Chemicals from the Glands of Ants

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1 Introduction

Ants are social insects, generally organized into large colonies where the numerous workers, infertile females, do most of the labours except procreation, which is reserved to the exiguous males and queens. All three castes use chemicals for communication, though as yet we know little about the substances specific to males and queens. The ants have inside their bodies a number of tiny glands in which they produce (or sequester) and store a curious variety of natural products. These distinctive and diminutive laboratories have been the subject of study of chemists and biologists in recent years. The substances studied generally have small molecules, sufficiently volatile to be studied by gas chromatography, and are presumed to have a pheromone function, though that has not been proven, or even tested in all cases. These glandular substances from ants are the subject of this review.

The ants belong to the family Formicidae, which is divided into eleven subfamilies:[1] *Ponerinae*, a primitive group common in Australia; *Myrmeciinae*, the 'bull ants' of Australia; *Dorylinae*, the Old World army ants; *Ecitoninae*, the New World army ants; *Leptanillinae*, *Pseudomyrmecinae*, and *Nothomyrmeciinae*, three small groups; *Myrmicinae*, the largest group, to which our temperate red ants belong; *Aneuretinae*, a fossil group with only one known species today; *Dolichoderinae*, a chiefly tropical group; and *Formicinae*, those that produce formic acid, and to which our black wood ants belong.

The exocrine glands (*i.e.* those secreting to the outside) of ants produce a range of substances for communication that fall under the general heading of '*semiochemicals*' (chemicals which convey information between organisms). *Pheromones* are only one type of semiochemical and transmit information between members of the same species. Semiochemicals used for interspecific communication are called *allelochemics*. Three main types of allelochemics are recognized; *allomones*, *kairomones*, and *synomones*. An allomone is a chemical emitted from an insect, which gives adaptive advantage to the odour-releasing individual (*e.g.* defensive and repellent secretions). In contrast, a kairomone gives an advantage to the receiver of the odour (*e.g.* substances that enable the predator to locate its prey). The chemical trails of the army ant, *Neivamyrmex nigrescens* are picked up by predators like the blind snake *Leptotyphlops dulcis*[2] and the beetle *Hellumorphoides texanus*,[3] which feed mainly on the brood of the ants. A synomone

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[1] R. R. Snelling, in 'Social Insects vol II', ed. H. R. Hermann, Academic Press, New York, 1981, p. 369.
[2] J. F. Watkins, F. R. Gehlbach, and R. S. Baldridge, *Southwest Nat.*, 1967, **12**, 455.
[3] R. W. Plesk, J. C. Kroll, and J. F. Watkins, *J. Kan. Entomol. Soc.*, 1969, **42**, 452.

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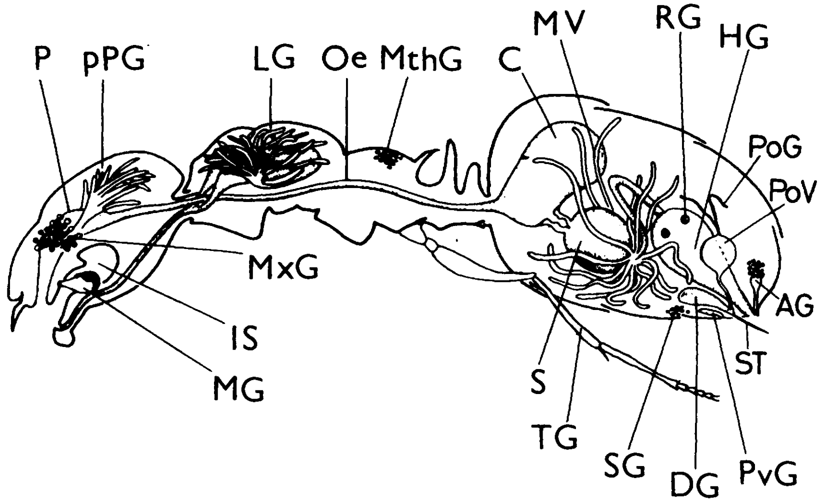

Figure 1 *Idealized section through a typical ant showing the location of the intestinal tract and the known exocrine glands. AG, anal-pygidial gland; C, crop; DG, Dufour gland; HG, hind gut; IS, infrabuccal sac; LG, labial gland; MG, mandibular gland; MthG, metathoracic or metapleural gland; MV, Malpighian vessels; MxG, maxillary gland; Oe, oesophagus; P, pharynx; PoG, poison gland; PoV, poison vesicle; pPG, postpharyngeal gland; PvG, Pavan gland; RG, rectal gland; S, stomach; SG, sternal gland; ST, sting lance; TG, tibial gland.* (Freely adapted from K. Dumpert, 'The Social Biology of Ants', Pitman Advanced Publishing Programme, London, 1981 and Paul Parey Verlag, Berlin)

benefits both the producer and recipient (*e.g.* floral scents that attract pollinating insects).

The location of the major exocrine glands in a typical ant is illustrated in Figure 1. In the head region are the mandibular, propharyngeal (maxillary), and the postpharyngeal glands. The mandibular glands are the major source of pheromones for a number of subfamilies of ants and many of these are described as 'alarm' pheromones. These alarm pheromones are released when ants are disturbed and generally increase the rate of movement and aggressiveness of the ants, although the overall behavioural responses produced are complex and not clearly defined. The labial glands associated with the digestive system open into the head region, but are actually situated in the thorax. The metapleural glands are also found in the thorax. Tibial glands in the hind legs, described in some species of *Crematogaster*, provide a unique source of trail pheromones[4,5] which are used by an insect to mark a route so that other insects of the same community are able to follow it. The poison and Dufour glands are the main glands in the abdomen. These two glands generally provide defensive allomones and in some cases the trail pheromones and sex attractants. The hind gut is the main source of the formicine trail substances. The supra-anal glands and Pavan's gland were once thought to be restricted to

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[4] R. H. Leuthold, *Psyche*, 1968, **75**, 233.

[5] D. J. C. Fletcher and J. M. Brand, *J. Insect Physiol.*, 1968, **14**, 783.

dolichoderine ants only, but Hölldobler and Engel[6] have recently reviewed tergal and sternal glands, and they believe that the anal glands are analogous to the tergal pygidial glands which are found in several sub-families.

Definitive behavioural activities have been assigned to a number of compounds found in the exocrine glands but many others appear to have no significant behavioural activity. Closely related species are often found to produce similar substances in a particular gland, although the qualitative and quantitative compositions are usually characteristic of the species. Although it is not always easy to explain why these species-specific mixtures of compounds are present, nevertheless they are diagonostically useful, especially for distinguishing between morphologically similar species. Furthermore, the investigations on the composition of exocrine glands can be helpful phylogenetically.

2 Venom Apparatus

It is thought that the original function of glands of the venom apparatus, which is attached to the sting lance, was the production of proteinaceous compounds that coated the eggs and allowed them to adhere to a substrate, and from this the venom of the sterile workers developed. The Dufour gland is a sac-like structure and is also attached to the sting. It is found in all Hymenoptera (bees, wasps, and ants) but its primary purpose is unknown. As its contents are oily, it has been suggested that it originally provided a lubricant for the eggs in the ovipositor. All the subfamilies of ants contain species that use venom to subdue their prey. However, in a number of species during phyletic development, an assortment of other functions have become assigned to the glands of the venom apparatus. These secondary functions include the production of communication pheromones, defensive allomones, and other deterrents.

A. Poison Gland Substances.—The characteristic chemical components found in the venoms of stinging ants are proteinaceous and alkaloidal. The formicine ants are stingless but their venoms often contain aqueous formic acid in concentrations up to 60%.[7] The amount of formic acid can occasionally be as large as 2 mg per ant but an amount around 600 μg per ant is considered usual. Formic acid constitutes more than 99% of formicine venom and it is the only volatile compound reported. However, the presence of peptides and free amino-acids in the venoms of *Formica polyctena*[7] and *Camponotus pennsylvanicus*[8] have also been reported. The major function of formic acid is to act as a defensive allomone against predators, although in some formicine ants it also acts as an alarm pheromone.[9]

Hefetz and Blum[10,11] have studied the biosynthesis of formic acid in the poison glands of formicine ants. Serine (1) is the major precursor and contributes both its

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[6] B. Hölldobler and H. Engel, *Psyche*, 1978, **85**, 285.

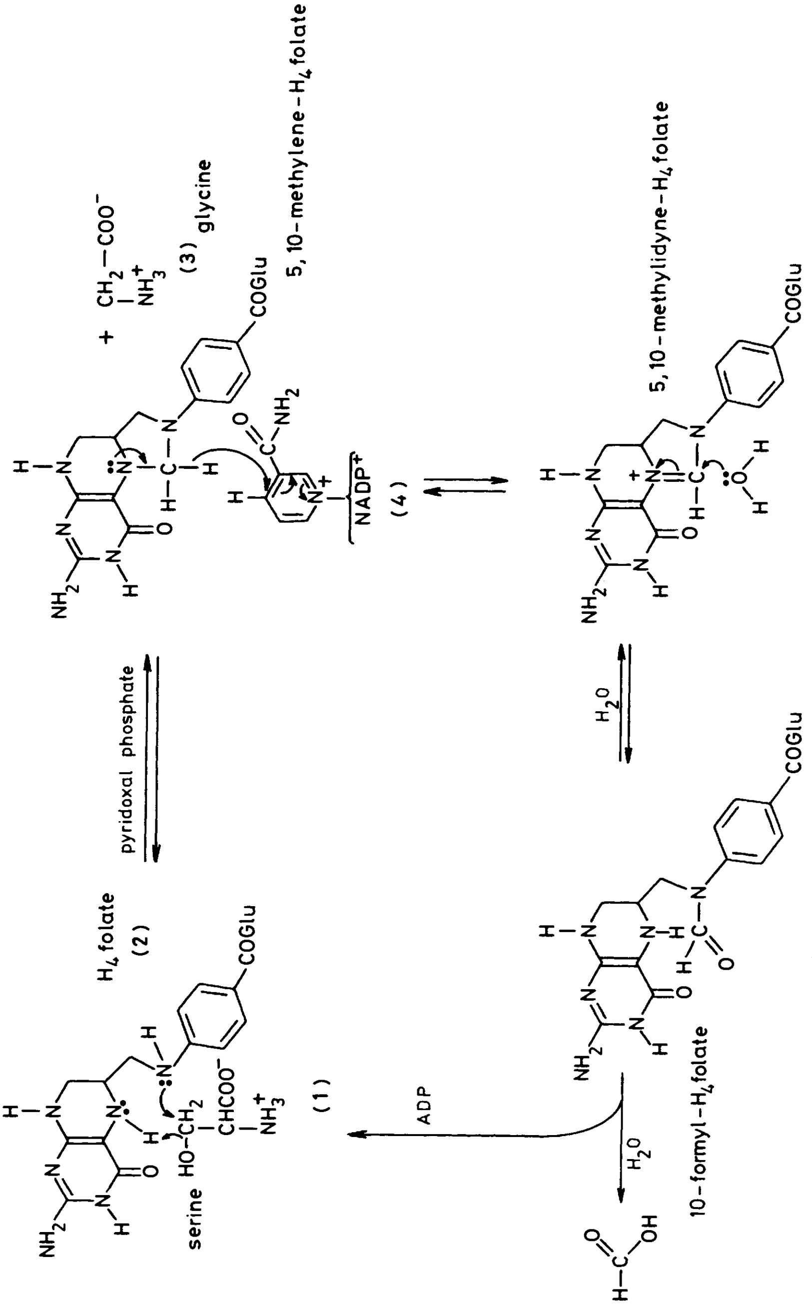
[7] M. F. H. Osman and J. Brander, *Z. Naturforsch., Teil B*, 1961, **16**, 749.

[8] H. R. Hermann and M. S. Blum, *Psyche*, 1968, **75**, 216.

[9] M. S. Blum and J. M. Brand, *Am. Zool.*, 1972, **12**, 553.

[10] A. Hefetz and M. S. Blum, *Science*, 1978, **201**, 454.

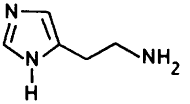
[11] A. Hefetz and M. S. Blum, *Biochim. Biophys. Acta*, 1978, **543**, 484.


serine
(1)
H4folate
(2)
pyridoxal phosphate
glycine
(3)
5,10-methylene-H4folate
NADP+
(4)
5,10-methylidyne-H4folate
(5)
H2O
10-formyl-H4folate
(6)
ADP
H2O
COGlu

Scheme 1

α- and β-carbons, but not its carboxyl carbon, to formic acid. The α-carbon of glycine can also be incorporated. The proposed biosynthetic pathway based on the studies of Hefetz and Blum is shown in Scheme 1. Serine (1) is converted into glycine (3) by donating its β-carbon to tetrahydrofolic acid (2). The N^5,N^{10}-methylene tetrahydrofolate (4) thus produced is oxidized to the methylidyne form (5) by $NADP^+$. The product (5) is hydrolysed to 10-formyltetrahydrofolate (6), which is further hydrolysed to produce formic acid and regenerate tetrahydrofolic acid. Hefetz and Blum[11] also demonstrated that the enzymes catalysing the reactions of Scheme 1 were present in the poison gland in much higher concentrations that any other tissue that was examined.

