The Chemistry of Aphids and Scale Insects

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1 Introduction

Aphids or plant lice (Homoptera: Aphidoidea) and scale insects or mealybugs (Homoptera: Coccoidea) represent two of the most successful groups of herbivores in the temperate and tropical regions of the Earth.[1] Unique biological adaptations, such as phloem feeding, surface protection by a hard or waxy covering, rapid growth, the telescoping of generations by asexual reproduction, and a variety of life forms, have permitted these insects to adapt to a wide range of plants, multiply explosively under favourable conditions, and survive topical applications of modern chemical insecticides. Thus, they represent an appreciable component in many terrestrial agroecosystems.

Some members of these groups may be classified as useful to man, yielding such important commercial products as dyes (cochineal, widely used before 1900), varnishes (shellac), and waxes. The scale insects *Trabutina mannipara* Ehrenburg and *Naiacoccus serpentinus* Green played a key role in world history; the nutritious manna they secrete when feeding on tamarisk trees (*Tamarix gallica*, var. 'mannifera' Ehr.) in the Sinai Peninsula helped the children of Israel to survive the march through the desert when they left Egypt,[2] and still represents an important food and export product of the area.

On the other hand, the reproductive potential, genetic adaptability, and feeding methods of aphids and scales cause them to be classified among the most destructive of agricultural pests. Pandemic prejudicial species include the cabbage aphid, *Brevicoryne brassicae* (L.); the greenbug, *Schizaphis graminum* (Rondani); the pea aphid, *Acyrthosiphon pisi* (Harris); the green peach aphid, *Myzus persicae* (Sulzer); the melon aphid, *Aphis gossypii* Glover; the woolly apple aphid, *Eriosoma lanigerum* (Hausmann); the grape phylloxera, *Viteus vitifolii* (Fitch); the black scale, *Saissetia oleae* (Bernard); citrus mealybugs (*Planococcus* and *Pseudococcus* species); the California red scale, *Aonidiella aurantii* (Maskell); the San José scale, *Quadraspidiotus perniciosus* (Comstock); and the oyster-shell

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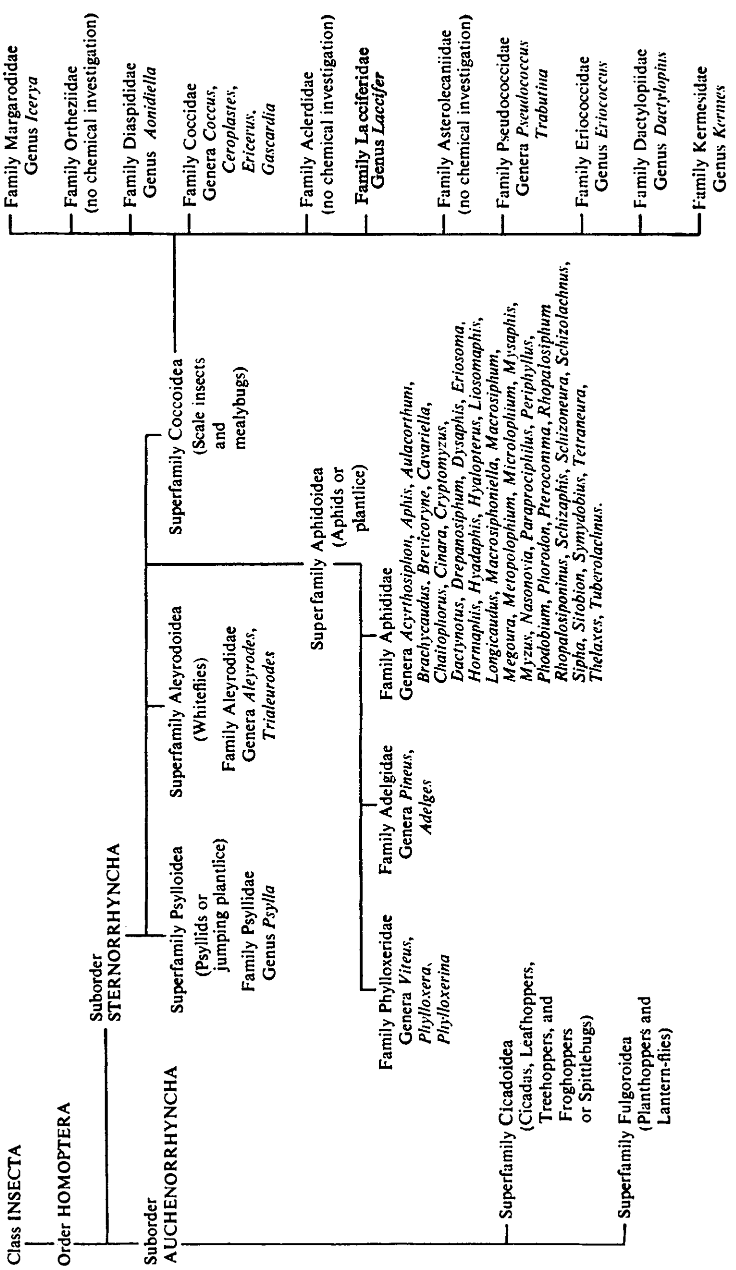
[1] (*a*) A. F. G. Dixon, 'Biology of Aphids', The Institute of Biology's Studies in Biology, No. 44, Edward Arnold, London, 1973; (*b*) 'Aphid Technology', ed. H. F. van Emden, Academic Press, London, 1972; (*c*) C. L. Metcalf, W. P. Flint, and R. L. Metcalf, 'Destructive and Useful Insects', McGraw-Hill, New York, 1962; (*d*) J. S. Kennedy and I. H. M. Fosbrooke, 'The Plant in the Life of an Aphid', in 'Insect/Plant Relationships', ed. H. F. van Emden, Blackwell, Oxford, 1973, pp. 129—140.

[2] Exodus 16: 4—5, 11—36; 'Ergebn. Sinai-Expedition der Hebräischen Universität, Jerusalem', various authors, Leipzig, 1929.


Class INSECTA
Order HOMOPTERA
Suborder AUCHENORRHYNCHA
Suborder STERNORRHYNCHA
Superfamily Psylloidea (Psyllids or jumping plantlice)
Family Psyllidae Genus *Psylla*
Superfamily Aleyrodoidea (Whiteflies)
Family Aleyrodidae Genera *Aleyrodes*, *Trialeurodes*
Superfamily Coccoidea (Scale insects and mealybugs)
Family Margarodidae Genus *Icerya*
Family Ortheziidae (no chemical investigation)
Family Diaspididae Genus *Aonidiella*
Family Coccidae Genera *Coccus*, *Ceroplastes*, *Ericerus*, *Gascardia*
Family Aclerdidae (no chemical investigation)
Family Lacciferidae Genus *Laccifer*
Family Asterolecaniidae (no chemical investigation)
Family Pseudococcidae Genera *Pseudococcus* *Trabutina*
Family Eriococcidae Genus *Eriococcus*
Family Dactylopiidae Genus *Dactylopius*
Family Kermesidae Genus *Kermes*
Superfamily Aphidoidea (Aphids or plantlice)
Family Phylloxeridae Genera *Viteus*, *Phylloxera*, *Phylloxerina*
Family Adelgidae Genera *Pineus*, *Adelges*
Family Aphididae Genera *Acyrthosiphon*, *Aphis*, *Aulacorthum*, *Brachycaudus*. *Brevicoryne*, *Cavariella*, *Chaitophorus*, *Cinara*, *Cryptomyzus*, *Dactynotus*, *Drepanosiphum*, *Dysaphis*, *Eriosoma*, *Hormaphis*, *Hyadaphis*, *Hyalopterus*, *Liosomaphis*, *Longicaudus*, *Macrosiphoniella*, *Macrosiphum*, *Megoura*, *Metopolophium*, *Microlophium*, *Mysaphis*, *Myzus*, *Nasonovia*, *Paraprociphilus*, *Periphyllus*, *Phodobium*, *Phorodon*, *Pterocomma*, *Rhopalosiphum* *Rhopalosiponinus*, *Schizaphis*, *Schizoneura*, *Schizolachnus*, *Sipha*, *Sitobion*, *Symydobius*, *Tetraneura*, *Thelaxes*, *Tuberolachnus*.
Superfamily Cicadoidea (Cicadas, Leafhoppers, Treehoppers, and Froghoppers or Spittlebugs)
Superfamily Fulgoroidea (Planthoppers and Lantern-flies)

Scheme 1

scale, *Lepidosaphes ulmi* (L.). These and many other widespread pests probably cause as much agricultural loss per year as any other major group of insects, largely through weakening plants, aborting fruit ripening, and transmitting plant diseases.

