

Attractants for Synanthropic Flies. Identification of Attractants and Coattractants for *Hippelates* Eye Gnats (Diptera: Chloropidae)

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Hippelates eye gnat attractants, emanated in fermented aqueous suspension of chicken whole-egg powder, were identified as trimethylamine and ammonia. From the same suspension, the coattractants, acetic and propionic acids, indole, and skatole, were also isolated and identified. An aqueous solution of trimethylamine and ammonia acidified with hydrochloric acid to pH 6.0 showed weak attractancy against the insects. The addition of linoleic acid to this aqueous solution increased the attractancy significantly. When acetic or propionic acid was used to acidify an aqueous mixture of trimethylamine, ammonia, and linoleic acid to pH 6.0, the attractancy of the resulting mixture significantly increased, reaching to about one-third of that of the fermented aqueous suspension of whole-egg powder. The addition of indole or skatole to the resulting mixture further enhanced the attractancy to the extent of that of the fermented aqueous suspension.

Hippelates eye gnats are severe pests and suspected vectors of organisms pathogenic to man and domestic animals (Dawson, 1960). The eye gnats breed over large expanses of land in the southern United States. In California, heavy populations of these pests prevail in the Coachella Valley of Riverside County and other intensively farmed valleys in southern California. Although many studies and attempts have been made toward controlling eye gnat populations by using various insecticides, no practical and effective area-wide larvicidal abatement measures have been formulated. This is largely due to the eye gnats building up resistance against insecticides (Mulla, 1962) and the high cost to treat large areas of the breeding habitat with chemicals. A promising alternative for the management of eye gnat populations is the use of attractants and attractive baits.

Eye gnats are attracted to a variety of putrefying proteins employed in measuring their population activity in the field (Burgess, 1951; Mulla et al., 1960b). Fermented aqueous suspension of chicken whole-egg powder was found to be highly attractive (Mulla et al., 1960b). Some physico-chemical factors influencing the attractancy of the fermented aqueous suspension and its distillate were studied (Hwang and Mulla, 1973a). As a result of these studies, an attractive material, prepared by lyophilizing the fermented aqueous suspension, was developed against synanthropic flies, and its efficacy was determined against the eye gnat *H. collusor* (Townsend) (Mulla et al., 1973).

During the course of investigations on chemical attractants emanated from the fermented aqueous suspension, we isolated and identified oleic and linoleic acids from the ether-soluble fraction of a distillate obtained from the fermented whole-egg slurry. Since these two unsaturated fatty acids per se were not attractive but enhanced the attractancy of the main attractants present in the water-soluble fraction of the distillate, they were designated as coattractants (Hwang and Mulla, 1971). The water-soluble fraction showed some attractancy against the eye gnats; therefore, it was concluded that the main attractants existed in this fraction. From the water-soluble fraction, we isolated a crystalline residue possessing weak attractancy against *H. collusor* (Hwang and Mulla, 1973b).

These studies led us to believe that the active principal

produced during fermentation of the aqueous suspension consisted of numerous compounds which, when present in certain proportions, were responsible for eliciting feeding response in eye gnats.

This paper reports the identification of the chemical attractants in the water-soluble fraction of the distillate from fermented aqueous suspension of whole-egg powder. At the same time, it reports the isolation and identification of other coattractants which are present in the fermented aqueous suspension. It also presents data on the attractancy of various compositions of these attractants and coattractants against field populations of *H. collusor*.

EXPERIMENTAL SECTION

Isolation and Identification of Attractants. The fermented aqueous suspension of chicken whole-egg powder (Hwang and Mulla, 1971) attractive to *H. collusor* was used for the isolation of attractants and coattractants. The suspension was distilled under atmospheric pressure (Figure 1). The distillate was acidified with diluted hydrochloric acid to pH 6.0 and extracted with ether. The water layer was separated, further acidified with hydrochloric acid to pH 3.0, and concentrated to dryness to yield a crude residue which was purified to give a purified residue (Hwang and Mulla, 1973b): mass spectrum (70 eV) *m/e* (rel intensity) 59 (6), 58 (13), 44 (5), 43 (4), 42 (6), 41 (4), 38 (33), 37 (4), 36 (100), 35 (13), 30 (7), 28 (23), 27 (4), 18 (32), 17 (40), 16 (38); (20 eV) 59 (32), 58 (12), 38 (22), 37 (5), 36 (65), 18 (12), 17 (100).