Proteinaceous venoms appear to be widely spread in the subfamilies, *Myrmeciinae*, *Ponerinae*, *Dorylinae*, *Pseudomyrmecinae*, and *Myrmicinae*. No information is available yet about the chemistry of venoms of other subfamilies. The presence of constituents with a wide range of pharmacological activities has been demonstrated in the venom of two species of *Myrmecia*.[12,13] The venom of *Pogonomyrmex badius*[14] contains histamine (7) and a series of free amino-acids, enzymes of six classifications and a number of other non-enzymic proteins. Similar constituents have also been found in *Myrmica ruginodis*.[15]



(7)

In contrast to the general proteinaceous themes exhibited by the venoms of many subfamilies of *Formicidae*, a number of species of ants in the *Myrmicinae* subfamily possess the ability to biosynthesize a variety of alkaloids in the venom gland. All the alkaloids reported in myrmicine venoms are summarized in Table 1.

The members of the genus *Solenopsis* undoubtedly lead the myrmicine ants as alkaloid chemists, possessing the ability to produce alkaloid-rich and low-protein venoms. In *Solenopsis geminata* around 19 μg of alkaloids are present in the poison gland of a single worker ant.[16] The ants belonging to the subgenus *Solenopsis* of the genus *Solenopsis* are referred to as *fire ants* because of the potency of their venoms, which exhibit pronounced necrotic,[17] haemolytic,[18] antibiotic,[19] and toxic[20] properties. The venoms of *Solenopsis* (*Solenopsis*) species are characterized by a predominance of 2-alkyl-6-methylpiperidines (19, 20). The alkyl group usually contains an odd number of carbon atoms in the C_7 to C_{15} range and may

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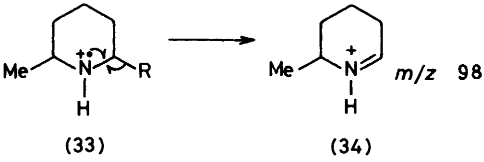
[12] J. C. Wanstall and I. S. de la Lande, *Toxicon*, 1974, **12**, 649.
[13] G. W. K. Cavill, P. L. Robertson, and F. B. Whitfield, *Science*, 1964, **146**, 79.
[14] J. O. Schmidt and M. S. Blum, *Science*, 1978, **200**, 1064.
[15] J. Jentsch, Proc. Int. Congr. Int. Union Study Soc. Insects, 6th, 1969, p. 69.
[16] A. B. Attygalle, Ph.D. thesis, University of Keele, 1983.
[17] D. C. Buffkin and F. F. Russel, *Toxicon*, 1972, **10**, 526.
[18] G. A. Adrouny, V. J. Derbes, and R. C. Jung, *Science*, 1959, **130**, 449.
[19] D. P. Jouvanez, M. S. Blum, and J. G. MacConnell, *Antimicrob. Agents Chemother.*, 1972, **2**, 291.
[20] J. R. Joyce, *Vet. Med. Small Anim. Clin.*, 1983, **78**, 1107.



(33) (34)

Scheme 2

sometimes contain a double bond. Both *cis*- and *trans*-isomers of 2,6-disubstituted piperidines are usually present, with either *trans*-isomer predominating as found in *S. invicta*[21,22] or *cis*-isomer predominating as in *S. xyloni* or *S. geminata*.[23] These ring configurational isomers are conveniently separated by g.l.c., with the *cis*-isomer eluting first on polar phases like Carbowax 20M. This may be because the nitrogen atom is less exposed when the 2,6-substituents are in di-equatorial positions as found in the *cis*-isomers. The double bonds, when present in the side chains, always appear to have a *Z*-configuration.[23] The absolute configurations of the chiral centres of these piperidines still remain unknown. The 2-alkyl-6-methylpiperidines (33) are well suited to be studied by gas chromatography–mass spectrometry, they all show the base peak or an intense ion at m/z 98 (34) due to the cleavage of the long alkyl group (Scheme 2). Baliah *et al.*[24] have provided an excellent review on synthetic methods for 2,6-disubstituted piperidines. The venom of *S. xyloni* contains, besides the usual piperidines, a 2-alkyl-6-methyl-2,3,4,5-tetrahydropyridine (21).[23]

Many species of *Solenopsis* belonging to the subgenus *Diplorhoptrum* are called *thief ants* because they steal brood from the nests of other species of ants. The raiding thief ants secrete offensive alkaloidal substances which repel the host ants from defending their brood. *Solenopsis* (*Diplorhoptrum*) *fugax* utilizes 2-butyl-5-heptylpyrrolidine (13) in this context.[25] This was demonstrated by applying the venom of *S. fugax*, synthetic pyrrolidine (13), or mineral oil on the brood of a few other species of ants and placing treated brood in the foraging areas of the respective ants. Ordinarily, if a larva is discovered by a worker it will immediately be transported back to the brood chamber. The worker ants picked up untreated or mineral oil treated larvae in a similar manner but clearly avoided picking up larvae contaminated with either the venom of *S. fugax* or synthetic pyrrolidine (13).[25]

In contrast to true fire ants (subgenus-*Solenopsis*) the thief ants are not noted for their stinging abilities. The subgenera, *Diplorhoptrum* and *Euophthalma* produce only very small quantities of alkaloids in their venoms. The venom of species of *Diplorhoptrum* and *Euophthalma* subgenera also contain 2-alkyl-6-methylpiperidines (19), but only *trans*-isomers were reported in contrast to both *cis*- and *trans*-isomers found in the ants of *Solenopsis* subgenus.[26] Furthermore the novel *N*-

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[21] J. G. MacConnell, M. S. Blum, and H. M. Fales, *Science*, 1970, **163**, 840.

[22] J. G. MacConnell, M. S. Blum, and H. M. Fales, *Tetrahedron*, 1971, **26**, 1129.

[23] J. M. Brand, M. S. Blum, H. M. Fales, and J. G. MacConnell, *Toxicon*, 1972, **10**, 259.

[24] V. Baliah, R. Jeyaraman, and L. Chandrasekaran, *Chem. Rev.*, 1983, **83**, 397.

[25] M. S. Blum, T. H. Jones, B. Holldobler, H. M. Fales, and T. Jaouni, *Naturwissenschaften*, 1980, **67**, 144.

[26] T. H. Jones, M. S. Blum, and H. M. Fales, *Tetrahedron*, 1982, **38**, 1949.

methylpiperidines (23) reported from *S. pergandei* and *S. carolinensis* appear to be unique to thief ants of *Diplorhoptrum* subgenus.[26] A unique mono-substituted piperideine (22) has also been reported from a *Solenopsis* (Diplorhoptrum) species.[26]

The South African species *Solenopsis punctaticeps* is more closely related to thief ants than fire ants. Although *S. punctaticeps* can sting, the reaction of humans to its venom is mild compared to that encountered with the sting of a true fire ant and its venom shows a marked difference from the fire ant venom by the absence of dialkylpiperidines—instead it is fortified with a number of 2,5-dialkylpyrrolines and -pyrrolidines (9, 10, and 13).[27,28]

The only bicyclic alkaloid known from *Solenopsis* is the pyrrolizidine (32). The four possible isomers have been synthesized and the stereochemistry of the ant isomer has been determined by comparison.[29] A recent enantioselective synthesis of the pyrrolizidine (32) has been reported[30] and the product was spectroscopically congruent with the natural product.

The alkaloidal venoms are not restricted only to the genus *Solenopsis*; many species of *Monomorium* also have an array of alkaloids in their venoms. Jones *et al.*[31] examined the venoms of a number of species of *Monomorium* and found that all produce mixtures of different proportions of *trans*-2,5-dialkylpyrrolidines (13), *trans*-2-alkyl-5-alkenylpyrrolidines (14), *trans*-2,5-dialkenylpyrrolidines (15), *trans*-2,5-dialkyl-*N*-methylpyrrolidines (16), *trans*-2-alkyl-5-alkenyl-*N*-methylpyrrolidines (17), *trans*-2,5-dialkenyl-*N*-methylpyrrolidines (18), 2,5-dialkyl-1-pyrrolines (9, 10), and 2,5-dialkenyl-1-pyrrolines (11, 12).[26,29] Although the purpose of these species-specific mixtures of alkaloids is not clear, at least they are useful for the chemotaxonomist since they provide a distinctive label to a species. The venom of the old world species *M. pharaonis* is particularly distinctive in containing, in addition to four dialkylpyrrolidines, two indolizidines (29, 31).[26,32,33] The indolizidine (Monomorine I) (29), which has an all-*cis* configuration, and *trans*-2-pentyl-5-(5′-hexenyl)pyrrolidine (Monomorine II) (14) were shown to attract Pharaoh's ant, *Monomorium pharaonis*, and to have some activity in a trail-following bioassay.[32,33] However, the true trail pheromone was later identified from the Dufour gland.[34]

Methyl 4-methylpyrrole-2-carboxylate (8), a minor constituent identified in the

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[27] D. J. Pedder, H. M. Fales, T. Jaouni, M. S. Blum, J. G. MacConnell, R. M. Crewe, and M. Robin, *Tetrahedron*, 1976, **32**, 2275.

[28] J. H. Jones, M. S. Blum, and H. M. Fales, *Tetrahedron Lett.*, 1979, **12**, 1031.

[29] T. H. Jones, M. S. Blum, H. M. Fales, and C. R. Thompson, *J. Org. Chem.*, 1980, **45**, 4778.

[30] S. Takano, S. Otaki, and K. Ogasawara, *J. Chem. Soc., Chem. Commun.*, 1983, 1172.

[31] T. H. Jones, M. S. Blum, R. W. Howard, C. A. McDaniel, H. M. Fales, M. B. DuBois, and J. Torres, *J. Chem. Ecol.*, 1982, **8**, 285.

[32] F. J. Ritter, I. E. M. Rotgans, E. Talman, P. E. J. Verwiel, and F. Stein, *Experientia*, 1973, **29**, 530.

[33] P. E. Sonnet and J. E. Oliver, *J. Heterocycl. Chem.*, 1975, **12**, 289.

[34] F. J. Ritter, I. E. M. Bruggemann-Rotgans, P. E. J. Verwiel, E. Talman, F. Stein, J. La Brijn, and C. J. Persoons, Int. Congr. Int. Union Study Soc. Insects, 8th, 1977, p. 41 (Chem. Abstr. 1978, **89**, 176608_f).

[35] J. H. Tumlinson, R. M. Silverstein, J. C. Moser, R. G. Brownlee, and J. M. Ruth, *Nature (London)*, 1971, **234**, 348.

[36] J. H. Tumlinson, J. C. Moser, R. M. Silverstein, R. G. Brownlee, and J. M. Ruth, *J. Insect Physiol.*, 1972, **18**, 809.

[37] R. G. Riley, R. M. Silverstein, B. Carroll, and R. Carroll, *J. Insect Physiol.*, 1974, **20**, 651.

venom of a few species of leaf-cutting ants, *Atta texans*,[35,36] *A. cephalotes*,[37] and *Acromyrmex octospinosus*[38] is the first substance to be identified as a component of ant trail pheromones. This pyrrole (8) was synthesized by Sonnet[39] and shown to be identical with the natural substance. The compound has a very high behavioural efficiency and the detection threshold is as low as 80 fg cm^{-1} of a trail. Artificial trails of the pyrrole (8) were followed by several leaf-cutting ants of the tribe Attini but two related species, *Atta sexdens* and *Acromyrmex niger*, did not show any significant response.[40] The pyrrole (8) is only one component in the trail pheromone of *Atta texana*; Tumlinson *et al.*[35] isolated at least four other active fractions but the structures of these other constituents remain unknown. Moser and Silverstein[41] have shown the existence of an active but non-volatile component besides the volatile component in the trail-marking substance of *A. texana*.

Initial laboratory experiments indicated that a practical method of ant control might result by incorporating the pyrrole (8) into toxic bait. In practice this made it easier for the ants to find the baits but did not increase the likelihood of the baits being picked up.[42] In field tests, pyrrole (8) was unable to reproduce all aspects of natural recruitment although it did induce trail-following behaviour.[43] Its addition to current baits would not be cost-effective[44] but it might be a worthwhile addition to the synthetic baits now being developed.[45]

An understanding of the stereochemistry necessary for a compound to exhibit pheromonal activity is aided by studies using structurally related compounds (sometimes called congeners). The studies of Sonnent and Moser[46] on the congeners of the pyrrole (8) show the absolute requirement of the 2,4-substitution pattern and the pyrrolic nitrogen atom. All the other ring-substitution isomers are inactive. *N*-Methylation also results in the reduction of activity.[47] The methyl group at position-4 can be replaced by a chlorine atom without loss of activity, and even when substituted with an ethyl group or a bromine atom the pyrrole shows a substantial degree of activity, indicating that the steric requirement at position-4 is not very stringent. In contrast, for substitution at the 2-position, activity of the pyrrole is retained only when the new substituent group is less bulky than the original. For example, compounds with the carboxy-group esterified with any alcohol higher than methanol were inactive.[46] An acetyl group at position 2 showed moderate activity but a free carboxy-group was inactive. Caputo *et al.*[48] have calculated the charge densities on the pyrrolic nitrogen for a variety of congeners and show the most active compounds to have the same charge of -0.51 electrons on the nitrogen atom. They have suggested that a close value for this

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[38] J. H. Cross, J. R. West, R. M. Silverstein, A. R. Jutsum, and J. M. Cherrett, *J. Chem. Ecol.*, 1982, **8**, 1119.

