VOLATILITY OF ORGANIC COMPOUNDS AS AN INDEX OF THE TOXICITY OF THEIR VAPORS TO INSECTS

By WILLIAM MOORE, 2
Head of Section of Research in Economic Zoology, Minnesota Agricultural Experiment Station

INTRODUCTION.

In a previous paper the writer pointed out the relationship between the toxicity of various benzene derivatives and their boiling points, citing the literature. The question arose whether a similar relationship of boiling point and toxicity existed among other volatile organic compounds. Early in the work it was discovered that boiling point was merely a convenient general index of the volatility of the compound and that the real relationship was probably between toxicity and volatility. It was at first thought that this relationship existed only with compounds having an action on lower organisms similar to that of chloroform and ether, but it was soon found to have a wider range of application.

METHOD OF EXPERIMENTATION

In general, the same methods were employed as in the previous work. In order to hasten the rate of diffusion of the vapor throughout the flask, the piece of filter paper, with the chemical to be tested, was suspended in the center of the flask by means of a fine wire. The lead foil covering the stoppers was attacked by some of the acids used in the experiments, making it necessary in these cases to coat the stoppers with collodion. Many of the chemicals produced anesthesia, and, although the flies showed no signs of life, they recovered upon being removed from the flask. A new method was therefore employed in determining the amount of the chemical necessary to kill in 400 minutes. Flasks containing varying quantities of the chemical were started and all were stopped 400 minutes later. These exposed to the smaller doses usually revived; with slightly stronger doses only a partial revival was noticed; while the larger quantities of the chemical resulted in death. In this manner the actual amount necessary to kill in 400 minutes was determined.

In studying the volatility 0.5 c. c. of the liquid was spread over a ground-glass plate and the time necessary for this quantity to evaporate noted. Solids were powdered, and 1 gm. was spread out on the glass to

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evaporate. After a certain period, varying according to the volatility of the compound, the solid was weighed again, the loss in weight being the amount evaporated in that period of time. These data were then reduced to gram-molecules evaporated in 400 minutes.

The insect used in the tests was the housefly (*Musca domestica* L.), reared under natural conditions.

**CHEMICALS TESTED**

In the selection of the organic compounds to be tested the object was to obtain a series differing widely in their chemical composition and toxicology. Their possible use as insecticides was not considered, since the object of the investigation was to discover the general laws of toxicity of volatile organic compounds to insects.

The chemicals might be conveniently divided into hydrocarbons, esters, acids, ethers, hydrocarbon derivatives containing hydroxyls, aldehydes, ketones, halogens, sulphur or nitrogen, terpenes or terpene derivatives, and alkaloids. The following list is thus divided:

**Hydrocarbons:**
- Petroleum ether (pentane and hexane).
- Gasoline (mostly heptane).
- Kerosene (mostly nonane and decane).
- Benzene.
- Toluene.
- Xylene.
- Naphthalene.
- Camphene.

**Acids:**
- Acetic acid.
- Butyric acid.
- Valeric acid.

**Aldehydes and ketones:**
- Acetone.
- Acetaldehyde.
- Chloral hydrate.
- Bromomethylphenylketone.
- Furfural.
- Menthone.

**Sulphurs:**
- Carbon bisulphid.
- Ethyl mercaptan.
- Allyl isosulphocyanate.
- Thiophene.

**Terpenes and their derivatives:**
- Camphene.
- Camphor.
- Menthone.
- Menthol.
- Pinene.
- Terpinol.
- Citral.

**Terpenes and their derivatives—Contd.**
- Eugenol.
- Isoeugenol.
- Geranyl acetate.

**Esters:**
- Methyl salicylate.
- Ethyl malonate.
- Ethyl acetooacetate.
- Amyl acetate.
- Amyl valerate.
- Propyl acetate.

**Ethers:**
- Ethyl ether.
- α-Naphthol ethyl ether.

**Hydroxyls:**
- Methyl alcohol.
- Ethyl alcohol.
- Amyl alcohol.
- Menthol.
- Thymol.

**Halogens:**
- Chloroform.
- Bromoform.
- Carbon tetrachlorid.
- Chloroform.
- Brometone.
- Ethylene bromid.

**Nitrogen:**
- Chloropicrin.
- Amyl nitrite.
- Nitrobenzene.
- Pyridin.

**Alkaloids:**
- Nicotin.
EXPERIMENTAL RESULTS

Eugenol, isoeugenol, and α-napthol ethyl ether were so slightly volatile that more than 400 minutes were required for the death of the flies; hence, they are not included in the results. Pinene, terpinol geranyl acetate, and to some extent citral on exposure to the air, tend to form a
Fig. 3.—Volatility and toxicity of the slightly volatile compounds on a larger scale than in figure 2.