Various characteristic spot tests for amines and ammonia were conducted according to Feigl (1954, 1960) and Shriner et al. (1956). The tests included the reaction with 2,4-dinitrochlorobenzene, the formation of dithiocarbamates, the formation of copper dithiocarbamate, the reaction with citric acid and acetic anhydride, the Hinsberg test, and the reaction with *p*-nitrobenzenediazonium chloride.

The purified residue (3.7 g) in aqueous sodium hydroxide solution (10%, 50 ml) was allowed to react with benzoyl chloride (10 g). The resulting benzamide was collected by filtration and recrystallized from hot water to give a pure benzamide (3.8 g): mp 121–122°C [lit. mp 124°C (Finan and Fothergill, 1962)]; ir (CHCl₃) 3540, 3420, 1680, 1605, and 1580 cm⁻¹; mass spectrum (70 eV) *m/e* (rel intensity) 121 (70), 105 (91), 77 (100), 51 (56), 50 (30), 44 (15) (Cotter, 1965).

The benzamide (1 g) was refluxed with 6 *N* hydrochloric

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acid (25 ml) for 5 hr. The mixture was washed with ether and evaporated to dryness, yielding ammonium hydrochloride (0.4 g): mass spectrum (70 eV) m/e (rel intensity) 38 (32), 37 (5), 36 (100), 35 (15), 18 (16), 17 (45), 16 (33).

After the benzamide was removed by filtration, the filtrate containing nonacylable fraction of the purified residue was added to an aqueous sodium hydroxide solution (10%, 50 ml). The alkaline solution was distilled under nitrogen. The distillate was absorbed in 2 *N* hydrochloric acid (100 ml). Evaporation of the acid solution gave trimethylamine hydrochloride (1.2 g): NMR (D_2O) δ 2.92 ppm; mass spectrum (70 eV) m/e (rel intensity) 59 (44), 58 (100), 43 (11), 42 (38), 38 (24), 37 (3), 36 (74), 35 (10), 30 (45), 28 (18), 18 (28), 15 (14).

Isolation and Identification of Coattractants. (1) The distillate from the fermented aqueous suspension of whole-egg powder was acidified to pH 6.0 and extracted with ether. The water layer was separated, further acidified to pH 3.0, and concentrated to dryness to give a crude residue as previously described. The distillate (800 ml) obtained during concentration of the acidified water layer was adjusted to pH 9.0 with 10% aqueous sodium hydroxide solution (Figure 1). Evaporation of the basic solution under diminished pressure gave a white residue (1.0 g). The residue was dissolved in water (5 ml), and the solution was acidified to pH 6.0 with hydrochloric acid and extracted three times with ether. The combined ether extracts were washed once with water (5 ml) and dried ($MgSO_4$). Evaporation of ether gave an oily material (0.32 g): ir (film) 3400–2400, 1700, 1460, 1420, 1280, and 940 cm^{-1} .

A Hewlett-Packard Model 5750B gas chromatograph equipped with dual flame ionization detectors and a Model 7123A recorder was used to analyze the oily material. A 10 ft \times 0.25 in. o.d. (wall thickness 0.035 in.) stainless steel column packed with 10% Carbowax 20M on 60–80 mesh, acid-washed Chromosorb W was used in the chromatograph. The GLC conditions used were as follows: injection port temperature, 250°C; detector temperature, 285°C; column temperature, 125–200°C at 1°C/min; carrier gas (N_2) flow rate, 25 ml/min at 65 psi; hydrogen flow rate, 46 ml/min; air flow rate, 428 ml/min. A 20% solution of the oily material in ether was prepared, and 0.2 μ l of the solution was injected into the GLC. Identification was made by comparison of the relative elution temperatures (RET) of the unknowns with those of authentic compounds. Acetic acid was used as an internal standard.

(2) The distillate (700 ml), obtained from the fermented suspension of whole-egg powder, was added with diluted hydrochloric acid (1.2%, 10 ml) and saturated aqueous sodium sulfate solution (10 ml) (Figure 1) (AOAC, 1970). The resulting solution was extracted three times with chloroform (50 ml each time). The combined chloroform extracts were washed with water and dried (Na_2SO_4). Evaporation of the solvent yielded a fine crystalline product (0.06 g): ir ($CHCl_3$) 3500–2400, 3500, 1705, 1610, 1600, 1595, and 680 cm^{-1} . The product showed strong positive reaction with Ehrlich's reagent [*p*-dimethylaminobenzaldehyde (1 g), 95% ethanol (95 ml), and concentrated hydrochloric acid (20 ml)] (Feigl, 1960).