[39] P. E. Sonnet, *J. Med. Chem.*, 1972, **15**, 97.

[40] S. W. Robinson, J. C. Moser, M. S. Blum, and E. Amante, *Insectes Soc.*, 1974, **21**, 87.

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[42] S. W. Robinson and J. M. Cherrett, *Bull. Entomol. Res.*, 1978, **68**, 159.

[43] S. W. Robinson, A. R. Jutsum, J. M. Cherrett, and R. J. Quinlan, *Bull. Entomol. Res.*, 1982, **72**, 345.

[44] K. Jaffe and P. E. Howse, *Anim. Behav.*, 1979, **27**, 930.

[45] A. R. Jutsum and J. M. Cherrett, *Bull. Entomol. Soc.*, 1981, **71**, 607.

[46] P. E. Sonnet and J. C. Moser, *Agr. Food Chem.*, 1972, **20**, 1191.

[47] P. E. Sonnet and J. C. Moser, *Environ. Entomol.*, 1973, **2**, 851; 1973, **56**, 976.

[48] J. F. Caputo, R. E. Caputo, and J. M. Brand, *J. Chem. Ecol.*, 1979, **5**, 273.

charge may be important in a compound with the correct steric properties to show chemorecognition.

Atta sexdens, a leaf-cutting ant species related to *A. texana* and *A. cephalotes* did not follow an artificial trail made of the pyrrole (8). Subsequently Cross *et al.*[49] identified 3-ethyl-2,5-dimethylpyrazine (24) from the poison glands of *Atta sexdens* as the major component of its trail pheromone. The pyrrole (8) was also isolated as a minor component but this substance does not evoke trail-following behaviour in *Atta sexdens*. Evershed *et al.*[50,51] identified the same pyrazine (24) as the sole component in the trail pheromone of *Myrmica rubra* and seven other related species of *Myrmica*. A quantitative study of the trail pheromone substances in the venom of Attine ants has been made by Evershed and Morgan.[52]

Recently a further pyrazine, 2,5-dimethylpyrazine (26), together with 3-ethyl-2,5-dimethylpyrazine (24) have been identified as the trail pheromone components of *Tetramorium caespitum*.[53,54] A complete identification of a multi-component trail pheromone of ants has been performed only in this case. A 30:70 mixture of 3-ethyl-2,5-dimethylpyrazine (24) and 2,5-dimethylpyrazine (26) constitutes the synergistic mixture that evokes the highest trail-following activity. A concentration of 40 and 90 pg cm^{-1} trail of the two respective synthetic pyrazines (24, 26) was equivalent in releasing trail-following activity to an artificial trail made of a single poison gland.

The ability to release trail-following activity by a number of congeneric pyrazines has been tested on *Tetramorium caespitum*.[54] The 2,5-substitution on the pyrazine ring is important because 2,3- and 2,6-dimethylpyrazines are inactive. Furthermore, when the ethyl of pyrazine (24) was replaced by a methyl group, the compound could still show some activity. Although many trail pheromones that originate from the poison glands[55] are not yet chemically identified, they might be expected to be nitrogenous compounds of a similar nature. Skatole (27) and anabaseine (28) are two further alkaloids isolated from two myrmicine ants, *Pheidole fallax*[56] and *Aphaenogaster fulva*[57] respectively. Anabaseine, a minor alkaloid in tobacco, acts as a weak attractant to *A. fulva*, but induces no trail-following behaviour.[57]

In 1980, Vander Meer *et al.*[58] identified the poison sac of queens of imported fire ant, *Solenopsis invicta*, as the storage site for the pheromone which enables the workers to recognize the queen. This pheromone orients and attracts the worker ants towards the queen. Using a bioassay method, Vander Meer *et al.* found that

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[49] J. H. Cross, R. C. Byler, U. Ravid, R. M. Silverstein, S. W. Robinson, P. M. Baker, J. S. De Oliveira, A. R. Jutsum, and J. M. Cherrett, *J. Chem. Ecol.*, 1979, **5**, 187.

[50] R. P. Evershed, E. D. Morgan, and M. C. Cammaerts, *Naturwissenschaften*, 1981, **67**, 374.

[51] R. P. Evershed, E. D. Morgan, and M. C. Cammaerts, *Insect Biochem.*, 1982, **12**, 383.

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[53] A. B. Attygalle and E. D. Morgan, *Naturwissenschaften*, 1983, **70**, 364.

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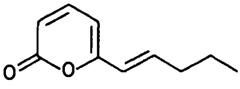
[55] A. B. Attygalle and E. D. Morgan, *Adv. Insect Physiol.*, 1984, **18**, in press.

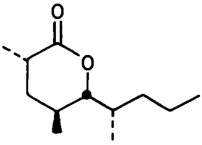
[56] J. H. Law, E. O. Wilson, and J. A. McCloskey, *Science*, 1965, **149**, 544.

[57] J. W. Wheeler, O. Olubajo, C. B. Storm, and R. M. Duffield, *Science*, 1981, **211**, 1051.

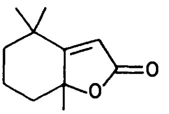
[58] R. K. Vander Meer, B. M. Glancey, C. S. Lofgren, A. Glover, J. H. Tumlinson, and J. Rocca, *Ann. Entomol. Soc. Am.*, 1980, 73, 609.



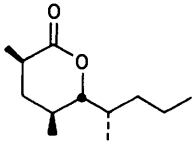
(35)



(36)



(37)



(38)

the characteristic 2-methyl-6-alkyl (or alkenyl)-piperidine alkaloids (19, 20) found in fire ant venom to be inactive as the queen recognition pheromones. These piperidines are found also in unmated (alate) queens but the alate queens are not overtly attractive to workers. The queen recognition pheromone is found only in the poison sac of mated queens. When the poison sacs were solvent extracted only the non-alkaloidal fraction was active, and therefore the pheromone was expected to be a minor non-alkaloid constituent in the poison sac.

Rocca *et al.*[59] isolated 5—25 μg of the compounds responsible for activity from 18 000 fire ant queens. Three components have been chemically identified: (*E*)-6-(1-pentenyl)-2*H*-pyran-2-one (35), tetrahydro-3,5-dimethyl-6-(1-methylbutyl)-2*H*-pyran-2-one (36), and dihydroactinidiolide (37).

The α-pyrone (35), the (±)-δ-lactone (36) [together with its 3-epimer (38)] and the dihydroactinidiolide (37) have all been synthesized.[59] [61] and the first two have been shown to be biologically active. The configurations at chiral atoms were assigned by comparing the i.r. and ^{1}H n.m.r. spectra with compounds of known configurations. The optical isomeric composition of the natural δ-lactone (36) is not yet determined.

The behaviour of *S. invicta* workers to the queen recognition pheromone has been studied by Lofgren *et al.*[62] This pheromone has the potential of being used in fire ant control because the worker ants move inanimate objects treated with pheromone (*e.g.* pieces of rubber *ca.* 20 mg, 'surrogate queens') into their nests. It could be useful to increase the rate of toxic bait pick-up.

The venom of the myrmicine ant *Myrmicaria natalensis* is distinctively aberrant and unusual. The reported[63] presence of monoterpene hydrocarbons, such as α-pinene, camphene, β-pinene, sabinene, β-myrcene, α-phellandrene, α-terpinene,

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[59] J. R. Rocca, J. H. Tumlinson, B. M. Glancey, and C. S. Lofgren, *Tetrahedron Lett.*, 1983, **24**, 1889 and 1892.

[60] J. R. Rocca, J. H. Tumlinson, B. M. Glancey, and C. S. Lofgren, *Tetrahedron Lett.*, 1983, **24**, 1893.

[61] T. Sakan, S. Isoe, and S. B. Hyeon, *Tetrahedron Lett.*, 1967, 1623.

[62] C. S. Lofgren, B. M. Glancey, A. Glover, J. Rocca, and J. Tumlinson, *Ann. Entomol. Soc. Am.*, 1983, **76**, 44.

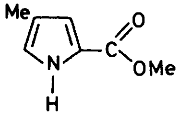
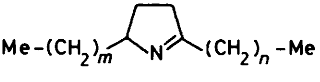
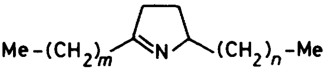
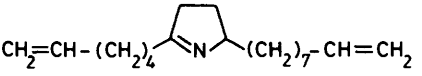
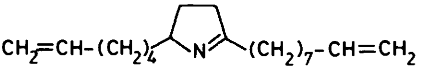
[63] J. M. Brand, M. S. Blum, H. A. Lloyd, and J. C. Fletcher, *Ann. Entomol. Soc. Am.*, 1974, **67**, 525.

limonene, and terpinolene, in the poison gland of *M. natalensis* may puzzle anyone interested in the phylogeny of the venom gland or the physiological action of these compounds. A similar mixture of monoterpenes is found in the poison gland secretions of *Myrmicaria eumenoides*, an opportunistic termite predator in west Africa.[64] When the synthetic terpenes were presented experimentally, α-pinene, β-pinene, myrcene, and limonene released 'alarm behaviour'.

The very highly volatile constituents present in nanogram quantities in the poison glands of *Myrmica rubra* and *M. scabrinodis* were reported to be simple alkanes, alcohols, and carbonyl compounds containing one to five carbon atoms.[65]

All reported evidence given so far clearly shows the diversity of ant venoms and probably the venom gland is the most versatile biosynthetic tissue that has been evolved by social hymenopterans.

Table 1 *Venom alkaloids of Myrmicine ants*

Structure		*Source*	*Ref.*
 (8)		*Atta texana*	35, 36
		A. cephalotes	37
		Acromyrmex octospinosus	38, 40
 (9)	$m = 1, n = 4$	*Solenopsis punctaticeps*	27
	$m = 1, n = 6$	*S. punctaticeps*	27
	$m = 3, n = 6$	*Monomorium latinode*	26
 (10)	$m = 1, n = 4$	*S. punctaticeps*	27
	$m = 1, n = 6$	*S. punctaticeps*	27
 (11)		*Monomorium* sp.	31
 (12)		*Monomorium* sp.	31

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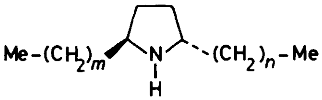
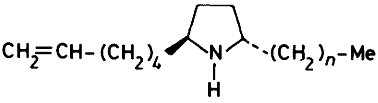
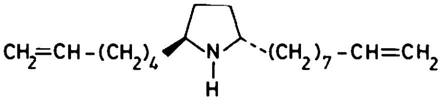
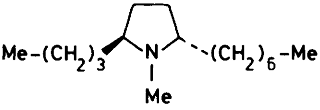
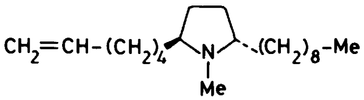
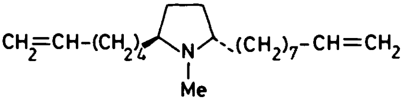
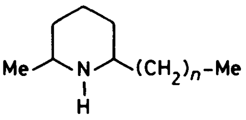
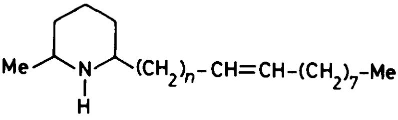
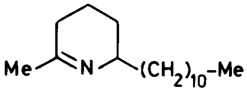
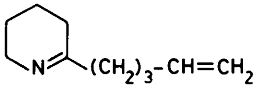
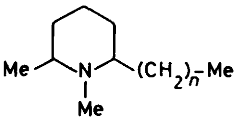
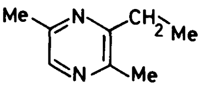
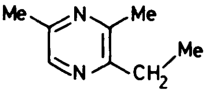
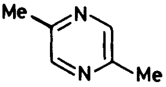
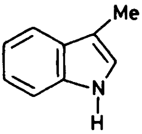
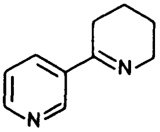
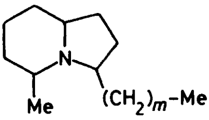
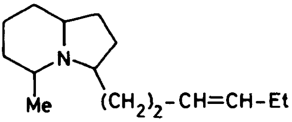
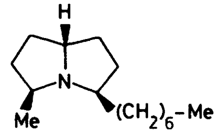
[64] P. E. Howse, R. Baker, and D. A. Evans, ref. 34, p. 44.