Fig. 4.—Comparison of the volatility and toxicity of the acetics.

Fig. 5.—Comparison of the volatility and toxicity of the esters.

Fig. 6.—Comparison of the volatility and toxicity of the halogen derivatives.
gummy mass without completely evaporating. The toxicity of these compounds, particularly piene and terpinol, is variable. Pinene usually fails to kill the flies, while terpinol may kill with a certain dose one day, while the following day the same dose is not fatal. Usually unless the flies die in a short time after the introduction of the material, they will survive the fumigation. These erratic results are no doubt due to the oxidation of the terpene on exposure to the air, thus producing a substance which is not so toxic to the insect. Inasmuch as many of the essential oils contain terpenes producing such gummy residues on exposure to the air, it is at once apparent why varying results have been reported as to their value as insecticides.

Table I and figures 1, 2, and 3 show that the toxicity of volatile organic compounds is closely correlated with their volatility. In general, the less volatile the chemical the more toxic it is even where the compounds are strikingly different in their chemical composition. When related compounds are considered, as in figures 4, 5, 6, and 7, this agreement is even more marked. Exceptions are noted, as in carbon bisulphid, ethyl mercaptan, and particularly chloropicrin. These exceptions are not due to vapor density, nor primarily to water solubility, but are no doubt due to their chemical composition or to some peculiar action of the chemical. Hydrocyanic acid, although not included in this paper, would be an exception, owing to its extreme solubility in water and the fact that such minute quantities are sufficient to inhibit the action of oxidizing enzymes. Chloropicrin may be likewise an enzym poison. The remarkable point of data here presented is not that there are a few exceptions, but the fact that there are so few exceptions among so large a number of very different chemicals which are strikingly different in their toxicological action on higher animals. It is interesting to note that ethyl alcohol is more toxic to insects than methyl alcohol, the reverse of that which takes place in higher animals.
TABLE I.—Relation of the volatility of organic compounds to their toxicity