The chemistry of these small insects is no less unusual than their biology. A large number of apparently polyketide-derived compounds dominates the picture of secondary metabolism of aphids and scales; some unique terpenoids have also been isolated. Essentially none of these compounds has any relationship with constituents of the host-plants. It seems possible that many substances are synthesized for the aphids and scales by species-specific endosymbiotes, using catabolic products of ingested carbohydrates and free amino-acids. These are the principal nutrients which the insects take in from phloem sap.* Many species can also be reared for multiple generations on artificial diets.[3] The symbiotic micro-organisms have been suggested as providers of necessary vitamins and steroids to the aphids, and may synthesize many additional compounds which accumulate in the insect's hemolymph. The importance of the endosymbiotes to the animals is shown by the rapid weakening and death observed in antibiotic-treated aphids,[1,4] and the elaborate mechanisms used to ensure passage of the micro-organisms from generation to generation.[5]

2 Systematics

The presently accepted taxonomic arrangement of the superfamilies Aphidoidea and Coccoidea and their close relatives is presented in Scheme 1. The close relationship of Homoptera to the true bugs (Hemiptera) has persuaded many authors to link these two groups, and indeed intermediate taxa are known. Other minor differences between recent authors involve family status and genus names. The arrangement given here is slightly modified from that according to Borrer and deLong,[6] using information received from Dr. V. F. Eastop of the British Museum (Natural History). Chemical structures have been established for secondary products isolated from species in the indicated genera.

3 Ecology

As a significant element in the ecosystem almost wherever they occur, aphids and scales are among the more important controlling elements on higher plants throughout the world (primary herbivores). On the other hand, they constitute significant food elements for vertebrate and invertebrate predators (prey of primary carnivores).

The complicated life cycles of many aphids frequently involve obligatory alter-

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* Some groups, especially scale insects in the family Diaspididae, are reported to feed on parenchyma or other non-phloem material.

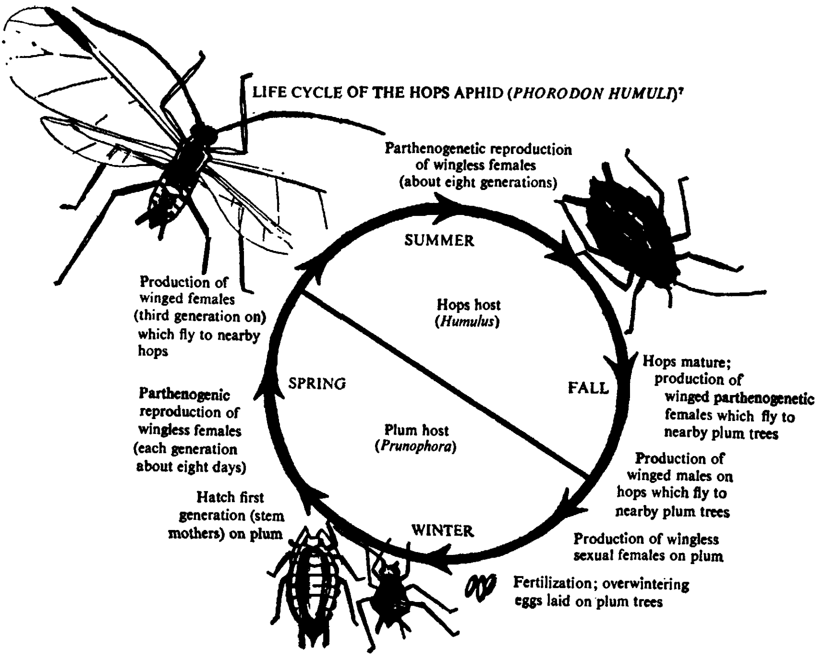
[3] J. L. Auclair and J. J. Cartier, *Ann. Soc. Entomol. Quebec*, 1964, **9**, 68; R. H. Dadd and T. E. Mittler, *Experientia*, 1966, **22**, 832; D. L. Krieger, *Ann. Entomol. Soc. Amer.*, 1971, **64**, 1176; D. H. Akey and S. D. Beck, *J. Insect Physiol.*, 1972, **18**, 1901, and references therein; see also J. B. Adams and H. F. van Emden, in ref. 1*b*, pp. 61—71.

[4] T. E. Mittler, *J. Insect Physiol.*, 1971, **17**, 1333.

[5] R. Hinde, *J. Insect Physiol.*, 1971, **17**, 1791.

[6] D. J. Borrer and D. M. deLong, 'An Introduction to the Study of Insects', Holt, Rinehart, and Winston, New York, 1971, 3rd edn.

nation of host plants and production of a variety of adult forms. A typical example (the hops aphid) is illustrated in Scheme 2.[7] Species are often purely parthogenetic in the tropics, with males as yet unknown, but multiple host plants are still frequent. Although scale insects often have more simple sexual cycles, their breadth of host-plant acceptance may be far greater than that of aphids.



Scheme 2

The abundance and dispersal of aphids and scales are strongly dependent upon weather (especially moisture) and availability of food-plants. Adverse conditions, crowding, host-plant senescence, or seasonal changes often lead to the production of alate (winged) individuals which disperse with the wind, covering from one to hundreds of miles before alighting and searching for satisfactory food-plants.[1] The factors which cause the aphids first to leave the host-plant in flight and then, after a given time (two hours to a full day), settle and search for a new host-plant have been extensively investigated.[1,8] Both

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[7] L. O. Howard, 'The Insect Book', Doubleday, New York, 1901, pp. 265—268.

[8] H. F. van Emden, 'Aphids as Phytochemists', in 'Phytochemical Ecology', ed. J. B. Harborne, Academic Press, New York, 1972, pp. 25—43.

nutrient value and secondary constituents of the plant determine acceptability to the aphid, which tests plants by multiple probes with its stylet and takes off again on a short flight if not satisfied. Young scale insect larvae are often dispersed by the wind or by birds; adult females are wingless. Adult males are usually alate, but without functional mouthparts, so the food-plant choice must be made by other chemoreceptors or different life forms.*

The excessive weakening of the plants attacked, through loss of nutrients, often results in stunted growth, reduced fecundity, minimal fruit maturation, permanent damage, and death. The weakened plant is further rendered more susceptible to attack by fungi and viruses. The latter are often carried from diseased to healthy plants on the homopteran stylets,[1,9] entering through the punctures made for phloem feeding.

The most important natural controls on the fantastic reproductive potential of aphids and scales (a single fundatrix could give rise to over 10^{16} individuals in one summer) are by fungal infection and parasitic microhymenoptera (Chalcidoidea and Ichneumoidea: Braconidae, Aphidiinae). Even so, where favourable plant conditions occur locally, these insects can rapidly destroy crops, trees, and fruits. Ideal conditions for adult multiplication and plant saturation may be created in agricultural monocultures which have suffered an indiscriminate application of insecticides; these tend to kill the parasitic wasps and other predators, but have little effect (except for the systemic poisons) on the phloem-feeding homopterans.