[65] M. C. Cammaerts, M. R. Inwood, E. D. Morgan, K. Parry, and R. C. Tyler, *J. Insect. Physiol.*, 1978, **24**, 207.

Structure		*Source*	*Ref.*
 (13)	$m = 1, n = 6$	*Solenopsis punctaticeps*	27
	$m = 3, n = 4$	*S. punctaticeps*	27
	$m = 3, n = 4$	*Monomorium* sp.	(*a*), 26
	$m = 3, n = 6$	*S. fugax*	25
	$m = 3, n = 6$	*S. punctaticeps*	27
	$m = 3, n = 6$	*M. latinode*	26
	$m = 4, n = 5$	*S. molesta*	28
	$m = 4, n = 5$	*S. texanas*	28
	$m = 5, n = 8$	*Monomorium* sp.	31
 (14)	$n = 4$	*Monomorium pharaonis*	(*a*)
	$n = 6$	*Monomorium* sp.	26
	$n = 8$	*Monomorium* sp.	31
 (15)		*Monomorium* sp.	31
 (16)		*M. latinode*	26
 (17)		*Monomorium* sp.	26
 (18)		*Monomorium* sp.	26

Structure		*Source*	*Ref.*
 (19)	$n = 6$	*S. richteri*	(*b*)
	$n = 8$	*S. carolinensis*	26
	$n = 8$	*Solenopsis* sp.	22
	$n = 8$	*S. richteri*	(*b*), 23
	$n = 10$	*S. littoralis*	26
	$n = 10$	*Solenopsis* sp.	22
	$n = 12$	*S. littoralis*	26
	$n = 14$	*S. invicta*	22, 23
 (20)	$n = 3$	*Solenopsis* sp.	22, 23
	$n = 5$	*S. invicta*	22, 23
	$n = 7$	*Solenopsis* sp.	22, 23
 (21)		*S. xyloni*	23
 (22)		*S.* (*Diplorhoptrum*)?	26
 (23)	$n = 8$	*S. carolinensis*	26
	$n = 10$	*S. pergandei*	26
 (24)		*Acromyrmex octospinosus*	38
		Atta sexdens	49
		Myrmica sp.	50, 51
		Tetramorium caespitum	53

Structure		*Source*	*Ref.*
 (25)		*Acromyrmex octospinosus*	38
 (26)		*Tetramorium caespitum*	53
 (27)		*Pheidole fallax*	(*c*)
 (28)		*Aphaenogaster fulva*	57
 (29) (30)	$m = 3$ $m = 5$	*M. pharaonis* (29) *Solenopsis* sp. (30)	32, 34 26, 29
 (31)		*M. pharaonis*	26

Structure	*Source*	*Ref.*
 (32)	*Solenopsis* sp.	29

[a] F. J. Ritter, I. E. M. Bruggemann-Rotgans, E. Verkuil, C. J. Persoons, in 'Pheromone and Defensive Secretion in Social Insects' ed. Ch. Noirot, P. E. House, and G. Le Masne, University of Dijon, Dijon, 1975. [b] J. E. MacConnell, R. N. Williams, J. M. Brand, and M. S. Blum, *Ann. Ent. Soc. Am.*, 1974, **67**, 134. [c] J. H. Law, E. O. Wilson, and J. A. McCloskey, *Science*, 1965, **149**, 544.

B. Dufour Gland Substances.—In 1841, Dufour first described this sac-like gland attached to the poison apparatus in ants and bees.[66] The Dufour gland of ants has a remarkable ability to synthesize hydrocarbons. Over 50 alkanes and alkenes have been identified in the Dufour gland and the compounds reported up to 1974 have been reviewed by Blum and Hermann.[67–69]

Aliphatic hydrocarbons within the range C_9 to C_{27} are present in the Dufour glands of myrmeciine,[70] ponerine,[70] pseudomyrmecine,[67] myrmicine,[67] formicine,[67] and dolichoderine[68] ants. The Dufour glands of ants are typically filled with linear hydrocarbons, but not exclusively so. Although hydrocarbons with an even number of carbon atoms are encountered as minor constituents, the odd-numbered hydrocarbons are always found in much larger quantities. Branched-chain hydrocarbons and many oxygenated compounds can also be encountered.

The formicine ants produce hydrocarbons, often undecane and tridecane, as the major class of compounds in their Dufour glands. Some species of *Formica* and *Camponotus* contain monomethylalkanes as minor constituents; for example, in *Camponotus intrepidus*, 3-methylalkanes comprise about 16% and 5-methylalkanes about 2% of the total hydrocarbons.[71] Over 95% of the total secretion of volatiles of *C. japonicus* and *C. obscuripes* is undecane.[72] Similarly, for *Formica nigricans*,[73] *F. rufa*,[73] *F. polyctena*,[73,74] and *Acanthomyops claviger*[75] undecane accounts for more than 50% of the Dufour gland secretion. In *Formica polyctena* a number of monomethylalkanes are present in small quantities, with the methyl branching at position 2, 3, 4, 5, or 7.[74] The Dufour glands of virgin queens of *F. polyctena* contain about 74% undecane, and this is also the major component of the worker glands. However, in the glands of mated queens undecane content is less than 1%, indicating that undecane may function as a pheromone for some behaviour related to swarming or pairing. Males did not, however, respond to streams of air laden

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[66] L. Dufour, *Mem. Pres. div. Sav. Acad. Sci. Inst. Fr.*, 1841, **7**, 265.

[67] M. S. Blum and H. R. Hermann, in 'Arthropod Venoms', ed. S. Bettini, *Handbook of Experimental Pharmacology, Vol. 48, Springer-Verlag, Berlin, 1978, p. 801.*

[68] M. S. Blum and H. R. Hermann, in 'Arthropod Venoms', ed. S. Bettini, Handbook of Experimental Pharmacology, Vol. 48, Springer-Verlag, Berlin, 1978, p. 871.

[69] M. S. Blum, 'Chemical Defences of Arthropods', Academic Press, New York, 1981.

[70] G. W. K. Cavill and P. J. Williams, *J. Insect Physiol.*, 1967, **13**, 1097.

[71] J. J. Brophy, G. W. K. Cavill, and J. S. Shannon, *J. Insect Physiol.*, 1973, **19**, 791.

[72] N. Hayashi and H. Komae, *Biochem. Syst. Ecol.*, 1980, **8**, 293.

[73] G. Bergström and J. Löfqvist, *J. Insect. Physiol.*, 1973, **19**, 877.

[74] J. Lofqvist and G. Bergström, *J. Chem. Ecol.*, 1980, **6**, 309.

[75] F. E. Regnier and E. O. Wilson, *J. Insect Physiol.*, 1968, **14**, 955.

with undecane alone or mixed with formic acid when tested in a climate chamber with high light intensity.[74]

In a number of species of *Lasius* also, the major component is undecane.[76] The composition of the glandular secretion of *Polyrhachis simplex* is very simple and consists of linear alkanes—over 90% tridecane and minor amounts of undecane, dodecane, pentadecane, and heptadecane.[77] Similarly, tridecane is the major component in the gland of an Australian *Polyrhachis* species examined by Brophy *et al.*[78] Undecane comprises nearly 50% of the total volatile secretions of *P. lamellidens.*[72]

Besides the alkanes, a number of alkenes are also found in the Dufour glands of formicine ants. Linear monoenes of C_{11}—C_{23} range are present in *Formica nigricens, F. rufa,* and *F. polyctena.*[73] It is interesting to find that the pentadecene in an Australian species of *Polyrhachis* is a mixture of Δ-6 and Δ-7 isomers. Similarly, heptadecene is a mixture of Δ-7 and Δ-8 isomers but 9-nonadecene, 9-heneicosene, 9-tricosene, and 9-pentacosene were not accompanied by positional isomers.[78] Similar mixtures of alkanes and alkenes of C_{10}—C_{18} range are found in the Dufour glands of a number of species of *Camponotus, Cataglyphis,* and *Polyrhachis* from Israel,[79] but in *Camponotus intrepidus* the alkenes constitute less than 0.2% of the total hydrocarbons[71] and are completely absent from *C. japonicus* and *C. obscuripes.*[72]

The formicine ants are notable for their ability to produce a variety of oxygenated compounds together with the hydrocarbons in their Dufour glands. These compounds, produced by a number of species of *Formica,*[80] *Lasius,*[76] *Camponotus,*[81,82] *Notoncus,*[78] and *Gigantiops,*[83] include a variety of primary aliphatic alcohols (C_{10}—C_{16}), simple ketones (C_{13}—C_{19}), alkylacetates (C_9OAc—$C_{18}OAc$), and a few terpenoid derivatives like α-farnesene,[80] farnesyl acetate,[76] all-*trans*-geranylgeraniol (39),[73] and geranylgeranyl acetate.[73] The Dufour gland of *Formica sanguinea* has alkyl acetates as the major components[80] (the average amount of decyl acetate is about 100 μg per ant).[80] Graham *et al.*[84] have studied decyl acetate biosynthesis in *F. schaufussi* to determine whether the ester is formed by the incorporation of molecular oxygen into a 2-ketone or by the esterification of acetic acid with an alcohol. The species *F. schaufussi* was specially suited because it has several hundred micrograms of decyl acetate in the Dufour gland. The radio-labelling studies of Graham *et al.* indicate that decyl acetate is synthesized *via* an esterification reaction.[84]

Methyl or ethyl ketones are encountered frequently in formicine Dufour glands, *e.g.* 2-tridecanone is a major constituent in *Gigantiops destructor*[83] and

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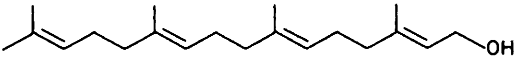
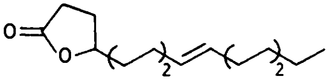
[76] G. Bergström and J. Lofqvist, *J. Insect Physiol.*, 1970, **16**, 2353.
[77] A. Hefetz and H. A. Lloyd, *J. Chem. Ecol.*, 1982, **8**, 635.
[78] J. J. Brophy, G. W. K. Cavill, J. A. McDonald, D. Nelson, and W. D. Plant, *Insect Biochem.*, 1982, **12**, 215.
[79] A. Hefetz and T. Orion, *Isr. J. Entomol.*, 1982, **16**, 87.
[80] G. Bergström and J. Löfqvist, *J. Insect Physiol.*, 1968, **14**, 995.
[81] G. Bergström and J. Löfqvist, *Entomol. Scand.*, 1972, **3**, 225.
[82] G. Bergström and J. Löfqvist, in 'Chemical Releasers in Insects', ed. A. S. Tahori, Gordon and Breach, New York, 1971, Vol. III, p. 195.
[83] M. S. Blum, T. H. Jones, W. I. Overal, H. M. Fales, J. O. Schmidt, and N. A. Blum, *Comp. Biochem. Physiol.*, 1983, **75B**, 15.
[84] R. A. Graham, J. M. Brand, and A. J. Markovetz, *Insect Biochem.*, 1979, **9**, 331.

Acanthomyops claviger[75] and it is also found in *Formica rufibarbis*.[80] A series of 2- and 3-alkylketones of C_{13}—C_{19} range is found in *Lasius* ants.[76] The Dufour gland content of *L. flavus* is unique in containing some hydroxy acids and the corresponding lactones.[76] 4-Hydroxyoctadec-9-enolide (40) and its free acid, and in minor amounts, the lower homologue with two carbon atoms less are found in the gland of *L. flavus*.[76]



(39)



(40)

Among the myrmicine ants the Dufour gland contents of a number of species of the genus *Myrmica* have been thoroughly investigated.[85–91] The presence of highly volatile oxygenated compounds such as simple alcohols, aldehydes, and ketones in the C_1—C_4 range have also been reported in myrmicine ants of the genus *Myrmica*.[65] Beside the general linear hydrocarbon theme, most species of *Myrmica* also have some terpenoid hydrocarbons, sometimes even as major components.[88] These terpenoid hydrocarbons were identified by Morgan and Wadhams, on mass spectral evidence, as farnesene, homofarnesene, and bishomofarnesene.[91] Subsequently, a trishomofarnesene has also been described from *M. scabrinodis*.[88] Parry[92] identified the farnesene isomer from the *Myrmica* ants as (*Z*, *E*)-α-farnesene (41) by comparison of its mass spectrum and g.l.c. retention times on different phases with those of a mixture of six farnesene isomers prepared from the dehydration of (*Z*)- and (*E*)-nerolidol (42). The structure of (*Z*, *E*)-α-farnesene was recently confirmed by total synthesis.[93] On the basis of their mass spectra, structures (43) and (44) have been proposed by Morgan and Wadhams[91] for the homofarnesene and bishomofarnesene isolated from the Dufour gland of *Myrmica* ants.