The same instrument with a 6 ft \times 0.125 in. o.d. (wall thickness, 0.016 in.) stainless steel column packed with 10% silicon gum rubber UCC-W982 on 80–100 mesh, acid-washed, DMCS-treated Chromosorb W was used for analyzing the fine crystalline product. The GLC conditions were as follows: injection port temperature, 260°C; detector temperature, 320°C; column temperature, 100–200°C at 4°C/min; carrier gas (N_2) flow rate, 20 ml/min

at 60 psi; hydrogen flow rate, 39 ml/min; air flow rate, 400 ml/min. A 6% chloroform solution of the fine crystalline product was made, and 3 μ l of the solution was injected into the GLC. Identification was also made by comparison of the RET of the unknowns with those of authentic compounds. Dodecane was used as an internal standard.

Bioassay Method. The bioassays of the aqueous compositions were carried out in the field against the eye gnat *H. collusor* using the Citrus Research Center olfactometer (Mulla et al., 1960a). The olfactometer consisted of four main parts: (1) eye gnat traps consisting of funnels and collection vials, (2) bait dishes, (3) a circular table with 20 holes and 8-mesh screen supporting the traps, and (4) an electric motor unit, speed controller, and reducer. The bait dishes (diameter 6 cm) were placed on the screens, test compositions (10 ml) placed in the bait dishes, and the eye gnat traps inverted over them. The motor unit rotated the table at a speed of 0.25 rpm. The eye gnats which were attracted by the test materials flew under the table and crawled through the support screen into the trap collection vials where they were killed by a deposit of a quick knockdown insecticide.

A standard batch of 1% fermented aqueous suspension of whole-egg powder (pH 6.0) showing potent attractancy was used along with the test materials for comparison. The standard suspension was prepared according to the procedure of Hwang and Mulla (1971) except that the concentration was adjusted to 1% instead of 2%. The tests were run until at least an average of 50 eye gnats were captured by the standard material. This procedure usually required 1–2 hr. Empty traps or traps containing water did not catch any insects, showing that there was no random capture. The attractancies were expressed as mean percent of the number in the standard. The statistical significance of the differences among the test samples was calculated at the 5% level by performing analysis of variance using Duncan's Multiple Range Test.

RESULTS AND DISCUSSION

Identification of Attractants and Their Biological Activity. A crystalline residue was isolated from the water-soluble fraction of a distillate obtained from the fermented aqueous suspension of whole-egg powder (Figure 1). In earlier studies, this purified residue possessed weak attractancy against *H. collusor* (Hwang and Mulla, 1973b). Since the purified residue was obtained from the basic fraction of the distillate of the fermented aqueous suspension and isolated as a hydrochloride salt, various spot tests for amines and ammonia were conducted. These tests indicated the absence of primary and secondary amines and the presence of a tertiary amine and the ammonium ion. The mass spectra (Figure 2) indicated that the purified residue contained both trimethylamine hydrochloride and ammonium chloride. The presence of ammonium chloride was further confirmed by the reaction of the purified residue with benzoyl chloride in an alkaline medium to produce benzamide which was identified by ir and mass spectra. From the benzamide, ammonium chloride was obtained on acid hydrolysis and identified by mass spectrum. Trimethylamine hydrochloride was isolated from the nonacylable fraction of the purified residue and identified by NMR and mass spectra.

From the above physico-chemical evidence, it was evident that the residue contained two components, trimethylamine hydrochloride and ammonium chloride. Since the basic compounds of the fermented suspension were captured as their hydrochlorides, the fermented aqueous suspension should have contained trimethylamine and ammonia.