Aphids and scales are heavily preyed upon by a variety of invertebrates, chiefly ladybugs (Coleoptera: Coccinellidae), true bugs (Reduviidae and Miridae), syrphid fly larvae, Neuropteran larvae (Chrysopidae), and midge maggots (Diptera: Cecidomyiidae and Chamaemyiidae). They are also often ingested by larger herbivores (including lepidopterous larvae and larger vertebrates) grazing on the plant, and probably represent a staple food for some insectivorous birds and reptiles. At least two species examined (*Aphis nerii* Fonscolombe, Aphididae and *Aspidiotus nerii* Bouché, Diaspididae) apparently ingest poisonous cardenolides from their host-plants (*Nerium oleander*, Apocynaceae, and various Asclepiadaceae). The first may advertise to vertebrate predators distasteful properties by a bright orange (aposematic or warning) coloration. Among its invertebrate predators, some continue to store the cardenolides, while others apparently metabolize them.[10]

While some animals feed on aphids and scales, others are attracted to the sweet honeydew they excrete from the anus. Certain species of ants form a mutualistic relationship with the homopterans, protecting them from predators, carrying them to new host-plants, and stimulating them with their antennae

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* Information on scale insects was received from Dr. D. J. Williams of the Commonwealth Institute of Entomology.

[9] M. A. Watson and R. T. Plumb, *Ann. Rev. Entomol.*, 1972, **17**, 425, and references therein.

[10] M. Rothschild, J. von Euw, and T. Reichstein, *J. Insect Physiol.*, 1970, 16, 1141; M. Rothschild, 'Secondary Plant Substances and Warning Coloration in Insects', in 'Insect/Plant Relationships', ed. H. F. van Emden, Blackwell, Oxford, 1973, pp. 59—83; M. Rothschild, J. von Euw, and T. Reichstein, *J. Entomol. (A)*, 1973, **48**, 89.

in order to obtain honeydew.[10a] For this reason, some aphids have been called 'ant cows'. Bees often facilitate their honey production by collecting honeydew from aphids, sometimes with disastrous results when the melezitose in the secretion crystallizes in the combs.[11]

The internal ecology of aphids and scales is also complicated. Each species houses one or more types of degenerate symbiotic micro-organism, which have been variously regarded as similar to Rickettsiae, gram-negative Eubacteria, Mycobacteria, or Mycoplasma,[12] within specialized structures (mycetomes) and cells (mycetocytes).[13] These symbiotes have been suggested to produce compounds useful to the insects but not sufficiently available from their diet or their own biosynthetic abilities, such as sterols,[3,14] amino-acids[15] (with possible fixation of N_2), vitamins,[15,16] and organosulphur compounds[17] (with fixation of inorganic sulphate). It is still in debate whether they also produce the many secondary polyketide-related compounds isolated from aphids and scales, normally regarded as products of biosynthetic pathways of micro-organisms rather than animals.

Although it is rarely mentioned in print, the attractive if fantastic hypothesis that mitochondria are merely further evolutionary degenerates of endosymbiotes is supported by both the close intracellular relationship of the homopteran symbiotes, and their suspected prodigious biosynthetic prowess. Removal of the nucleic acid to the outside of such degenerate organisms, accompanied by control of their enzyme systems by the cells in which they are housed, might give a useful biochemical system not unlike that in which mitochondria participate (for a discussion of and a conservative view against this suggestion, see ref. 13, pp. 69—74).

4 Secondary Compounds of Scale Insects

The commercial production of dyes, varnishes, and waxes from scale insects has facilitated the chemical investigation of secondary metabolic products of these organisms. Nevertheless, the structural complexity of these compounds is such that only recently have some definitive results come to light.

A. Lac Resin.—The Indian scale insect *Laccifer lacca* Kerr (also known as *Tachardia lacca*) produces a hard secretion which accumulates along infested branches, eventually swallowing up the insects themselves and remaining as a thick cylinder. Removed by melting, the secretion is known as stick-lac;[18] when

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[10a] M. J. Way, *Ann. Rev. Entomol.*, 1963, **8**, 307.

[11] C. S. Hudson and S. F. Sherwood, *J. Amer. Chem. Soc.*, 1918, **40**, 1456.

[12] C. Vago and M. Laporte, *Ann. Soc. entomol. France, N.S.*, 1965, **1**, 181; R. Hinde, *J. Insect Physiol.*, 1971, **17**, 2035; D. McLean and E. Houk, *ibid.*, 1973, **19**, 625; E. J. Houk, *ibid.*, 1974, **20**, 471.

[13] P. Buchner, 'Endosymbiosis of Animals with Plant Microorganisms', Interscience, New York, 1965, pp. 23—34, 58—66, 232—345, 619—829.

[14] P. Ehrhardt, *Experientia*, 1968, **24**, 82.

[15] R. Fink, *Z. Morphol. Ökol. Tiere*, 1952, **41**, 78.

[16] P. Ehrhardt, *Z. vergl. Physiol.*, 1968, **60**, 416.

[17] P. Ehrhardt, *Biol. Zbl.*, 1969, **88**, 335.

[18] M. S. Wadia, R. G. Khurana, V. V. Mhaskar, and Sukh Dev, *Tetrahedron*, 1969, **25**, 3841.

ground and washed with water, eliminating most of the pigments, it is called seed-lac. A number of varieties exist, depending upon the host-plant, but they are physically and chemically very similar, showing principally quantitative variation in the several components. Further industrial purification of seed-lac gives the more homogeneous shellac of commerce, a useful hard varnish for which no perfect synthetic substitute is yet known.

Laboratory fractionation of Palas seed-lac (from *L. lacca* on *Butea monosperma* Lamk., Leguminosae[19]) gave by water extraction 2% residual pigments (with some carbohydrates also). Subsequent extraction with 78% aqueous ethanol left behind waxes (5%) and insect and plant debris. The ethanol extract could be fractionated with ether to give insoluble hard resin (57%) with the desirable properties of commercial shellac, and more soluble soft resin (19%) and neutral components (5%).

The hard and soft resins, prepared similarly from a variety of lac samples, are complex oligomers of hydroxy-acids, joined by ether[20] and ester linkages. Although both resin types contain essentially the same acids, the proportions and intermolecular bonds are different. Careful purification of hard resin by fractional precipitation from benzene–dioxan mixtures gave a series of 12 fractions,[21] quite different in content and in proportions of the constituent hydroxy-acids. Further purification of one fraction by progressive solution in ethyl acetate–dioxan and precipitation from dioxan with benzene gave an apparently pure oligomer denominated 'pure lac resin' (12% of the original hard resin). This was chosen for detailed structural studies.[22]

The principal hydroxy-acids of lac resin are probably *threo*-aleuritic acid [= 9,10,16-trihydroxypalmitic acid (1)],[18,23] jalaric acid (2),[18,24] and laccijalaric acid (3).[25] An important minor constituent of some fractions is butolic acid (4).[26] Other minor acids detected include myristic, palmitic, palmitoleic, and other C_{14}—C_{18} straight-chain acids, C_{16} ω-hydroxy-acids, C_{14} and C_{16} 9,10-dihydroxy-acids, and 6-oxotetradecanoic acid.[23,27]

The sesquiterpenic aldehyde-acids (2) and (3) have been suggested to give rise to complex mixtures [(5)—(12)] when the resin is hydrolysed by alkali. This unusual reaction would be basically a Cannizzaro-type disproportionation,

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[19] R. G. Khurana, A. N. Singh, A. B. Upadhye, V. V. Mhaskar, and Sukh Dev, *Tetrahedron*, 1970, **26**, 4167.

[20] R. Madhav, T. R. Seshadri, and G. B. V. Subramanian, *Indian J. Chem.*, 1967, **5**, 182; T. R. Seshadri, N. Sriram, and G. B. V. Subramanian, *ibid.*, 1971, **9**, 524.