A recent micro-degradation study provided the confirmatory evidence for the structure of homofarnesene and bishomofarnesene.[94] One of the products from the micro-ozonolysis of farnesene was 4-oxopentanal, whereas the homofarnesene and bishomofarnesene isomers from *Myrmica* ants gave 4-oxopentanal indicating the

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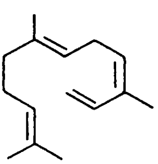
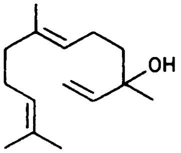
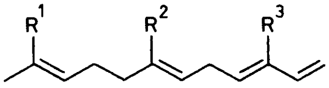
[85] A. B. Attygalle, M. C. Cammaerts, and E. D. Morgan, *J. Insect Physiol.*, 1983, **29**, 27.
[86] A. B. Attygalle, R. P. Evershed, E. D. Morgan, and M. C. Cammaerts, *Insect Biochem.*, 1983, **13**, 507.
[87] M. C. Cammaerts, R. P. Evershed, and E. D. Morgan, *J. Insect Physiol.*, 1981, **27**, 59.
[88] E. D. Morgan, K. Parry, and R. C. Tyler, *Insect Biochem.*, 1979, **9**, 117.
[89] E. D. Morgan, R. C. Tyler, and M. C. Cammaerts, *J. Insect Physiol.*, 1977, **23**, 511.
[90] M. C. Cammaerts-Tricot, E. D. Morgan, R. C. Tyler, and J. C. Braekman, *J. Insect Physiol.*, 1976, **22**, 927.
[91] E. D. Morgan and L. J. Wadhams, *J. Insect. Physiol.*, 1972, **18**, 1125.
[92] K. Parry, M.Sc. Thesis, University of Keele, 1978.
[93] L. J. Thompson, Ph.D. Thesis, University of Keele, 1982.
[94] A. B. Attygalle and E. D. Morgan, *J. Chem. Soc. Perkin Trans 1*, 1982, 949.



(41)



(42)



(43) $R^1 = R^3 = Me$ $R^2 = Et$

(44) $R^1 = R^2 = Et$ $R^3 = Me$

presence of an ethyl group at C-7. Similarly, farnesene and homofarnesene gave propanone but bishomofarnesene gave butanone, indicating the presence of an ethyl group at C-11 of the bishomofarnesene.[94] The configurations of the double bonds of these two isomers are still not determined. A similar homofarnesene isomer has been reported from four species of attine ants[95,96] and α-farnesene from *Aphaenogaster longiceps*.[97] Hydrocarbon themes, similar to those in *Myrmica* ants, are shown by the Dufour glands of *Pogonomyrmex*[98] and *Novomesser*.[99]

Dufour gland secretions of dolichoderine ants also show the linear and methyl-branched alkane and alkene pattern,[100,101] but no terpenoids have been found. Some of the low molecular weight hydrocarbons (out of the large number reported) from the total extracts of a few species of *Iridomyrmex* may have arisen from the Dufour gland.[102] No information is available about the chemistry of the Dufour glands of other subfamilies.

The primary functions of the Dufour gland appear to be defence and communication. Blum[103] has suggested that the diverse chemical compounds found in the Dufour gland could function to overstimulate the olfactory receptors of predators, and thus act as a deterrent. According to Bergström and Löfqvist,[82] these compounds are often used as alarm pheromones—as, for example, undecane in *Lasius niger*[76] and *Acanthomyops claviger*.[75] Tridecane however, which is almost the only substance in the Dufour gland of *Polyrhachis simplex*, did not provoke any

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[95] R. P. Evershed and E. D. Morgan, *Insect Biochem.*, 1980, **10**, 81.

[96] R. P. Evershed and E. D. Morgan, *Insect Biochem.*, 1981, **11**, 343.

[97] G. W. K. Cavill, P. J. Williams, and F. B. Whitfield, *Tetrahedron Lett.*, 1967, **23**, 2201.

[98] F. E. Regnier, M. Nieh, and B. Hölldobler, *J. Insect Physiol.*, 1973, **19**, 981.

[99] K. Vick, W. A. Drew, D. J. McGurk, E. J. Eisenbaum, and G. R. Waller, *Ann. Entomol. Soc. Am.*, 1969, **62**, 723.

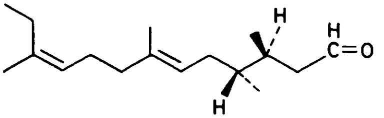
[100] G. W. K. Cavill and E. Houghton, *J. Insect Physiol.*, 1974, **20**, 2049.

[101] G. W. K. Cavill and E. Houghton, *Aust. J. Chem.*, 1973, **26**, 1131.

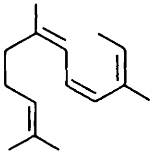
[102] J. J. Brophy, G. W. K. Cavill, N. W. Davies, T. D. Gilbert, R. P. Philp, and W. D. Plant, *Insect Biochem.*, 1983, **13**, 381.

[103] M. S. Blum, *Bull. Entomol. Soc. Am.*, 1974, **20**, 30.

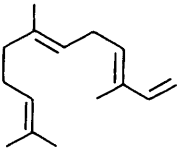
sustained alarm behaviour.[77] Bradshaw *et al.*[104] have demonstrated that in the African weaver ant *Oecophylla longinoda*, undecane from the Dufour gland and formic acid from the poison gland act synergistically to release a 'mass attack' reaction. Similarly, in *Formica rufa*, some of the hydrocarbons of the Dufour gland as well as the formic acid act as alarm pheromones and the combination of both releases a more intense alarm behaviour.[105] The Dufour glands of slave-keeping formicine ants such as *Formica subintegra*, *F. pergandei*, and *F. sanguinea* produce large quantities of C_{10}—C_{14} acetates, which are sprayed during slave raids to excite and attract the slave-maker ants but panic and disperse the slave-defender species.[80,106] The role of Dufour gland hydrocarbons in slave-keeping ants has been demonstrated by Lofqvist.[107] Formic acid from the Dufour gland is the main defence substance in *F. rufa* and *F. sanguinea*. However, it is rather harmless by itself because it is hydrophilic and when sprayed on a lipophilic cuticle it forms droplets which can affect only a small area. The hydrocarbons and acetates from the Dufour gland are lipophilic and promote the spreading of formic acid. The experiments of Löfqvist have shown the higher toxicity of formic acid and hydrocarbon or acetate mixtures compared with formic acid alone. Cammaerts *et al.*[87] have demonstrated that the ants of the genus *Myrmica* use their Dufour gland contents as a home-range marking pheromone. The ants move rapidly over any



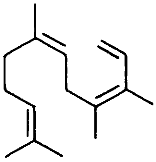
(45)



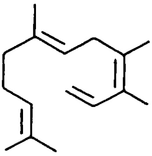
(46)



(47)



(48)



(49)

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[104] J. M. S. Bradshaw, R. Baker, and P. E. Howse, *Physiol. Entomol.*, 1979, **4**, 39.
[105] J. Löfqvist, *J. Insect Physiol.*, 1976, **22**, 1331.
[106] F. E. Regnier and E. O. Wilson, *Science*, 1971, **172**, 267.
[107] J. Löfqvist, *Oikos*, 1977, **28**, 137.

area marked with their own Dufour gland secretions, but more slowly on an alien-marked territory until they have over-marked it with their own Dufour gland contents.[85] The evidence so far available suggests that each species of ant has its own characteristic mixture of hydrocarbons and other compounds and that, at least in the *Myrmica* species which have been studied in detail, they are able to recognize this mixture and distinguish it from other species.[87]

In addition to the roles discussed above, some ant species utilize trace components of the Dufour gland secretion as trail pheromones. The few compounds identified as such include one sesquiterpenoid aldehyde, faranal (45),[108] and a few sesquiterpenoid alkenes (41, 46—49).[109,110] Although monomorine I (29) and monomorine III (14) from the poison glands of Pharaoh's ant, *Monomorium pharaonis* show some activity in trail following tests,[32,33] the true trail pheromone originates from the Dufour gland and was identified as (+)-(3*S*,4*R*)-3,4,7,11-tetramethyltrideca-6*E*,10*Z*-dienal (faranal) (45).[34,108] The stereochemistry and geometry of faranal have been established by stereospecific synthesis by several groups.[111-117] Faranal has an interesting structural relationship to juvenile hormones and the farnesene homologue found in *Myrmica* species.[94] In studies of faranal, Kobayashi *et al.*[111] found that the 3-epimer (3*R*,4*R*) is also weakly active when tested separately, though the preference of the ants for the (3*S*,4*R*)-optical isomer is unambiguous when tested in a choice test. The (3*R*)-enantiomer does not interfere with the activity of (3*S*) since ants follow a trail made of a mixture. The importance of the (4*R*)-configuration for activity has been shown by Koyama *et al.*[118] According to their results the geometry of the C-10 double bond is unimportant; both the *cis*- and *trans*-isomers show similar activity. Furthermore, the substitution at C-11 is not so important for the manifestation of trail-releasing activity—an ethyl or a methyl group at C-11 has activity, although the 7-methyl cannot be replaced by an ethyl group without losing the activity.[118]

The trail pheromone from the Dufour gland of the fire ant *Solenopsis invicta* is definitely multi-component but there is some ambiguity about its composition. According to Williams *et al.*[109,119] the major component is (2*Z*,4*Z*,6*Z*)-3,7,11-trimethyl-2,4,6,10-dodecatetraene (*Z*,*Z*,*Z*-allofarnesene) (46). They synthesized the eight isomers of allofarnesene[119] and found the *Z*,*Z*,*Z*-isomer to be congruent

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[108] F. J. Ritter, I. E. M. Bruggemann-Rotgans, P. E. J. Verviel, C. J. Persoons, and E. Talman, *Tetrahedron Lett.*, 1977, 2617.

[109] H. J. Williams, M. R. Strand, and S. B. Vinson, *Experientia*, 1981, **37**, 1159.

[110] R. K. Vander Meer, F. D. Willams, and C. S. Lofgren, *Tetrahedron Lett.*, 1981, 1651.

[111] M. Kobayashi, T. Koyama, K. Ogura, S. Seto, F. J. Ritter, and I. E. M. Bruggemann-Rotgans, *J. Am. Chem. Soc.*, 1980, **102**, 6602.

[112] K. Mori and H. Ueda, *Tetrahedron Lett.*, 1981, **22**, 461.

[113] K. Mori and H. Ueda, *Tetrahedron*, 1982, **38**, 1227.

[114] D. W. Knight and B. Ojhara, *Tetrahedron Lett.*, 1981, **22**, 5101.

[115] D. W. Knight and B. Ojhara, *J. Chem. Soc., Perkin Trans. 1*, 1983, 955.

[116] R. Baker, D. C. Billington, and N. Ekanayake, *J. Chem. Soc., Chem. Commun.*, 1981, 1234.

[117] R. Baker, D. C. Billington, and N. Ekanayake, *J. Chem. Soc., Perkin Trans 1*, 1983, 1387.

[118] T. Koyama, M. Matsubara, K. Ogura, I. E. M. Bruggemann, and A. Vrielink, *Naturwissenschaften*, 1983, **70**, 469.

[119] H. J. Williams, M. R. Strand, and S. B. Vinson, *Tetrahedron*, 1981, **37**, 2763.

with the ant substance. However, all isomers with Z-4 configuration showed trail-following activity.

According to Vander Meer *et al.*[110] four of the components of the trail pheromone from the Dufour gland of *S. invicta* are (3*Z*,6*E*)-3,7,11-trimethyldodeca-1,3,6,10-tetraene (*Z*,*E*-α-farnesene) (41), (3*E*,6*E*)-3,7,11-trimethyldodeca-1,3,6,10-tetraene (*E*,*E*-α-farnesene) (47), (3*Z*,6*Z*)-3,4,7,11-tetramethyldodeca-1,3,6,10-tetraene (*Z*,*Z*-homofarnesene) (48), and (3*Z*,6*Z*)-3,4,7,11-tetramethyldodeca-1,3,6,10-tetraene (*Z*,*E*-homofarnesene) (49). The two farnesenes were obtained by dehydrating (*E*)-nerolidol (42) and showed activity at a pheromonal level. *Z*,*E*-α-Farnesene (41) was the most active component and shows activity even at 100 fg cm^{-1} trail. The other three components were 10—100 times less active.[120] The homofarnesenes have not yet been synthesized. It is interesting to note that four components (41, 47—49) were able to duplicate the recruitment response of a Dufour gland when heptadecane (another component of the Dufour gland) was added to the mixture; heptadecane itself is inactive.

Barlin *et al.*[121] have made a preliminary survey of the trail pheromones of other species of *Solenopsis*. They report the main component of *S. richteri* to have a molecular weight of 218 and a molecular formula of $C_{16}H_{26}$. They assume that the trail pheromones of *S. xyloni* and *S. geminata* are similar and possess a molecular formula $C_{17}H_{28}$.