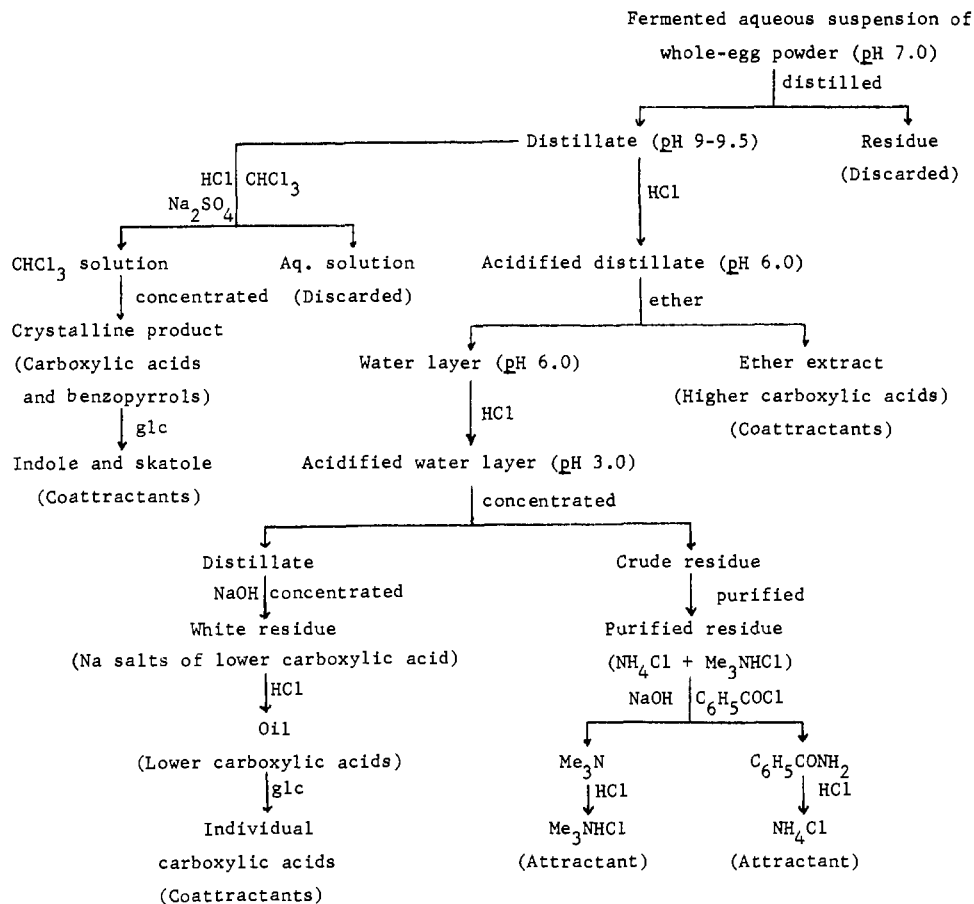


Figure 1. Fractionation scheme for isolating the attractants and the coattractants.

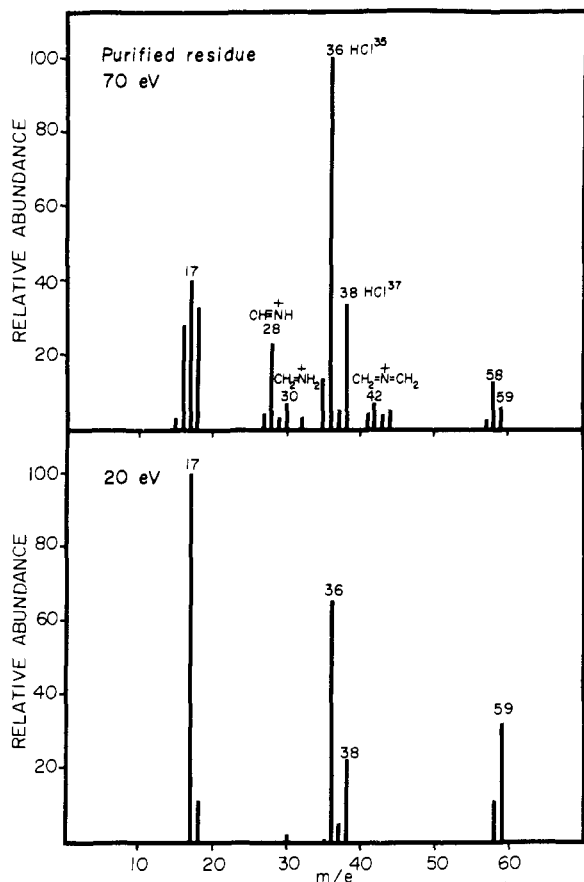


Figure 2. Mass spectra of the purified residue at 70 and 20 eV.