[21] A. B. Upadhye, M. S. Wadia, V. V. Mhaskar, and Sukh Dev, *Tetrahedron*, 1970, **26**, 4177.

[22] A. B. Upadhye, M. S. Wadia, V. V. Mhaskar, and Sukh Dev, *Tetrahedron*, 1970, **26**, 4387.

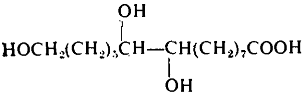
[23] H. Singh, R. Madhav, T. R. Seshadri, and G. B. V. Subramanian, *Tetrahedron*, 1967, **23**, 4795.

[24] M. S. Wadia, R. G. Khurana, V. V. Mhaskar, and Sukh Dev, *Tetrahedron Letters*, 1964, 513.

[25] A. N. Singh, A. B. Upadhye, M. S. Wadia, V. V. Mhaskar, and Sukh Dev, *Tetrahedron*, **25**, 3855.

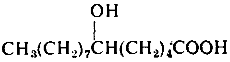
[26] J. W. Christie, F. D. Gunstone, and H. G. Prentice, *J. Chem. Soc.*, 1963, 5768; R. G. Khurana, M. S. Wadia, V. V. Mhaskar, and Sukh Dev, *Tetrahedron Letters*, 1964, 1537.

[27] J. W. Christie, F. D. Gunstone, H. G. Prentice, and S. C. Sen Gupta, *J. Chem. Soc.*, 1964, 1537.



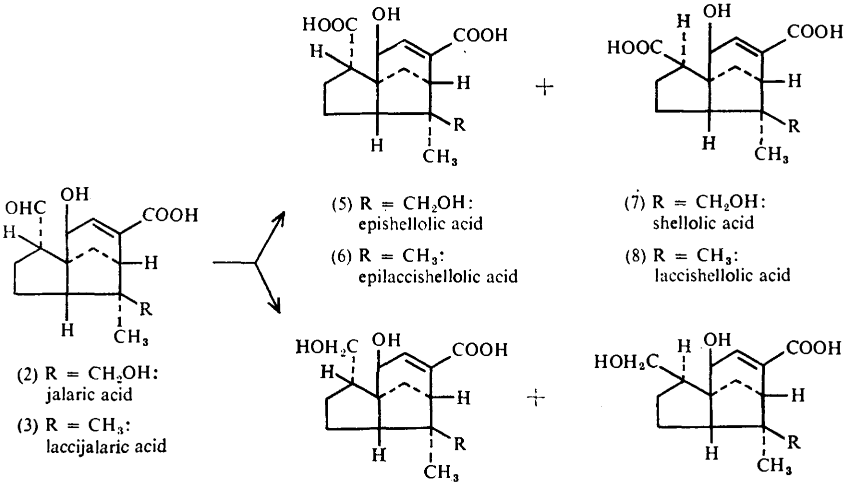
$HOCH_2(CH_2)_5\overset{OH}{\overset{|}{C}}H{-}\underset{OH}{\underset{|}{C}}H(CH_2)_7COOH$

(1) aleuritic acid



$CH_3(CH_2)_7\overset{OH}{\overset{|}{C}}H(CH_2)_4COOH$

(4) butolic acid



(2) R = CH_2OH: jalaric acid

(3) R = CH_3: laccijalaric acid

(5) R = CH_2OH: epishellolic acid

(6) R = CH_3: epilaccishellolic acid

(7) R = CH_2OH: shellolic acid

(8) R = CH_3: laccishellolic acid

(9) R = CH_2OH: epilaksholic acid

(10) R = CH_3: epilaccilaksholic acid

(11) R = CH_2OH: laksholic acid

(12) R = CH_3: laccilaksholic acid

possible in these aldehydes which are too sterically hindered to undergo normal aldol condensation.[18,24]

There is still some doubt, however, as to whether the unique building-blocks of the resin are only (1), (2), and (3), with (5)—(12) arising only as artefacts; a recent publication has indicated the presence of further components, including epishellolic acid (5), in untreated lac resin.[28]*

An extensive series of chemical modifications and hydrolyses led to a definition of the oligomer linkage points in the fraction called 'pure lac resin',[22] but the exact structure of this individual compound is still uncertain. The molecular weight is 2432, comprising two molecules of aleuritic acid linked through the carboxyl (with all three hydroxyls free), and one probably linked through the

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* In ref. 28, the names jalaric (2) and laccijalaric (3) acids are changed to epijalaric and epilaccijalaric, respectively, to correspond to the configurational nomenclature of epishellolic acid (5). Although this change may be rationally defensible, we prefer not to follow it as it will promote confusion with the older, well-established names for (2) and (3).

[28] T. R. Seshadri, N. Sriram, and G. B. V. Subramanian, *Indian J. Chem.*, 1971, **9**, 528.

9- and 16-hydroxyls; one molecule of laccijalaric acid linked through the 5-hydroxyl; and five molecules of jalaric acid: three linked through the 5-hydroxyl and possibly the carboxyl, one linked through the carboxyl only, and one linked through the 5-hydroxyl and the CH_2OH, and possibly the carboxyl; in all, eight intermolecular bonds are present.

B. Pigments.—All known pigments of scales are polyketide anthraquinones, sometimes condensed further with amino-acid or carbohydrate moieties (see Schemes 3 and 4).[29,30]* While the lac pigments, in spite of their large production and potential commercial value,[30] have had limited use, the colours isolated from the Mexican scale *Dactylopius coccus* Costa (feeding principally on *Opuntia* cacti) and the Mediterranean scale *Kermes ilicis* Linnaeus (feeding principally on *Quercus coccifera*, an oak), were among the most important commercial dyes before the advent of synthetics. Their names (carmine and Venetian red) conjure up to the mind certain rich shades of natural coloration which, because of their high saturation, low brilliance, and permanent character, have not yet been fully duplicated by aniline dyes.

The structural formulations of carminic and kermesic acid and the lac pigments have had a rather chequered history, due to the difficult chemical nature of these compounds which are poorly crystalline, form solid mixtures, and decompose at very high temperatures. The first is an unusual *C*-glycoside with only one position free on the aromatic nucleus. The structure presently accepted (13) is well founded upon degradative and spectroscopic evidence.[31,32] Likewise, the recently revised structure for erythrolaccin (14),[33] the principal pigment from seed-lac, is surely correct (by unambiguous synthesis). Laccaic acids A (15) and B (16)[34,35] are appreciably more complicated; like carminic and kermesic (17)[36]†

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* The 'ommochrome' pigment of lac larvae, lacciferic acid (H. Singh, T. R. Seshadri, and G. B. V. Subramanian, *Tetrahedron Letters*, 1966, 1101), is now regarded as a mixture of laccaic acids A, B, and C, with the latter existing partly as a protein complex: B. V. Ramachandran, A. V. Rama Rao, and I. N. Shaikh, *Indian J. Chem.*, 1970, **8**, 783.

† Kermesic acid has also been found in stick-lac from Thailand, along with laccaic acids A, B, and C, and emodin (27).[30]

[29] R. H. Thomson, 'Naturally Occurring Quinones', Academic Press, New York, 1971, 2nd ed., pp. 418—422, 443, 453, and 455—472.

[30] K. Venkataraman and A. V. Rama Rao, in 'Some Recent Developments in the Chemistry of Natural Products', ed. S. Rangaswami and N. V. Subba Rao, Prentice-Hall of India, New Delhi, 1972, pp. 341—352.

[31] J. C. Overeem and G. J. M. van der Kerk, *Rec. Trav. chim.*, 1964, **83**, 1023.