It is possible to conclude that the Dufour gland has evolved a long way from its suggested original function of providing a lubricant for the sting or for eggs during oviposition,[122] and that it has assumed novel duties acting as an important social organ to carry out a number of functions in defence and communication.

3 Mandibular Gland Substances

Mandibular glands are found in most insects and probably in all ants. Apart from the variation in size (in *Camponotus* it is remarkably large and extends up to the abdomen[123]), the mandibular glands appear to be similar in anatomy in all ant species.

The mandibular gland secretions have both defensive and pheromonal functions and a variety of natural products have been identified in the secretions.[66–68,124] Different subfamilies of ants appear to biosynthesize different classes of compounds. Duffield has made a comparative study of the mandibular gland chemistry of formicine and ponerine ants.[125]

A. Sulphides.—Some ponerine ants have the ability to produce alkyl sulphides in their mandibular glands, *e.g. Paltothyreus tarsatus* secretes dimethyl disulphide and dimethyl trisulphide, both of which release alarm behaviour.[126,127] Ants of the

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[120] R. K. Vander Meer, *Fl. Entomol.*, 1983, **66**, 139.

[121] M. R. Barlin, M. S. Blum, and J. M. Brand, *J. Insect Physiol.*, 1976, **22**, 839.

[122] R. L. Robertson, *Aust. J. Zool.*, 1968, **16**, 133.

[123] U. Maschwitz and E. Maschwitz, *Oecologia*, 1974, **14**, 289.

[124] K. Parry and E. D. Morgan, *Physiol. Entomol.*, 1979, **4**, 161.

[125] R. M. Duffield, *Diss. Abs. Int. B*, 1977, **37**, 3761.

[126] G. Casnati, A. Ricca, and M. Pavan, *Chim. Ind.* (*Milan*), 1967, **49**, 57.

[127] R. M. Crewe and D. J. C. Flecher, *J. Entomol. Soc. S. Afr.*, 1974, **37**, 291.

species *Megaponera foetens* use dimethyl disulphide and dimethyl trisulphide to co-ordinate attacks on their termite prey. Scout ants, on finding a nest of termites, release these alkyl sulphides from their mandibular glands to attract sister workers who dig into the termite galleries in response to other unidentified pheromones from the mandibular glands.[128] Benzylmethyl sulphide has also been identified but appears to show no behavioural activity. Biosynthetic studies have shown that the thiomethyl group of methionine is incorporated into these alkyl sulphides.[129,130]

B. Pyrazines.—Alkylpyrazines have been detected in the mandibular glands of several species of ponerine and dolichoderine ants. Recently pyrazines have also been identified in a few species of formicine and one species of myrmicine ants. Table 2 lists the alkylpyrazines reported from the mandibular glands of ants. All the pyrazines so far identified from the mandibular glands of ants are trisubstituted. Except for the unique trialkylpyrazine (52) recently reported from the myrmicine ant, *Aphaenogaster rudis*,[131] all the other pyrazines show 2,5-dimethyl-3-alkyl (50) or 2,6-dimethyl-3-alkyl (51) substitution patterns.

Gas chromatography combined with mass spectrometry is an ideal technique for the detection and identification of the pyrazines because the mass spectra of the pyrazines are well characterized. The retention times on gas chromatography and the molecular ion from mass spectrometry are useful for determining the length of the alkyl chain. Brophy and Cavill[132] and Wheeler *et al.*[131] provide useful compilations of mass spectral data of pyrazines.

The alkylpyrazines from mandibular glands have been reported to act as alarm pheromones.[133–135] In *Odontomachus troglodytes*, the males retreated from an alkylpyrazine source whereas the workers were attracted to, and attacked, the pheromone source.[136] Some of the reported alkylpyrazines have interesting side chains like citronellyl[137] and styryl.[138] Akita and Ohta[139] have reported a recent preparation of (*Z*)- and (*E*)-2,5-dimethyl-3-styrylpyrazine. The ability to biosynthesize alkylpyrazines does not appear to be unique to ants because many other insects including wasps,[131,140] beetles,[141] and flies[142] also produce a variety of alkylpyrazines.

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[128] C. Longhurst, R. Baker, and P. E. Howse, *J. Chem. Ecol.*, 1979, **5**, 703.

[129] R. M. Crewe and F. P. Ross, *Nature (London)*, 1975, **254**, 448.

[130] R. M. Crewe and F. P. Ross, *Insect Biochem.*, 1975, **5**, 839.

[131] J. W. Wheeler, J. Avery, O. Olubajo, M. T. Shamin, C. B. Storm, and R. M. Duffield, *Tetrahedron*, 1982, **38**, 1939.

[132] J. J. Brophy and G. W. K. Cavill, *Heterocycles*, 1980, **14**, 477.

[133] J. W. Wheeler and M. S. Blum, *Science*, 1973, **182**, 501.

[134] R. M. Duffield, M. S. Blum, and J. W. Wheeler, *Comp. Biochem. Physiol.*, 1976, **54B**, 439.

[135] M. V. Brown and B. P. Moore, *Insect Biochem.*, 1979, **9**, 451.

[136] C. Longhurst, R. Baker, P. E. Howse, and W. J. Speed, *J. Insect Physiol.*, 1978, **24**, 833.

[137] J. J. Brophy, G. W. K. Cavill, and W. D. Plant, *Insect Biochem.*, 1981, **11**, 307.

[138] G. W. K. Cavill and E. Houghton, *Aust. J. Chem.*, 1974, **27**, 879.

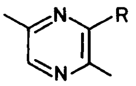
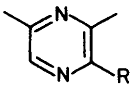
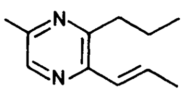
[139] Y. Akita and A. Ohta, *Heterocycles*, 1982, **19**, 329.

[140] A.-K. Borg-Karlson and J. Tengo, *J. Chem. Ecol.*, 1980, **6**, 827.

[141] B. P. Moore and W. V. Brown, *Insect Biochem.*, 1981, **11**, 493.

[142] R. Baker, R. H. Herbert, and R. A. Lomer, *Experientia*, 1982, **38**, 232.

Table 2 *Alkylpyrazines identified from mandibular glands of ants*

Structure		*Source-species*	*Subfamily*	*Ref.*
 (50)	R = ethyl	*Iridomyrmex purpureus*	Dolichoderinae	208
	R = propyl	*I. humilis*	Dolichoderinae	100, 138
		I. purpureus	Dolichoderinae	208
	R = n-butyl	*I. purpureus*	Dolichoderinae	208
	R = isobutyl	*Anochetus sedilloti*	Ponerinae	136
		Calomyrmex sp.	Formicinae	135
	R = s-butyl	*Anochetus sedilloti*	Ponerinae	136
	R = pentyl	*A. sedilloti*	Ponerinae	136
	R = isopentyl	*Odontomachus hastatus*	Ponerinae	133
		O. clarus	Ponerinae	133
		O. troglodytes	Ponerinae	136
		Ponera pennsylvanica	Ponerinae	134
		Hypoponera opacior	Ponerinae	134
		Iridomyrmex humilis	Dolichoderinae	100, 138
		Rhytidoponera metallica	Ponerinae	137
		Calomyrmex sp.	Formicinae	135
		Notoncus ectatommoides	Formicinae	78
	R = 2-methyl-butyl	*Calomyrmex* sp.	Formicinae	135
	R = styryl	*Iridomyrmex hymilis*	Dolichoderinae	100, 138
	R = citronellyl	*Rhytidoponera metallica*	Ponerinae	137
 (51)	R = ethyl	*Odontomachus brunneus*	Ponerinae	133
		O. troglodytes	Ponerinae	136
	R = propyl	*O. brunneus*	Ponerinae	133
	R = butyl	*O. brunneus*	Ponerinae	133
		O. troglodytes	Ponerinae	136
		Anochetus sedilloti	Ponerinae	136
		Brachyponera sennaarensis	Ponerinae	136
	R = i-butyl	*Anochetus sedilloti*	Ponerinae	136
	R = s-butyl	*A. sedilloti*	Ponerinae	136
	R = pentyl	*Odontomachus brunneus*	Ponerinae	133
		O. troglodytes	Ponerinae	136
		Brachyponera sennaarensis	Ponerinae	136
	R = hexyl	*Odontomachus troglodytes*	Ponerinae	136
 (52)		*Aphaenogaster rudis*	Myrmicinae	131

C. Ketones and Alcohols.—Secondary alcohols and their corresponding ketones are the most common chemicals found in the mandibular glands of ants[67,69]—even in those of some ponerine ants where these compounds are found instead of the usual pyrazines.[143,144] In *Bothroponera soror* different components in the mandibular gland secretion release different behavioural responses.[144] For example, 2-undecanone releases alerting and orientation responses and 2-undecanol an attraction response. The mandibular gland secretions of doryline[67] and pseudomyrmecine[67] ants also contain mainly aliphatic ketones.

The mandibular gland secretions of myrmicine and formicine ants have been more extensively studied than those of other subfamilies. Among the myrmicine ants, species which belong to the genus *Myrmica* are able to biosynthesize an abundance of homologous 3-alkanones and the corresponding 3-alkanols of the C_6—C_{11} range,[145–148] however, 3-octanone and 3-octanol are the major active components.[146] The 3-octanol of *Myrmica* ants is chiefly 3-(−)-(*R*)-octanol with small amounts of the (*S*)-enantiomer.[149] Only the (*R*)-enantiomer shows biological activity. The 4-methyl-3-heptanone in the mandibular glands of *Atta texana* is biosynthesized with stereospecific exactitude to yield the (*S*)-(+)-isomer alone, and only this enantiomer is pheromonally active.[150] Similarly, only the (3*R*,4*S*)-isomer of 4-methyl-3-hexanol is found in *Tetramorium impurum*.[151,152] Although it is difficult to generalize on the little information available, it would not be surprising if all 3-alkanols of myrmicine ants are found to have (3*R*)-configuration. The optical isomeric composition of (4*E*)-4,6-dimethyl-oct-4-ene-3-one (53) (manicone), an alarm pheromone of *Manica mutica* and *M. bradleyi*, is not yet determined.[153] A number of syntheses of manicone (53) are available.[154–157]

Usually the myrmicine ants produce 3-alkanones only,[145–148,158] but rarely, 2-alkanones[158] and 4-alkanones[159] are also encountered in the mandibular glands. On the other hand, the formicine ants produce a number of positional isomeric ketones; those with the carbonyl group at 2,[76,77] 3,[83,160] and 4[77] position are frequently found.

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[143] R. M. Duffield and M. S. Blum, *Ann. Entomol. Soc. Am.*, 1973, **66**, 1357.

[144] C. Longhurst, R. Baker, and P. E. Howse, *J. Insect Physiol.*, 1980, **26**, 551.

[145] M. C. Cammaerts, R. P. Evershed, and E. D. Morgan, *J. Insect Physiol.*, 1983, **29**, 659.

[146] M. C. Cammaerts, R. P. Evershed, and E. D. Morgan, *Physiol. Entomol.*, 1982, **7**, 119.

[147] M. C. Cammaerts, R. P. Evershed, and E. D. Morgan, *J. Insect Physiol.*, 1981, **27**, 225.

[148] E. D. Morgan, M. R. Inwood, and M. C. Cammaerts, *Physiol. Entomol.*, 1978, **3**, 107.

[149] A. B. Attygalle, E. D. Morgan, R. P. Evershed, and S. J. Rowland, *J. Chromatogr.*, 1983, **260**, 411.

[150] R. G. Riley, R. M. Silverstein, and J. C. Moser, *Science*, 1974, **183**, 760.

[151] J. M. Pasteels, J. C. Verhaeghe, R. Ottinger, J. C. Braekman, and D. Daloze, *Insect Biochem.*, 1981, **11**, 675.

[152] J. M. Pasteels, J. C. Verhaeghe, J. C. Braekman, D. Daloze, and B. Tursch, *J. Chem. Ecol.*, 1980, **6**, 467.

[153] H. M. Fales, M. S. Blum, R. M. Crewe, and J. M. Brand, *J. Insect Physiol.*, 1972, **18**, 1077.

[154] T. Nakai, T. Mimura, and T. Kurokawa, *Tetrahedron Lett.*, 1978, **32**, 2895.

[155] J. A. Katzenellenbogen and T. Utawanit, *J. Am. Chem. Soc.*, 1974, **96**, 6153.

[156] P. J. Kocienski, J. M. Ansell, and R. W. Ostrow, *J. Org. Chem.*, 1976, **41**, 3625.

[157] K. Banno and T. Mukaiyama, *Chem. Lett.*, 1976, **3**, 279.

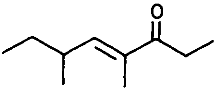
[158] C. Longhurst, R. Baker, and P. E. Howse, *Insect Biochem.*, 1980, **10**, 107.

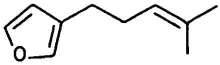
[159] O. Olubajo, R. M. Duffield, and J. W. Wheeler, *Ann. Entomol. Soc. Am.*, 1980, **73**, 93.