Table I. Attractancy of Trimethylamine and Ammonia against *H. collusor*

Material ^a	Mean attractancy, ^b % of standard
Me ₃ N	3.9c
Me ₃ N, linoleic acid	22.3a
NH ₃	2.9c
NH ₃ , linoleic acid	13.2b
Me ₃ N, NH ₃	7.9b
Me ₃ N, NH ₃ , linoleic acid	24.5a

^a pH adjusted to 6.0 by addition of HCl. Concentrations of Me₃N, NH₃, and linoleic acid were 1.2, 0.8, and 0.3%, respectively. ^b Based on six tests with four replicates in each test. Means followed by the same letter are not significantly different from one another at the 5% probability level.

To determine the biological activity of trimethylamine and ammonia against *H. collusor*, three aqueous solutions, each containing (1) trimethylamine (1.2%), (2) ammonia (0.8%), and (3) trimethylamine (1.2%) and ammonia (0.8%), were made. To ascertain the effect of the co-attractants on the activity of the attractants, linoleic acid (0.3%, 75% purity) was added to each of these solutions. These six preparations were adjusted to pH 6.0 with hydrochloric acid and bioassayed.

Table I shows the results of the bioassay tests. The aqueous solutions of trimethylamine and ammonia at pH 6.0 both showed weak attractancy which was significantly enhanced by the addition of linoleic acid. The solution of trimethylamine and ammonia at pH 6.0 showed significantly greater activity than the individual components. The addition of linoleic acid to the solution containing these two basic compounds also increased the attractancy significantly. As previously reported, linoleic acid alone

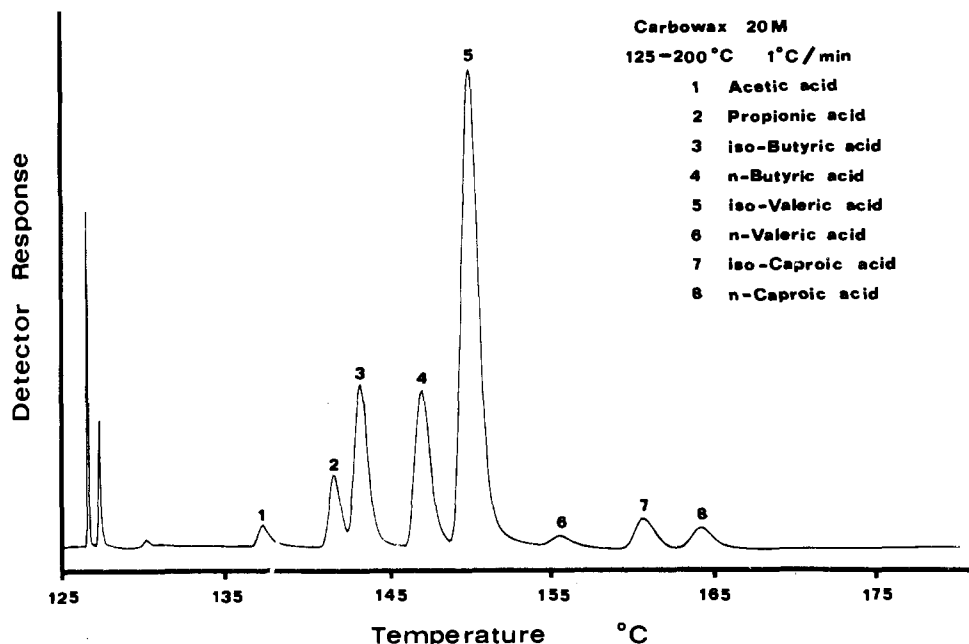


Figure 3. Gas chromatogram of lower carboxylic acids isolated from the fermented aqueous suspension of whole-egg powder.

did not possess any attractancy (Hwang and Mulla, 1971).

Ammonia has been known to be emitted by decaying organic matter and was reported to be an oviposition lure for the house fly (Vanskaya, 1941) and the apple maggot (Dean, 1941). In these earlier works, ammonia was used in aqueous solution or generated by the action of alkali, a buffer, or even water on ammonium salts, urea, amino acids, or foodstuffs. In the case of *Hippelates* eye gnat attractants, ammonium hydroxide per se in various concentrations did not attract the insects (Y.-S. Hwang and M. S. Mulla, unpublished data) whereas it exhibited a low level of attractancy only when it was neutralized to pH 6.0 with hydrochloric acid. Trimethylamine was also active only under weakly acidic conditions.