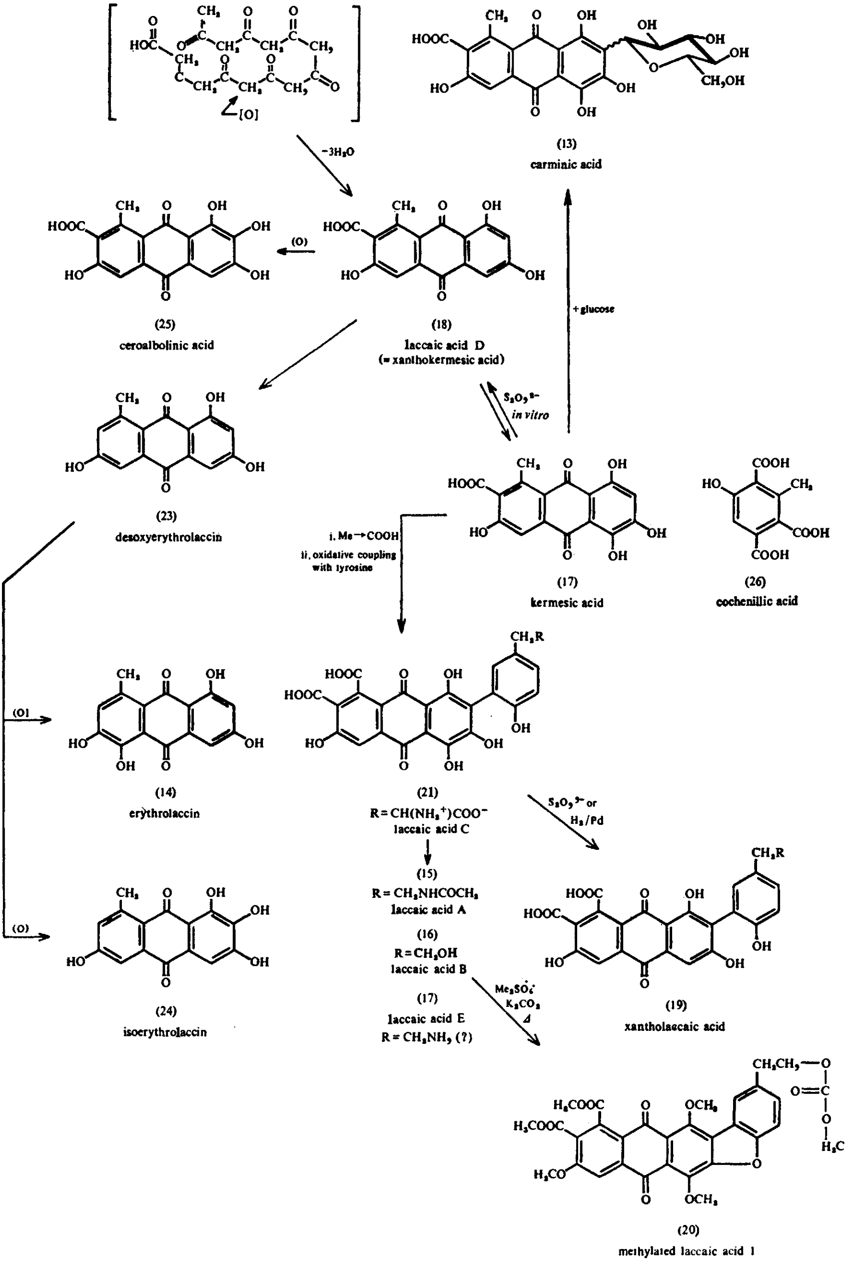
[32] S. B. Bhatia and K. Venkataraman, *Indian J. Chem.*, 1965, 3, 92.

[33] P. Yates, A. C. Mackay, L. M. Pande, and M. Amin, *Chem. and Ind.*, 1964, 1991; N. S. Bhide, A. V. Rama Rao and K. Venkataraman, *Tetrahedron Letters*, 1965, 33; N. S. Bhide and A. V. Rama Rao, *Indian J. Chem.*, 1969, 7, 996.

[34] R. Burwood, G. Read, K. Schofield, and D. E. Wright, *J. Chem. Soc.*, 1965, 6067; 1967, 842; R. Burwood, G. Read, and K. Schofield, *Tetrahedron Letters*, 1966, 3059; N. S. Bhide, E. D. Pandhare, A. V. Rama Rao, I. N. Shaikh, and K. Venkataraman, *Tetrahedron Letters*, 1967, 2437; N. S. Bhide, E. D. Pandhare, A. V. Rama Rao, I. N. Shaikh, and R. Srinivasan, *Indian J. Chem.*, 1969, 7, 987.

[35] E. D. Pandhare, A. V. Rama Rao, R. Srinivasan, and K. Venkataraman, *Tetrahedron*, 1966, Supplement 8, 229; E. D. Pandhare, A. V. Rama Rao, and I. N. Shaikh, *Indian J. Chem.*, 1969, 7, 977.

[36] D. D. Gadgil, A. V. Rama Rao, and K. Venkataraman, *Tetrahedron Letters*, 1968, 2223.


[O]
-3H₂O
(13)
carminic acid
(O)
(25)
ceroalbolinic acid
(18)
laccaic acid D
(= xanthokermesic acid)
+glucose
S₂O₄²⁻
in vitro
(23)
desoxyerythrolaccin
i. Me→COOH
ii. oxidative coupling with tyrosine
(17)
kermesic acid
(26)
cochenillic acid
(O)
(14)
erythrolaccin
(21)
R = CH(NH₃⁺)COO⁻
laccaic acid C
S₂O₄²⁻ or H₂/Pd
(15)
R = CH₂NHCOCH₃
laccaic acid A
(16)
R = CH₂OH
laccaic acid B
(17)
laccaic acid E
R = CH₂NH₂ (?)
(19)
xantholaccaic acid
Me₂SO₄
K₂CO₃
Δ
(O)
(24)
isoerythrolaccin
(20)
methylated laccaic acid I

Scheme 3

acids, they undergo the purpurin–xanthopurpurin transformation [→ (18), (19)][35,36] upon reduction. Furthermore, when methylated under forcing conditions, they undergo partial ring-closure to furanoid compounds and in some cases even suffer carbonation from the K_2CO_3 catalyst [→ (20)].[35] Additional compounds in this series include laccaic acids C (21),[37] D [= xanthokermesic acid (18)],[36,38] and E (22),[30] desoxyerythrolaccin (23),[38,39] isoerythrolaccin (24),[39] and ceroalbolinic acid (25)[40] from the Mexican *Ceroplastes albolineatus* Cockerell and the Japanese *C. rubens* Maskell. The correctness of the present formulations for the structures of these pigments is greatly supported by the unified simplicity of their biogenetic scheme, starting from a hypothetical octaketide (Scheme 3).[36] All except laccaic acids A, B, C, and E and the erythrolaccins give cochenillic acid (26)[31,32] upon oxidation.

A number of simpler, carboxyl-free anthraquinones related to the widespread emodin (27), the derived purpurin (28), and 7-acetylemodin (29) occur free and/or as glycosides in Australian *Eriococcus* species.[41,42] All of these compounds [(27)—(33)] are apparently derived from a cyclization mode of the presumed octa- or nona-ketide precursors different from that which produces the lac pigments (Scheme 4).[42]

C. Waxes.—The wax secreted copiously by certain coccids is collected by many peoples around the world and used in medicine, for making candles, and in diverse other household activities. The prototype wax scale [*Ericerus pela* (Chavannes)] is thus used in China; the related *Gascardia cerifera* (F.) similarly serves the people of India, and *Ceroplastes* scale insects have been used for millenia for the production of wax by many peoples in Central and South America.

Although a large but varying fraction of scale wax is composed of standard long-chain esters,[43–46*] analysis of hydrolysates has turned up some surprising constituents. Most waxes also seem to include a small amount of straight-chain hydrocarbons, containing from 15 to 33 or more carbon atoms (both even and odd numbers), with the higher molecular weights usually predominating.[45] Many also contain a surprisingly large percentage of free fatty acids in the

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[*] The 'long-chain ketone $C_{23}H_{46}O$' mentioned in ref. 41 may well be an ester, $C_{46}H_{92}O_2$ or $C_{69}H_{138}O_3$.