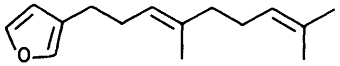
[160] J. W. S. Bradshaw, R. Baker, and P. E. Howse, *Physiol. Entomol.*, 1979, **4**, 15.

D. Aldehydes.—Apart from the terpenoid aldehydes, some simple aliphatic aldehydes are also found in the mandibular glands of ants. Some of the common compounds are 2,6-dimethyl-5-heptenal,[75,76] hexanal,[160] and 2-hexenal.[161]

E. Terpenes.—A variety of terpenoid compounds are found in the mandibular glands of ants, especially among formicine and some myrmicine ants. Some of the compounds encountered are citral,[75,162,163] neric acid,[162] geranic acid,[162] citronellol,[163] citronellal,[75,76] geraniol,[162,163] farnesol,[162] 2,3-dihydrofarnesal,[76] β-pinene,[162] geranylcitronellal,[76] and geranylgeranial.[76] Perillene (54)[158,161,164] and dendrolasin (55)[165] are two furanoid terpenes that are characteristically found. A convenient method to synthesize these 3-substitute furanoids is available.[166]

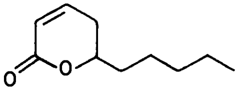

(53)

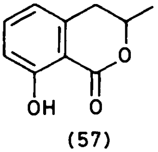

(54)


(55)

Some investigations have been made on the biosynthesis of terpenoids in ants. In *Acanthomyops claviger* the use of acetate and mevalonate as precursors is evident from incorporation studies.[167] Similar biosynthetic studies have been made on dendrolasin.[168]

F. Lactones.—Massiolactone (56) identified from the workers of carpenter (*Camponotus*) ants is a powerful skin irritant.[169] Recently a related lactone (35), first identified as a queen recognition pheromone originating from the poison glands of *Solenopsis invicta*,[59] has been found in the mandibular glands of male carpenter ants.[170] Mellein (57) is another lactone from the mandibular glands of carpenter ants[171] and has also been identified in the gaster of *Rhytidoponera metallica.*[137]


(56)


(57)

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[161] C. Longhurst, R. Baker, and P. E. Howse, *Experientia*, 1979, **35**, 870.

[162] H. Schildknecht, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 214.

[163] M. S. Blum, F. Padovani, and E. Amante, *Comp. Biochem. Physiol.*, 1968, **26**, 291.

[164] R. Bernardi, C. Cardani, D. Ghiringhella, A. Selva, A. Baggini, and M. Pavan, *Tetrahedron Lett.*, 1967, **40**, 3893.

[165] A. Quilico, F. Piozzi, and M. Pavan, *Tetrahedron*, 1957, **1**, 177.

[166] S. P. Tanis, *Tetrahedron Lett.*, 1982, **23**, 3115.

[167] G. M. Happ and J. Meinwald, *J. Am. Chem. Soc.*, 1965, **87**, 2507.

[168] E. E. Waldner, C. Schlatter, and H. Schmidt, *Helv. Chim. Acta*, 1969, **52**, 15.

[169] G. W. K. Cavill, D. V. Clark, and F. B. Whitfield, *Aust. J. Chem.*, 1968, **21**, 2819.

[170] T. H. Jones and H. M. Fales, *Tetrahedron Lett.*, 1983, **24**, 5439.

[171] J. M. Brand, H. M. Fales, E. A. Sokoloski, J. G. MacConnell, M. S. Blum, and R. M. Duffield, *Life Sci.*, 1973, **13**, 201.

G. Benzenoid Compounds.—Some benzenoid aromatic compounds have been detected in the mandibular glands of myrmicine and formicine ants. Benzaldehyde has been identified as a defensive secretion in an attine ant.[172] Phenylethanol constitutes 15% of the mandibular secretion of *Camponotus clarithorax*.[173] *o*-Aminoacetophenone from *Mycocepurus goeldi* acts as an attractant for these 'perfume ants',[174] so called because of the grape-like fragrance of *o*-aminoacetophone. A related compound, methyl anthranilate is found in the mandibular glands of some *Camponotus*[171] ants, *Aphaenogaster fulva*[175] and *Xenomyrmex floridanus*.[175] Male ants of some species of *Camponotus*[176] and the workers of *Bothroponera soror*[144] and *Gnamptogenys pleurodon*[177] secrete methyl 6-methylsalicylate.

H. An Overview.—The diverse groups of chemical compounds mentioned above demonstrates the biosynthetic versatility of the ant mandibular gland. Pheromonal and defensive roles have been attributed to a number of these chemicals but the role of most remains obscure. In a few, the role of individual constituents of the mandibular secretion has been worked out. For example, in *Bothroponera soror*[144] 2-undecanone releases an alerting and orientation response, 2-undecanol an attraction response, and methyl 6-methylsalicylate releases stinging activity.

A similar study on weaver ants, *Oecophylla longinoda*, showed that the components hexanal and 1-hexanol release alerting and attraction responses while 2-butyloct-2-enal and 3-undecanone act as markers for attack.[160,178] The multifunctional role of mandibular gland secretions of an Australian desert ant, *Calomyrmex*, has also been described.[179] The composition of the mandibular gland secretions is species- and sometimes caste-specific[180] and is therefore useful in differentiating between morphologically similar species and in chemosystematics.

4 Postpharyngeal Gland Substances

The postpharyngeal glands of the ants are a pair of glove-shaped structures overlying the brain. These glands can occupy a large portion of the head and open separately into the posterior portion of the pharynx[181] (Figure 1). The function of the postpharyngeal gland remains unknown. It may play a part in larval feeding[182] or have a digestive function[183] (although the lipase activity has been found to be very low[184]). Phillips and Vinson[185] had claimed that the glands function as a

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[172] M. S. Blum, F. Padovani, F. Curley, and R. E. Hawk, *Comp. Biochem. Physiol.*, 1969, **29**, 461.

[173] H. A. Lloyd, M. S. Blum, and R. M. Duffield, *Insect Biochem.*, 1975, **5**, 489.

[174] M. S. Blum, J. M. Brand, and E. Amante, *Experientia*, 1981, **37**, 816.

[175] R. M. Duffield, J. W. Wheeler, and M. S. Blum, *Fl. Entomol.*, 1980, **63**, 203.

[176] J. M. Brand, R. M. Duffield, J. G. MacConnell, M. S. Blum, and H. M. Fales, *Science*, 1973, **179**, 388.

[177] R. M. Duffield and M. S. Blum, *Experientia*, 1975, **31**, 466.

[178] J. W. S. Bradshaw, R. Baker, and P. E. Howse, *Nature (London)*, 1975, **258**, 230.

[179] E. J. Brough, *Z. Tierpsychol.*, 1978, **46**, 279.

[180] J. W. S. Bradshaw, R. Baker, and P. E. Howse, *Physiol. Entomol.*, 1979, **4**, 27.

[181] S. A. Phillips and S. B. Vinson, *J. Ga. Entomol. Soc.*, 1980, **15**, 215.

[182] E. Bugnion, *Bull. Soc. Ent. Egypte*, 1930, **40**, 85.

[183] J. Forbes and A. M. McFarlane, *J. New York Entomol. Soc.*, 1961, **69**, 92.

[184] B. L. Ricks and S. B. Vinson, *Entomol. Exp. Appl.*, 1972, **15**, 329.

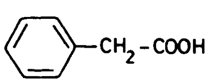
[185] S. A. Phillips and S. B. Vinson, *Ann. Entomol. Soc. Am.*, 1980, **73**, 257.

cephalic caecum and that the major lipid components come from the food but Thompson *et al.*[186] have recently discovered that the major class of compounds in the postpharyngeal glands of *Solenopsis invicta* queens is hydrocarbons. The gland may have a special function in *S. invicta* queens, however, as it becomes disproportionately large in virgin queens and is filled with fluid prior to their nuptial flight.[186]

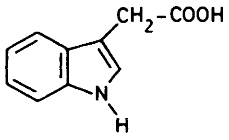
Very few chemical analyses have been reported on the composition of the postpharyngeal gland. Usually the contents are simply described as a yellow oil. Vinson *et al.*[187] found the composition of the hexane-soluble material of postpharyngeal glands of newly mated *S. invicta* queens to be 63% hydrocarbons, 19% free fatty acids, 13% glycerol esters, 6% steroids, and a trace of wax esters. The hydrocarbon fraction was analysed by Thompson *et al.*[186] who found four major methyl-branched hydrocarbons of the C_{28}—C_{29} range. Vander Meer *et al.*[188] found that the total hydrocarbon content of the gland showed a marked increase at 15 days after mating, which suggested that the queen has the biosynthetic capacity to produce these materials herself. The increase in hydrocarbon levels of the postpharyngeal glands coincides with wing muscle histolysis. The hydrocarbon level decreased to the original level after 15 days and during this period the free fatty acid and triacylglycerol concentrations remained the same. The postpharyngeal glands of *S. invicta* workers contain microgram quantities of (*Z*)-9-tricosene accompanied by tricosane and heneicosane among other minor hydrocarbons.[16]

5 Metapleural Gland Substances

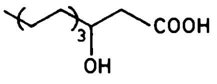
Metapleural glands, located in the thorax, are found in most ants. Although the functions of this gland are still obscure, its secretions are known to consist mainly of carboxylic acids. At least in *Atta sexdens rubropilosa*, a leaf-cutting and fungus-growing ant, it has been suggested that the metathoracic gland secretions are involved in the control of fungus gardens. The compounds identified from the metathoracic gland of *A. sexdens rubropilosa* are phenylacetic acid (58), 3-indoleacetic acid (59),[189] 3-hydroxydecanoic acid (60),[190] 3-hydroxyoctanoic acid, and 3-hydroxyhexanoic acid. The last two acids are minor components. 3-



(58)



(59)



(60)

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[186] M. J. Thompson, B. M. Glancey, W. E. Robbins, C. S. Lofgren, S. R. Dutky, J. Kochansky, R. K. Vander Meer, and A. R. Glover, *Lipids*, 1981, **16**, 485.

[187] S. B. Vinson, S. A. Phillips, and H. J. Williams, *J. Insect Physiol.*, 1980, **26**, 645.

[188] R. K. Vander Meer, B. M. Glancey, and C. S. Lofgren, *Insect Biochem.*, 1982, **12**, 123.

[189] H. Schildknecht and K. Koob, *Angew. Chem.*, 1970, **82**, 181.

[190] H. Schildknecht and K. Koob, *Angew. Chem.*, 1971, **83**, 110.

Indoleacetic acid (59) is one of the widely distributed plant growth substances. Phenylacetic acid (58) can also function as a growth regulator, either alone or even more effectively in combination with indole acid (59). The natural compound myrmicacin (60) is laevorotary and acts as a growth inhibitor at higher concentrations. It is indicated that myrmicacin (60) and the other two related hydroxy-acids are used by the harvester ants (*Messor*) to prevent germination of grass seeds in their granaries and by the leaf-cutting ants (*Atta*) to prevent germination of undesirable fungal spores on their fungus gardens. However, phenylacetic acid (58), indoleacetic acid (59), and myrmicacin (60), when present in low concentrations stimulate growth as demonstrated by artificial fungus-growing experiments.[191] The same acids (58), (59), and (60) were found in *Myrmica rubra*, but the indole acid (59) was absent in *Messor barbarus* and phenylacetic acid in *Acromyrmex subterraneus*.[162] Iwadara and Iwanami[192] have briefly reviewed pollen germination-inhibitory activity, animal cell growth-inhibiting activity, and antimicrobial activity of myrmicacin and other related compounds excreted by ants.

6 Substances from the Hind Gut

Although the hind gut is not an exocrine gland in the strict sense, it is the source of several natural products in ants. The hind gut is the source of the trail pheromones for all formicine ants that have been investigated.[55] In the case of *Lasius fuliginosus* it was first observed that the activity could be extracted from the hind gut into water and this aqueous extract was used to lay artificial trails.[193] The activity disappeared to a large extent when the extract was basified and reappeared at the original level when it was re-acidified. Later Huwyler *et al.*[194,195] found the active material to be composed of an acidic and a non-acidic fraction.

Six fatty acids, namely, hexanoic, heptanoic, octanoic, nonanoic, decanoic, and dodecanoic acids have been identified as pheromone components in the acidic fraction. Commercial samples of the six acids when tested individually could evoke trail-following behaviour in *L. fuliginosus* workers. However, the activity towards an appropriate mixture of the acids has not been examined. Furthermore, the composition of the non-acidic fraction of the hind gut material remains unknown. Huwyler *et al.*[194] have further reported that the trail pheromone isolated from the rectal fluid of the related species *L. niger* is non-acidic and can be recovered from the gas chromatographic effluent.