A mixture of trimethylamine, ammonia, and linoleic acid adjusted to pH 6.0 was thus proven to show considerable activity in inducing feeding response of *H. collusor*. Nevertheless, its activity was much lower than that of the fermented aqueous suspension of whole-egg powder. It was, therefore, assumed that other chemical factors, which synergized the activity of the attractants (trimethylamine and ammonia), might exist in the fermented suspension. Consequently, the fermented suspension was exhaustively analyzed and many attempts were made in searching these active factors.

Isolation, Identification, and Activity of Coattractants. The distillate from the fermented aqueous suspension of whole-egg powder, upon acidification to pH 6.0 and ether extraction, gave an ether extract and a water layer (see Experimental Section and Figure 1). Isolation of the acidic fraction from the water layer yielded an oily material, the IR spectrum of which coincided with those of lower aliphatic carboxylic acids.

In GLC analysis of the oily material on the Carbowax 20M column, eight peaks were repeatedly obtained. Figure 3 shows the typical separation of the mixture of lower carboxylic acids. The carboxylic acids [relative elution temperature (RET) to the standard (acetic acid)] thus identified were acetic (1.00), propionic (1.03), isobutyric (1.04), *n*-butyric (1.07), isovaleric (1.09), *n*-valeric (1.13), isocaproic (1.17), and *n*-caproic (1.19) acids. *n*-Butyric, isovaleric, and isocaproic acids were also found earlier in

Table II. Effects of Various Carboxylic Acids on the Attractancy of *Hippelates* Eye Gnat Attractants

Aqueous mixture ^a acidified to pH 6.0 by	Mean attractancy, ^b % of standard
HCl	15.2b
Acetic acid	31.7a
Propionic acid	26.2a
Isobutyric acid	2.7c
<i>n</i> -Butyric acid	12.5b
Isovaleric acid	4.4c
<i>n</i> -Valeric acid	0.6d
Isocaproic acid	0.4d
<i>n</i> -Caproic acid	0.6d

^a The aqueous mixture consisted of trimethylamine (1.2%), ammonia (0.8%), and linoleic acid (0.3%).

^b Based on six tests with four replicates in each test. Means followed by the same letter are not significantly different from one another at the 5% probability level.

the ether extract of the distillate obtained from the fermented suspension (Hwang and Mulla, 1971).

To study the effects of these lower carboxylic acids on the activity of the combination of the attractants (trimethylamine and ammonia) and the coattractant (linoleic acid), an aqueous mixture of trimethylamine (1.2%), ammonia (0.8%), and linoleic acid (0.3%) was made. The aqueous mixture was neutralized to pH 6.0 individually with each of the carboxylic acids identified above. For comparison, the aqueous mixture was also neutralized to pH 6.0 with hydrochloric acid. These preparations were subjected to field bioassays against *H. collusor*.

Table II shows the attractancy of the preparations. When acetic and propionic acids were used to acidify the aqueous mixture of trimethylamine, ammonia, and linoleic acid instead of hydrochloric acid, the attractancy of the resulting mixtures increased significantly over that acidified with hydrochloric acid. By using acetic acid in place of hydrochloric acid, the attractancy doubled and was almost one-third as potent as that shown by the standard. The attractancy of the aqueous mixture acidified with *n*-butyric acid was about the same as that acidified with hydrochloric acid. Using isobutyric, isovaleric, *n*-valeric, isocaproic, and *n*-caproic acids in acidification of the

Table III. Effects of Indole and Skatole on the Attractancy of *Hippelates* Eye Gnat Attractants

Aq mixture ^a plus	Mean attractancy, ^b % of standard
None	46.6a
Indole (0.01%)	111.3c
Skatole (0.01%)	79.4b

^a The aqueous mixture consisted of trimethylamine (1.2%), ammonia (0.8%), and linoleic acid (0.3%) acidified to pH 6.0 with acetic acid. ^b Based on 12 tests with 4 replicates in each test. Means followed by the same letter are not significantly different from one another at the 5% probability level.

aqueous mixture resulted in lowering the attractancy significantly. It was found previously that addition of *n*-butyric, isovaleric, and isocaproic acids to the water layer decreased the attractancy of the resultant mixtures significantly (Hwang and Mulla, 1971).