<table>
<thead>
<tr>
<th>Name of compound</th>
<th>Volatility in gram-molecules evaporating in 400 minutes</th>
<th>Toxicity in millions of a gram-molecule killing in 400 minutes</th>
<th>Name of compound</th>
<th>Volatility in gram-molecules evaporating in 400 minutes</th>
<th>Toxicity in millions of a gram-molecule killing in 400 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl ether</td>
<td>4.4245</td>
<td>4318.4</td>
<td>Furfural</td>
<td>0.0457</td>
<td>20.8</td>
</tr>
<tr>
<td>Petroleum ether</td>
<td>3.5841</td>
<td>713.3</td>
<td>Brommethylphenylketone</td>
<td>0.0282</td>
<td>2.4</td>
</tr>
<tr>
<td>Ethyl mercaptan</td>
<td>2.1541</td>
<td>109.9</td>
<td>Butyric acid</td>
<td>0.0241</td>
<td>25.8</td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>1.0776</td>
<td>671.8</td>
<td>Ethyl acetacetate</td>
<td>0.0192</td>
<td>24.8</td>
</tr>
<tr>
<td>Acetone</td>
<td>1.5617</td>
<td>954.3</td>
<td>Amyl valerate</td>
<td>0.0182</td>
<td>11.2</td>
</tr>
<tr>
<td>Carbon bisulphid</td>
<td>1.3616</td>
<td>286.3</td>
<td>Valeric acid</td>
<td>0.0113</td>
<td>15.3</td>
</tr>
<tr>
<td>Chloroform</td>
<td>1.2870</td>
<td>804.6</td>
<td>Allyl isosulphoecyanate</td>
<td>0.0085</td>
<td>2.2</td>
</tr>
<tr>
<td>Carbon tetrachlorid</td>
<td>7.067</td>
<td>161.9</td>
<td>Nitrobenzene</td>
<td>0.0058</td>
<td>1.8</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>4.432</td>
<td>331.2</td>
<td>Ethyl malonate</td>
<td>0.0054</td>
<td>9.6</td>
</tr>
<tr>
<td>Benzene</td>
<td>4.057</td>
<td>142.5</td>
<td>Menthone</td>
<td>0.0049</td>
<td>2.9</td>
</tr>
<tr>
<td>Chlorperin</td>
<td>3.443</td>
<td>1.7</td>
<td>Methyl salicylate</td>
<td>0.0033</td>
<td>1.0</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>2.936</td>
<td>60.0</td>
<td>Camphene</td>
<td>0.0032</td>
<td>44.0</td>
</tr>
<tr>
<td>Thiophene</td>
<td>2.659</td>
<td>102.2</td>
<td>Chloral hydrate</td>
<td>0.0030</td>
<td>48.0</td>
</tr>
<tr>
<td>Propyl acetate</td>
<td>2.610</td>
<td>103.4</td>
<td>Naphthalene</td>
<td>0.0013</td>
<td>3.9</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>2.343</td>
<td>273.2</td>
<td>Nicotin</td>
<td>0.0010</td>
<td>2.4</td>
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<tr>
<td>Toluene</td>
<td>2.018</td>
<td>147.5</td>
<td>Camphor</td>
<td>0.0069</td>
<td>5.2</td>
</tr>
<tr>
<td>Ethylene bromid</td>
<td>1.266</td>
<td>28.6</td>
<td>Kerosene</td>
<td>0.0067</td>
<td>11.9</td>
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<tr>
<td>Pyridine</td>
<td>1.347</td>
<td>21.7</td>
<td>Chloretone</td>
<td>0.0005</td>
<td>3.6</td>
</tr>
<tr>
<td>Xylene</td>
<td>1.241</td>
<td>64.9</td>
<td>Menthol</td>
<td>0.0019</td>
<td>3.2</td>
</tr>
<tr>
<td>Amyl acetate</td>
<td>0.627</td>
<td>44.8</td>
<td>Thymol</td>
<td>0.0014</td>
<td>9.9</td>
</tr>
<tr>
<td>Gasoline</td>
<td>0.050</td>
<td>42.0</td>
<td>Brometone</td>
<td>0.0009</td>
<td>1.1</td>
</tr>
<tr>
<td>Amyl nitrite</td>
<td>0.9712</td>
<td>41.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bromoform</td>
<td>0.486</td>
<td>7.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amyl alcohol</td>
<td>0.2460</td>
<td>38.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION OF RESULTS

Holt, working with the cockroach, states that the toxicity of a volatile organic compound increases as the boiling point increases, up to a certain point, beyond which an increase in boiling point is accompanied by a decrease in toxicity. In the writer's own work the results show an increase in toxicity up to where the compound is so slightly volatile (b. p. 225° to 250° C.) as to be of no value. Holt used a fixed quantity of each compound in uniform flasks, giving the time required as an index of toxicity. Under such conditions a larger quantity of a high boiling point compound than would volatilize was placed in the flask. Although such compounds required longer to kill the cockroaches in Holt's flasks, the amount of vapor which produced the death was much less than was considered to be the case. The apparent decrease in toxicity in his experiments was really an increase, since the dose was greatly diminished, although the period of time was increased. The question naturally arises as to why the volatility of a chemical should be related to its toxicity. The following seems to be a reasonable explanation. The vapor present in the air is taken into the tracheae of the insects and is

condensed upon reaching their finer divisions. If the compound is very volatile, it will evaporate and readily pass out of the insect, while if very slightly volatile it will remain in the insect, and will penetrate the tissues and produce the poisonous reactions which lead to the insect's death. In higher animals, when the compound is taken into the lungs, it is rapidly removed by the blood and carried to all parts of the body, giving it an opportunity to react chemically with the tissues. For this reason the toxicity of volatile organic compounds is more closely correlated with the chemical composition when introduced into the higher animals, while in insects toxicity is more closely associated with volatility than with chemical composition.

SUMMARY

In general, the toxicity of a volatile organic compound is correlated closely with its volatility.

A decreasing volatility is accompanied by an increased toxicity.

The boiling point of the chemical is a general index of its volatility.

Compounds with boiling points of 225° to 250° C. are usually so slightly volatile that they do not produce death except after very long exposures.

The structure of the respiratory system of the insect is probably responsible for the remarkable influence of volatility on the toxicity of the vapor of volatile organic compounds.
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