A similar mixture of fatty acids has been reported to constitute the trail pheromone of the myrmicine ant *Pristomyrmex pungens*.[196,197] The glandular source of the trail pheromone of this species remains unknown, although it is probably not the hind gut because no other myrmicine ant so far investigated has the trail pheromones originating from this organ. The mixture of saturated and

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[191] H. Schildknecht, P. B. Reed, F. D. Reed, and K. Koob, *Insect Biochem.*, 1973, **3**, 439.

[192] T. Iwadara and Y. Iwanami, *Yakugaku*, 1979, **28**, 309.

[193] W. Hangartner, *Z. Vergl. Physiol.*, 1967, **57**, 103.

[194] S. Huwyler, K. Grob, and M. Viscontini, *J. Insect Physiol.*, 1975, **21**, 299.

[195] S. Huwyler, K. Grob, and M. Viscontini, *Helv. Chim. Acta*, 1973, **56**, 976.

[196] N. Hayashi and H. Komae, *Z. Naturforsch.*, 1973, **28c**, 626.

[197] N. Hayashi and H. Komae, *Experientia*, 1977, **33**, 424.

unsaturated fatty acids of C_{14}—C_{20} range falls out of line when compared with the chemical structures identified as trail pheromone components of other myrmicine ants. Out of the nine fatty acids reported, three were saturated and identified as tetradecanoic, hexadecanoic, and octadecanoic acids. The remaining five unsaturated acids have been only partially identified as hexadecenoic acid, octadecenoic acid, octadecadienoic acid, octadecatrienoic acid, eicosatetraenoic acid, and eicosapentenoic acid. The positions of the double bonds and the configurations have not been determined. Furthermore, the query as to whether these acids really are the trail pheromone components of *P. pungens* or not remains because the activity of the synthetic analogues has not been reported.

The hind gut is also the source of the trail pheromones of a number of species of ponerine and ecitonine ants but nothing is known yet about their chemistry.[55]

7 Anal-pygidial Gland Substances

All ant subfamilies, except formicine ants, possess an anal-pygidial gland (also referred to as anal or supra-anal glands). Dolichoderine ants are unique in producing in their anal-pygidial glands a group of cyclopentanoid monoterpenes known as the iridoids (Table 3). Iridomyrmecin (69) was the first of these to be discovered,[198] using conventional large-scale isolation techniques, in the Argentine ant *Iridomyrmex humilis*, which is a common pest species. The compound was said by Pavan to have insecticidal properties.[199] Five years later Cavill *et al.*[200] isolated iridomyrmecin from *I. nitidus*. In all, three iridolactones (66, 67, and 69) and two iridodials (65, 68) have been isolated from dolichoderine ants. The substances have now all been known for some time and their chemistry has been thoroughly reviewed by Weatherston[201] and there is also a more recent summary[68] up to 1975. They are structurally related to nepetalactone, a substance which is physiologically active for cats from the catnip plant *Nepeta cataria*.[202]

Robinson, recognizing the probable biochemical precursor of the iridoids, devised a biomimetic synthesis of iridomyrmecin (69) and isoiridomyrmicin (66) from (*S*)-citronellal.[203,204] All the iridoids, including the alkaloid actinidine (70),[205] which at one time was thought to be an artefact of isolation, are now proposed to arise from citronellal.[206] The four simpler cyclopentanoids listed in Table 3 (61—64) presumably arise by further degradation from the same source.

Other terpenoid ketones found in the anal-pygidial gland of dolichoderines are 6-methylhept-5-en-2-one[207] (71) (from 13 species,[68] *I. purpureus*,[208] and *Tapinoma*

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[198] M. Pavan, *Ric. Sci.*, 1949, **19**, 1011.

[199] M. Pavan, *Ric. Sci.*, 1950, **20**, 1853.

[200] G. W. K. Cavill, D. L. Ford, and H. D. Locksley, *Aust. J. Chem.*, 1956, **9**, 288.

[201] J. Weatherston, *Quart. Rev.*, 1967, **21**, 287.

[202] J. Meinwald, *Chem. Ind.*, 1954, 488.

[203] K. J. Clark, G. I. Fray, R. H. Jaeger, and R. Robinson, *Angew. Chem.*, 1958, **70**, 704.

[204] K. J. Clark, G. I. Fray, R. H. Jaeger, and R. Robinson, *Tetrahedron*, 1959, **6**, 201.

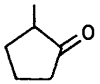
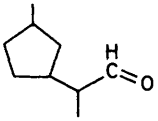
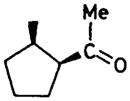
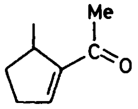
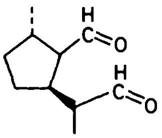
[205] J. W. Wheeler, T. Olagbemiro, A. Nash, and M. S. Blum, *J. Chem. Ecol.*, 1977, **3**, 241.

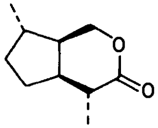
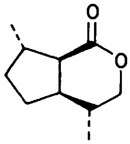
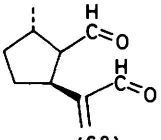
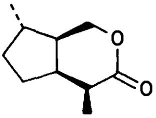
[206] G. W. K. Cavill and D. V. Clark in 'Naturally Occurring Insecticides', ed. M. Jacobson and D. G. Crosby, Marcel Dekker, New York, 1971, p. 271.

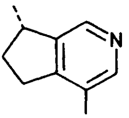
[207] G. W. K. Cavill, D. L. Ford, and H. D. Locksley, *Chem. Ind.*, 1956, 465.

[208] G. W. K. Cavill, P. L. Robertson, J. J. Brophy, R. K. Duke, J. McDonald, and W. D. Plant, *Insect Biochem.*, 1984, **14**, 505.

Table 3 *Cyclopentanoids identified from anal-pygidial glands of ants*

Structure	*Source-species*	*Ref.*
 (61)	*Azteca instabilis*	(*a*)
	A. nigriventris	(*a*)
	A. velox	(*a*)
 (62)	*Iridomyrmex purpureus*	208
 (63)	*Azteca nigriventris*	(*a*)
	A. velox	(*a*)
 (64)	*Azteca instabilis*	(*a*)
	A. nigriventris	(*a*)
	Iridomyrmex purpureus	208
 (65) Iridodial	*Azteca chartifex*	(*a*)
	A. instabilis	(*a*)
	A. parzensis	(*a*)
	A. velox	(*a*)
	Conomyrma pyramicus	(*b*)
	Dolichoderus scabridus	211
	Iridomyrmex conifer	200, 207
	I. detectus	200, 207, 211
	I. nitidiceps	211, 217
	I. purpureus (=*detectus*)	208
	I. pruinosus	(*b*)
	I. rufoniger	211
	Tapinoma nigerrimum	(*b*), (*c*), 210
	T. sessile	(*b*)
	T. simrothi	209

Structure	*Source-species*	*Ref.*
 (66) Isoiridomyrmecin	*Dolichoderus scabridus*	211
	Iridomyrmex nitidus	200, 207, 211
	Tapinoma sessile	(*b*)
 (67) Isodihydro-neptalactone	*Iridomyrmex nitidus*	(*d*)
	I. nitidiceps	217
	I. purpureus	208
 (68) Dolichodial	*Dolichoderus clarki*	(*e*), 211
	D. dentata	211
	D. scabridus	211
	Iridomyrmex detectus	(*e*), 211
	I. humilis	(*f*), 100
	I. myrmecodiae	211
	I. nitidiceps	217
	I. rufoniger	211
 (69) Iridomyrmecin	*Iridomyrmex humilis*	(*b*), (*g*), 200
	I. nitidiceps	217
	I. pruinosus	(*b*)
	Tapinoma simrothi	209

Structure	*Source-species*	*Ref.*
 (70) Actinidine	*Conomyrma* sp.	205
	Iridomyrmex nitidiceps	217
	I. purpureus (=*detectus*)	208

[a] J. W. Wheeler, S. L. Evans, M. S. Blum, and R. L. Torgerson, *Science*, 1975, **187**, 254. [b] D. J. McGurk, J. Frost, G. R. Waller, E. J. Eisenbraun, K. Vick, W. A. Drew, and J. Young, *J. Insect Physiol.*, 1968, **14**, 841. [c] M. Pavan and R. Trave, *Insectes sociaux*, 1958, **5**, 299. [d] G. W. K. Cavill and D. V. Clark, *J. Insect Physiol.*, 1967, **13**, 131. [e] G. W. K. Cavill and H. Hinterberger, *Aust. J. Chem.*, 1961, **14**, 143. [f] G. W. K. Cavill, E. Houghton, F. J. McDonald, and P. J. Williams, *Insect Biochem.*, 1976, **6**, 483. [g] R. Fusco, R. Trave, and A. Vercellone, *Chim. Ind. (Milan)*, 1955, **37**, 251.

simrothi[209]), 2-methylheptan-4-one (72) (from *Tapinoma nigerrimum*,[210] *T. sessile*,[68] and *T. simrothi*[209]), 4-methylhexan-2-one (73) (from *Dolichoderus clarki*[211]), and 4-hydroxy-4-methyl-2-pentanone (74) (from *Tapinoma simrothi*[209]) but linear ketones, *e.g.* 2-heptanone (seven species[68]), 2-pentanone (*Azteca* sp. and *Monacis bispinosa*[68]), and 4-heptanone (*Tapinoma simrothi*[209]) are also found widely distributed.

It is curious that citronellal itself is not found in the Dolichoderinae, though it is found in both formicine and myrmicine species. Iridodials are also found in two other unrelated groups of insects, the phasmids or stick insects (together with neptalactone)[212,213] staphylinid beetles (rove beetles),[214,215] and a longhorn beetle (*Aromia moschata*).[216]

The toxicity of iridoids to other insects is not clear, but evidently it is not great. Iridodial (65) and dolichodial (69) are unstable compounds and produce a sticky gel and so probably act defensively. The iridolactones are stable and probably act as alarm substances. In a recent investigation of the Australian cocktail ant *I. nitidiceps*, Cavill's group found that iridodial (65) and isovaleric acid were the major components of the anal-pygidial gland.[217] Behavioural tests showed that isovaleric acid was primarily an alarm substance and iridodial was deduced to be the essential repellent.[217] The body of the Australian meat ant (*I. purpureus*) contains chiefly iridodial and 6-methylhept-5-en-2-one (71) (presumably from the anal-pygidial gland) and smaller quantities of other iridoids and as a minor component, the new compound 1,3,3-trimethyl-2,7-dioxabicyclo-[2,2,1]-heptane (75), evidently derived from methylheptenone (71).[208]

Some recent reports on anal-pygidial gland show the presence of aromatic

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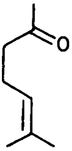
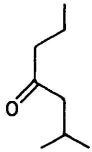
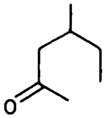


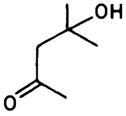
(71)



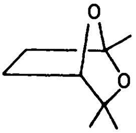
(72)



(73)



(74)



(75)

compounds. 3-Hydroxybenzaldehyde is found along with other components such as isogeraniol, heptadecane, and heptadecene in the pygidial gland secretions of the ponerine ant *Rhytidoponera metallica.*[218] Similarly, methylacetophenone and hydroxymethylacetophenone are reported from the dolichoderine ant *Hypoclinea.*[219]

8 Other Glands

Very little information is available on the chemistry of other glands. An enzyme analysis of the labial gland of larvae of *Solenopsis invicta* has been reported.[220]

A Pavan's gland constituent, (*Z*)-9-hexadecenal has been identified as a trail pheromone component in *Iridomyrmex humilis.*[221,222] The geometry of the C-9 double bond is important for the activity because the (*E*)-9-hexadecenal could evoke only insignificant trail-following activity.[223,224] The analogues, (*Z*)-7-tetradecenyl formate, (*E*)-7-tetradecenyl formate, and tetradecyl formate were also inactive. Van Vorhis Key and Baker have biologically tested this trail pheromone.[225,226]

Conclusion

This review has demonstrated the wide variety of substances that have been found in ant glands. Some of them have provided a challenge and inspiration to the synthetic chemist, some of them are yet to be synthesized, some, to the chemist interested in solving structural and synthetic problems are disappointingly simple.

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Nevertheless their isolation and identification in the tiny quantities available are a triumph of modern micro-chemical methods. To the behavioural biologist, the chemist has thrown down a challenge to explain the purpose of all these diverse substances and to the taxonomist to use the substances to make more certain identification of species and their grouping together into genera and tribes. But all scientists can together marvel at the variety of enzymes that must be available to the insects to make these substances and the great diversity of gland contents that has been thrown up through evolution.

There are many other facets to the subject which cannot be covered here. To mention one example, many of these substances (the terpenoids, pyrazines, alcohols, ketones, and aromatic compounds) also have distinctive odours for humans, and seem to be detectable in very roughly the same kind of concentrations in ants and man, while other substances, notably the hydrocarbons, convey no odour message to man. Possibly even the fragrance chemist has something to learn from ant chemistry.

Acknowledgement. The valuable assistance of Miho Yamakawa in the preparation of this manuscript is gratefully acknowledged.