Acetic acid was reported to be attractive to *Drosophila* species (Barrows, 1907) and to oriental fruit moth (Frost, 1937), *n*-butyric acid to picture wing flies (Ortalidae) (Howlett, 1912), *n*-caproic acid to Japanese beetle (Langford and Cory, 1946; Muma et al., 1945), to green June beetle (Beckham and Dupree, 1952; Muma, 1944), and to the adults of Pacific and sugarbeet wireworms (Lehman, 1932), and *n*-valeric acid to Japanese beetle (Langford and Cory, 1946), to ortalid fly and stable fly (Howlett, 1912), and to codling moth (Van Leeuwen, 1939, 1948). Additionally, *n*-valeric acid was identified as the sex pheromone produced by the sugar beet wireworm, *Limonius californicus* (Mannerheim) (Jacobson et al., 1968), and *n*-caproic acid was shown to be a potent attractant for *Ocella parva* (Adams), a small, flowerfeeding, nonbiting fly similar in appearance to *Hippelates* spp. (Jantz and Beroza, 1967). None of the lower carboxylic acids identified here, however, individually showed attractancy against *Hippelates* eye gnats.

It is thus apparent that a higher degree of attractancy can be obtained by acidifying an aqueous mixture of trimethylamine, ammonia, and linoleic acid with acetic or propionic acid to pH 6.0. However, the attractancy obtained thus far could only account for about one-third of the original attractancy shown by the fermented aqueous suspension of whole-egg powder. Consequently, further pursuit of other chemical factors became necessary.

The fermented aqueous suspension of whole-egg powder and its distillate showed a positive reaction with the Ehrlich's reagent indicating the presence of pyrroles or benzopyrroles. According to the procedure of AOAC (1970) for the isolation of benzopyrroles, a fine crystalline product was obtained, the ir spectrum of which showed that the product contained carboxylic acids and benzopyrroles. The fine crystalline product produced a strong positive reaction to the Ehrlich test.

The GLC separation of a chloroform solution of the fine crystalline product on the UCC-W982 column repeatedly gave three major peaks, two of which were identified as indole (RET 1.02, dodecane as standard) and skatole (RET 1.05). Figure 4 shows the typical separation of the benzopyrroles on this column.

To test the activity of the benzopyrroles, an aqueous mixture of trimethylamine (1.2%), ammonia (0.8%), and linoleic acid (0.3%) was prepared and acidified to pH 6.0 with acetic acid. The resulting aqueous mixture and its combinations with indole (0.01%) and with skatole (0.01%) were bioassayed against *H. collusor*.

Table III shows the attractancy of these preparations. The aqueous mixture of trimethylamine, ammonia, linoleic

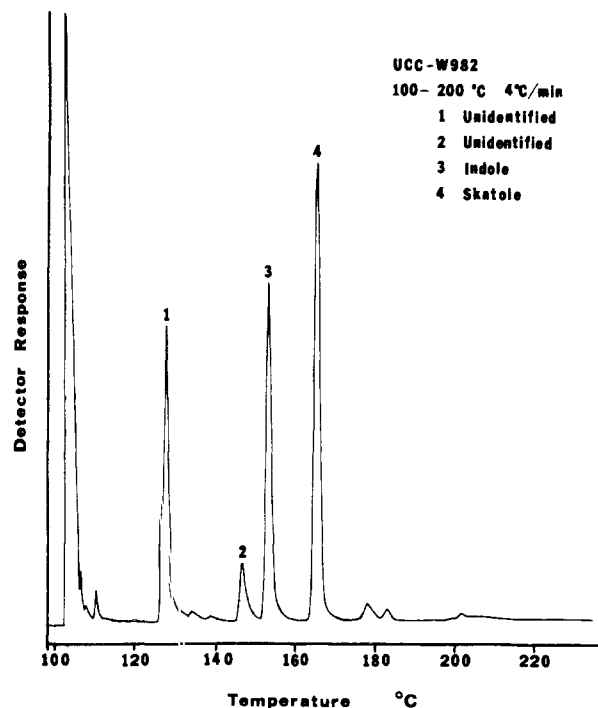


Figure 4. Gas chromatogram of benzopyrroles isolated from the fermented suspension of whole-egg powder.

acid, and acetic acid showed good activity which was significantly increased by the addition of indole and skatole. The addition of indole invested significantly greater attractancy than that of skatole, indicating the former was a better coattractant than the latter. These two attractant preparations were as potent as the fermented aqueous suspension. Indole and skatole per se in various concentrations did not attract the insects.