[37] A. V. Rama Rao, I. N. Shaikh, and K. Venkataraman, *Indian J. Chem.*, 1969, **7**, 188.

[38] A. R. Mehandale, A. V. Rama Rao, I. N. Shaikh, and K. Venkataraman, *Tetrahedron Letters*, 1968, 2231.

[39] A. R. Mehandale, A. V. Rama Rao, and K. Venkataraman, *Indian J. Chem.*, 1972, **10**, 1041.

[40] T. Rios, *Tetrahedron*, 1966, **22**, 1507; D. D. Gadgil, A. V. Rama Rao, and K. Venkataraman, *Tetrahedron Letters*, 1968, 2229; K. Doi, *Sci. Rep. Hirosaki Univ.*, 1972, **18**, 37 (*Chem. Abs.*, 1972, **77**, 72 697v).

[41] A. W. K. Chan and W. D. Crow, *Austral. J. Chem.*, 1966, **19**, 1701.

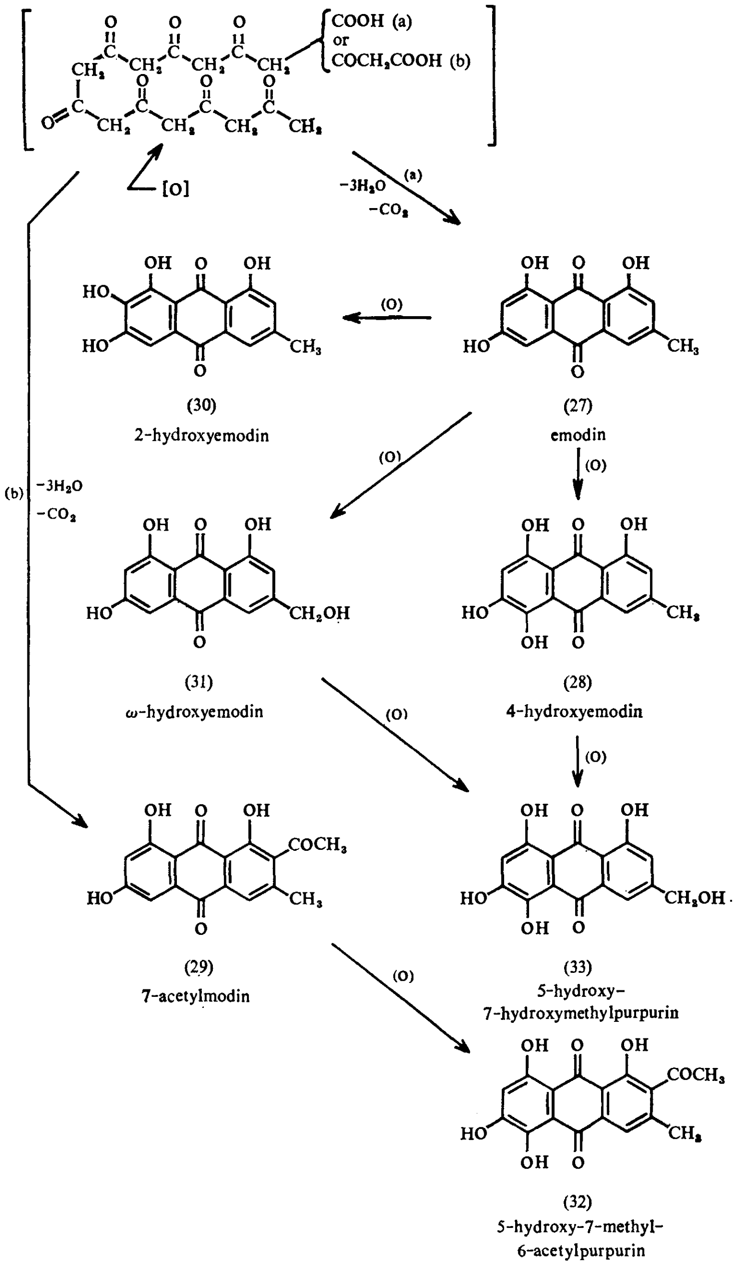
[42] H. J. Banks and D. W. Cameron, *Chem. Comm.*, 1970, 1577.

[43] Y. Tamaki, *Botyu-Kagaku*, 1969, **34**, 86.

[44] E. Faurot-Bouchet and G. Michel, *J. Amer. Oil Chemists' Soc.*, 1964, **41**, 418.

[45] Y. Tamaki, *Nogyo Gijutsu Kenkyusho Hokoku* (Bulletin of the National Institute of Agricultural Sciences), *C*, 1970, 1.

[46] A. C. Chibnall, S. H. Piper, A. Pollard, E. F. Williams, and P. N. Sahai, *Biochem. J.*, 1934, **28**, 2189.


COOH (a)
or
COCH₂COOH (b)
[O]
(a)
−3H₂O
−CO₂
(O)
(30)
2-hydroxyemodin
(27)
emodin
(b)
−3H₂O
−CO₂
(31)
ω-hydroxyemodin
(28)
4-hydroxyemodin
(29)
7-acetylmodin
(33)
5-hydroxy-7-hydroxymethylpurpurin
(32)
5-hydroxy-7-methyl-6-acetylpurpurin

Scheme 4

26—34 carbon range;[44] in the case of *Gascardia madagascarensis* Targioni-Tozzetti, these are mostly hydroxylated on a carbon near the middle of the chain.[44] The wax of the lac insect (*Laccifer lacca*), by way of contrast, contains mostly free alcohols.[46] The wax of the cochineal insect, *Dactylopius coccus*, is principally 15-keto-n-tetratriacontanyl-13-keto-n-dotriacontanoate.[47]* The ester waxes generally possess over 50, often up to 70 carbon atoms, with the ester function near the middle of the chain.[43,45] Unsaturated and/or shorter-chain waxes are occasionally found;[43,48] the corresponding acids and alcohols are commoner in the body lipids of the insects than in the waxes.[43,49] A major esterified acid of the citrus pest *Pseudococcus comstocki* (Kuwana) is the dibasic tetradecane-1,14-dioic acid.[50]

In *Ceroplastes rubens* Maskell, a fair portion of the esterified alcohols and acids in the wax may consist of modified diterpenes, which have been named rubabietic acid (34), rubenic acid (35), and rubenol (36).[51] It is possible that these stuctures may need revision in light of modern methods of physical analysis.

The waxes of first and second instar *Ceroplastes* contain mostly eicosanoic acid,[43,45] suggesting that not only the thickness of the coating, but also the chain length of its constituents grows along with the insects.

Saponification of the wax of the Mexican *Ceroplastes albolineatus* gave not only n-alkanols and n-alkanoic acids, but also an exceptional series of sesterterpenes (C_{25}), including the parent geranylfarnesol (37).[52] Also found were four tricyclic compounds [(38)—(41)], two acids and two alcohols, having the same fundamental skeleton (but a different stereochemistry) as the fungal ophiobolins [*e.g.* (42)].[53] The structure of the major alcohol, ceroplastol-I (38), was established by *X*-ray crystallographic analysis of its *p*-bromobenzoate.[54] The structures of ceroplastol-II (39),[55] ceroplasteric acid (40),[54] and albolic acid (41)[56] followed from spectral measurements and chemical interrelations [the double bond isomerized from the exocyclic to the endocyclic location upon treatment of the compounds (38) and (40) with toluene-*p*-sulphonic acid in pyridine]. Albolineol (42a), also found in the hydrolysate, is apparently a bicyclic precursor to, or fragmentation product of, (38).[56a]

A further sesterterpene acid (gascardic acid), not possessing the ophiobolane skeleton but having many elements in common with the *Ceroplastes* sesterter-

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* Similar scale waxes, with both elements always hydroxylated on the twentieth carbon in from the end of the chain, have been studied recently by J. Meinwald and co-workers (Ninth IUPAC Symposium on the Chemistry of Natural Products, Ottawa, June 1974).