Indole is formed by the bacterial tryptophanase reaction on tryptophan (Hopkins and Cole, 1903; Happold and Hoyle, 1935; Happold, 1950). Both indole and skatole can be produced from tryptophan by rumen microorganisms (Lewis and Emery, 1962). Photolysis of tryptophan in water also yields the benzopyrroles (Melchior, 1957). It was thus assumed that enzymatic hydrolysis of proteins in the aqueous suspension of whole-egg powder by microorganisms produced tryptophan which was degraded to the benzopyrroles enzymatically or possibly photolytically under the greenhouse lighting conditions. The benzopyrroles thus produced, in conjunction with other active components, contributed to the overall attractancy of the fermented suspension.

Indole was reported as an attractant for blowflies (Cragg, 1950; Cragg and Ramage, 1945; Cragg and Thurston, 1950), and skatole for *Sarcophaga bullata* Parker (Graenicher, 1935) and for houseflies (Pospisil, 1958). A mixture of skatole and terpinyl acetate attracted palm weevil (Hagley, 1965). However, the benzopyrroles in combination with other active components in the fermented aqueous suspension have not been known to attract *Hippelates* eye gnats until the present time.

In these studies on the chemical attractants for *Hippelates* eye gnats, we have now identified the natural chemical attractants and coattractants emanated from putrefied egg protein. We have documented that an aqueous mixture of trimethylamine, ammonia, linoleic acid, acetic or propionic acid, and indole or skatole at pH 6.0 shows potent attractancy against these insects. Its attractancy is as strong as that of the starting fermented aqueous suspension used in the isolation and as the

standard in the bioassays. Discovery of these attractants offers a good potential and a new tool for the control of *Hippelates* eye gnats.

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Synthesis and Laboratory and Field Evaluation of a New, Highly Active and Stable Insect Growth Regulator

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The insect growth regulator 6,7-epoxy-1-(*p*-ethylphenoxy)-3-ethyl-7-methylnonane (Ro 10-3108) is an efficient agent for plant protection. Stability studies in the laboratory (uv, hydrolysis) and persistency studies outdoors show that this compound, in contrast to most known insect growth regulators, is sufficiently stable for practical purposes. Ro 10-3108 gave good control of natural populations of summerfruit tortrix moth and scale insects. The favorable toxicological data as well as the biodegradability of Ro 10-3108 make this compound a promising candidate for several fields of application. A technically feasible synthesis of the compound is given.

In the last several years compounds which mimic the effects of insect juvenile hormones by preventing adult development have received a great deal of attention as possible insect control agents. Hundreds of chemical structures with juvenile hormone activity have been synthesized and investigated (Menn and Beroza, 1972; Sláma et al., 1974). Efforts of chemists and entomologists have been directed mostly toward four classes of insect growth regulators (IGR's): derivatives of juvabione and dehydrojuvabione (Suchý et al., 1968), compounds having a farnesyl type skeleton (Mori, 1971), alkyl 3,7,11-trimethyl-2,4-dodecadienoates (Henrick et al., 1973), and

aromatic ethers with a geranyl type side chain (cf. Bowers, 1971; Pallos et al., 1971; Sarmiento et al., 1973). We concentrated our efforts on compounds of the latter type, keeping in mind that any successful IGR must have a better field stability than the previously described candidates (cf. Bagley and Bauernfeind, 1972; Sláma et al., 1974, pp 275 ff).

MATERIALS AND METHODS

Synthesis. Compounds 1 (Wright et al., 1974), 2, and 3 (cf. Table I) were synthesized by hydrogenation of the unsaturated compounds which result from alkylation of *p*-ethylphenol with the appropriate allylic bromide followed by epoxidation (cf. Bowers, 1969). In addition, a synthetic scheme was adopted for compound 3 (Ro 10-3108) which allows its preparation in kilogram quantities and which avoids major purification steps (cf. Figure 1). Starting from 7-methyl-6-nonen-3-one (Hoffmann et al.,

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