[47] A. C. Chibnall, A. L. Latner, E. F. Williams, and C. A. Ayre, *Biochem. J.*, 1934, **28**, 313.

[48] M. Kono and T. Maruyama, *J. Agric. Chem. Soc. Japan*, 1939, **15**, 177, quoted in ref. 45.

[49] Y. Tamaki and S. Kawai, *Botyu-Kagaku*, 1967, **32**, 63.

[50] Y. Tamaki, *Lipids*, 1968, **3**, 186.

[51] M. Kono and T. Maruyama, *J. Agric. Chem. Soc. Japan*, 1938, **14**, 318, quoted in ref. 45.

[52] T. Rios and S. Pérez C., *Chem. Comm.*, 1969, 214.

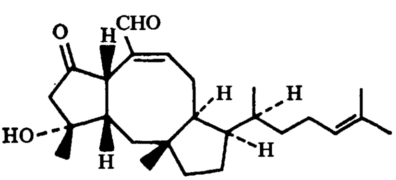
[53] T. Rios and F. Colunga, *Chem. and Ind.*, 1965, 1184.

[54] Y. Iitaka, I. Watanabe, I. T. Harrison, and S. Harrison, *J. Amer. Chem. Soc.*, 1968, **90**, 1092.

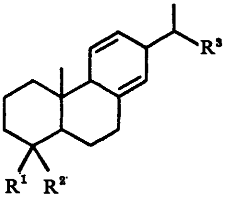
[55] T. Rios and L. Quijano, *Tetrahedron Letters*, 1969, 1317.

[56] T. Rios and F. Gómez G., *Tetrahedron Letters*, 1969, 2929.

[56a] T. Rios, L. Quijano, and J. Calderón, *J.C.S. Chem. Comm.*, 1974, 728.



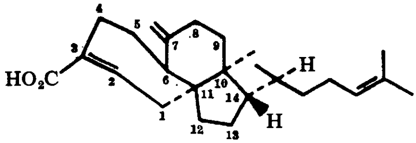
(42) ophiobolin C



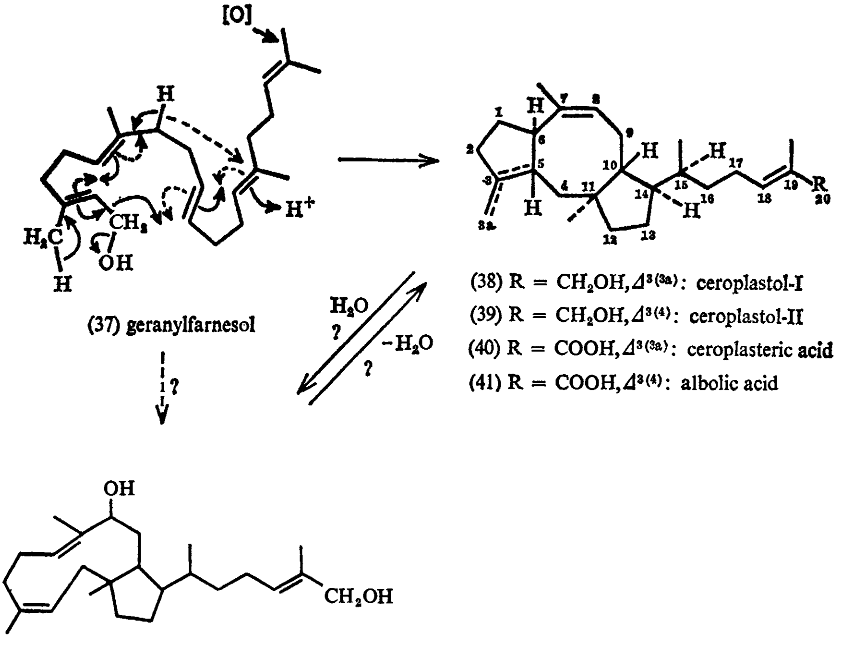
(34) R^1 = COOH, R^2,R^3 = CH_3
rubabietic acid

(35) R^1 = COOH, R^2,R^3 = CH_3, CH_2OH
rubenic acid

(36) R^1 = CH_2OH, R^2,R^3 = CH_3, CH_2OH
rubenol



(42b) gascardic acid



(37) geranylfarnesol

(38) R = $CH_2OH, \Delta^{3(3a)}$: ceroplastol-I

(39) R = $CH_2OH, \Delta^{3(4)}$: ceroplastol-II

(40) R = $COOH, \Delta^{3(3a)}$: ceroplasteric acid

(41) R = $COOH, \Delta^{3(4)}$: albolic acid

(42a) albolineol

penes, has been isolated from *Gascardia madagascarensis*[56b] and subjected to a variety of interesting chemical reactions, leading to the determination of its

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[56b] G. Brochère and J. Polonsky, *Bull. Soc. chim. France*, 1960, 963.

structure (42b).[56b,56c] Its biogenetic pathway from a presumed geranylfarnesyl pyrophosphate precursor includes migration of the methyl group from C-11 to C-10.[56c]

D. Honeydew.—Most scales (and many aphids) excrete copious quantities of clear, sweet liquid known as honeydew.[57] In addition to minor metabolic products, this fluid contains many compounds, either unchanged or in slightly modified form, which are present in the excess sap of the plant which is ingested by the scale or aphid. It is often used by animals, from ants (which tend aphids and scales as if they were domestic cattle[10a]) and bees to hummingbirds and man. Aphid and scale honeydew has the trisaccharide melezitose, synthesized within the insect, as a frequent major component.[11,43,45,58] Other important compounds detected (varying in composition and concentration with the homopteran and host-plant species) include ribitol, glucosucrose (also synthesized in the insect), *d*-mannitol, raffinose, stachyose, maltose, sucrose (usually a principal component), trehalose, glucose,[57,59] and a variety of both common[59] and unusual[60] amino-acids (such as β-alanine, γ-aminobutyric acid, methionine sulphoxide, homoserine, and dopa). The nutritional value of honeydew, though somewhat variable, is sufficient to make of it an excellent potential source of carbohydrate food.

E. Manna.—The true 'celestial manna' which brought the people of Israel through the march across the Sinai Peninsula in good health during the Exodus, was extensively studied by a Hebrew University expedition in 1927.[2] It is apparently produced by the scale insects *Trabutina mannipara* and *Naiacoccus serpentinus*, feeding on the desert tamarisk trees. Precisely as documented in the Biblical account, it drops to the ground during the night like a light snow; spoils rapidly in the morning sun, unless baked; and is very nutritious. Chemical analysis indicated sucrose and invert sugar as principal components.[61]

North Iraquian manna, claimed to be very similar, is nonetheless chemically distinct from the celestial manna of Sinai. It has been claimed to be an exudate of trees (oaks and/or *Fraxinus ornus* L., the common European ash) which have been pierced by homopterans, not a secretion of the homopterans themselves.

[56c] R. Scartazzini, Diss. Nr. 3899, E. T. H., Zurich, 1966; and D. Arigoni, J. Polonsky, R. Scartazzini, G. Settim, and G. Wolff, unpublished work, reported by J. R. Hanson, in 'Terpenoids and Steroids', ed. K. H. Overton (Specialist Periodical Reports), The Chemical Society, London, 1974, Vol. 4, p. 174.

[57] R. H. Hackman and V. M. Trikojus, *Biochem J.*, 1952, **51**, 653; H. E. Gray and G. Fraenkel, *Physiol. Zool.*, 1954, **27**, 56; W. H. Ewart and R. L. Metcalf, *Ann. Entomol. Soc. Amer.*, 1956, **49**, 441; J. S. D. Bacon and B. Dickinson, *Biochem J.*, 1957, **66**, 289; T. E. Mittler, *J. Exp. Biol.*, 1958, **35**, 74; J. L. Auclair, *Ann. Rev. Entomol.*, 1963, **8**, 439.

[58] Y. Tamaki, *Seibutsu Kagaku*, 1968, 17; S. Kawai and Y. Tamaki, *Jap. J. Appl. Entomol. Zool.*, 1969, **13**, 150.

[59] R. A. Gray, *Science*, 1952, **115**, 129; Y. Tamaki, *Jap. J. Appl. Entomol. Zool.*, 1964, **8**, 227, and references therein; H. S. Salama and A. M. Rizk, *J. Insect Physiol.*, 1969, **15**, 1873; M. Saleh and H. S. Salama, *ibid.*, 1971, **17**, 1661.

[60] J. B. Maltais and J. L. Auclair, *Canad. J. Zool.*, 1952, **30**, 191; Y. Tamaki, *Jap. J. Appl. Entomol. Zool.*, 1964, **8**, 159, and references therein.

[61] A. Fodor and R. Cohn, in ref. 2, p. 89.

In addition to nearly 15% of fat, protein, fiber, and ash,[62,63] it also may include, like insect honeydew, appreciable amounts of melezitose (10—12%),[63] or trehalose (~ 7%).[64] Only 10% of the carbohydrates are reducing;[62,63] most of the remainder is sucrose, and raffinose was also detected.[62]

Neither natural Arabian manna contains mannitol or mannose, but these have been detected in other manna-like materials (solid honeydews), apparently also produced from scale insect/tree interactions.

F. Pheromones.—Presumed sex pheromones have been detected in females of three species of scale: *Matsucoccus resinosae* Bean and Godwin (red pine scale),[65] *Aonidiella citrina* Coquillet (yellow scale),[66] and *A. aurantii* (Maskell) (California red scale).[67] Partial isolation of the sex attractant from the latter has been reported.[68] Very little chemical work was done on the natural pheromone, but it was observed to co-chromatograph on Carbowax 20M with methyl and ethyl myristates, compounds isolated in the same work[68] (this is one of the few reports of the occurrence of an ethyl ester in nature; as the pheromone was collected by passage of air over the feeding scales, however, the myristyl esters could originate from either the animals or the citrus fruits). The chromatographic behaviour and chemical reactions of the pheromone suggested that it might be an acetate of an unsaturated branched-chain alcohol.[68,69]

5 Secondary Compounds of Aphids

A. Triglycerides.—Early workers verified three unusual facts concerning aphid lipids: (i) they were almost exclusively composed of triglycerides; (ii) they amounted to as much as one-third of the weight of the insects, without forming an external secretion like the waxy covering of many scale insects; and (iii) in many cases, they contained almost exclusively myristic acid, with other acids being of short chain length (C_6, C_8).[70]

Further investigation, with isolation of individual compounds, led to the identification of trimyristin and 2-*trans,trans*-sorboyl-1,3-dimyristin from temperate-zone species,[71,72] and 2-*trans,trans*-sorboyl-1,3-dipalmitin from the more tropical *Aphis nerii* Fonscolombe.[73] The unusual sorbic acid-containing

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[62] Z. I. Sabry and N. A. Atallah, *Nature*, 1961, **190**, 915.
[63] H. Colin and H. Belval, *Bull. Assoc. Chim.*, 1937, **54**, 12.
[64] J. Leibowitz, *Biochem. J.*, 1944, **38**, 205.
[65] C. C. Doane, *J. Econ. Entomol.*, 1966, **59**, 1539.
[66] D. S. Moreno, G. E. Carman, R. E. Rice, J. G. Shaw, and N. S. Bain, *Ann. Entomol. Soc. Amer.*, 1972, **65**, 443; D. S. Moreno, *ibid.*, p. 1283.
[67] H. Tashiro and D. L. Chambers, *Ann. Entomol. Soc. Amer.*, 1967, **60**, 1166; H. Tashiro, D. L. Chambers, D. Moreno, and J. Beavers, *ibid.*, 1969, **62**, 935.
[68] J. D. Warthen, jun., M. Rudrum, D. S. Moreno, and M. Jacobson, *J. Insect Physiol.*, 1970, **16**, 2207.
[69] W. Roelofs, personal communication.
[70] F. E. Strong, *Hilgardia*, 1963, **34**, 43.
[71] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.*, 1965, 5651.
[72] Y. Shimizu, *Naturwiss.*, 1971, **58**, 366.
[73] K. S. Brown, jun., D. W. Cameron, and U. Weiss, *Tetrahedron Letters*, 1969, 471.

glycerides are apparently restricted to aphids; it has been recently demonstrated that they are biosynthesized within the aphids from acetate.[74] The glycerides have been reported to possess antifungal activity,[72] but the erratic test results suggest that this may be due to sorbic acid (formed by hydrolysis and known to possess antibiotic properties).

A significant use of these triglycerides by the aphids is in defence. When disturbed or attacked, aphids produce from their cornicles (rodlike projections on their abdomens) a supercooled liquid which rapidly becomes a sticky solid upon contact with any surface;[75] this is almost totally composed of a low-melting triglyceride mixture, sometimes similar to but rarely identical with that in the total body lipids.[76] The esterified acids are almost wholly palmitic, myristic, sorbic, and n-hexanoic (= caproic); the latter is, like sorbic acid, esterified to the central oxygen of the glycerol.[77] Lesser acids found in aphid triglycerides include stearic, oleic, and lauric.[76]

The triglyceride mixtures seem to be species-specific with wide variation between species, but no good systematic correlation can be constructed in accord with accepted taxonomic divisions, using the proportions of the various acids in the triglycerides.[76] The proportions are not normally changed by the diet, genetic selection, colour, form, or food-plant of an aphid species, again indicating that the compounds are synthesized *de novo* by the aphids (or their symbiotes). However, they may vary in widely separate populations, or be affected by ambient temperature; the sorbic acid glyceride isolated from a temperate population (Rhode Island, USA) of the normally tropical *Aphis nerii** had an appreciably lower melting point (53—54 °C) than that from Arizona or Brazilian populations (2-sorbo-1,3-dipalmitin, m.p. 62—63 °C), and appeared to be 2-sorbo-1,3-dimyristin.[78] Presuming that the melting point of this compound is important in the properties of the supercooled and potentially antifungal defensive secretion, it might be expected that colder-climate populations would synthesize triglycerides with shorter-chain acids.[73,76]

An investigation of 30 aphid species for acid proportions in the triglycerides of the cornicle secretion compared with those in the total body lipids indicated wide variation and appreciable discrepancies.[76] Although there is a strong trend toward higher concentrations of myristoyl (lower-melting) and sorboyl (more anti-fungal) triglycerides in the cornicle secretion with relation to total lipids, several exceptions are evident. Successive drops from the cornicles of a continuously stimulated aphid show compositions progressively closer to those of body lipids.[76]

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* The temperate populations have been separated from *A. nerii* by some specialists; the foodplant preferences are identical, however.

[74] R. T. Aplin and P. Fairweather, manuscript in preparation.

[75] A. F. G. Dixon, *Entomol. Mon. Mag.*, 1958, **94,** 8; J. S. Edwards, *Nature*, 1966, **211,** 73; F. E. Strong, *Ann. Entomol. Soc. Amer.*, 1967, **60,** 668.

[76] R. K. Callow, A. R. Greenway, and D. C. Griffiths, *J. Insect Physiol.*, 1973, **19,** 737; A. R. Greenway and D. C. Griffiths, *ibid.*, p. 1649.

[77] K. S. Brown, jun. and A. M. Duffield, unpublished results.

[78] Y. Shimizu, personal communication (to U. Weiss).

As was found in the case of scale wax, triglycerides from immature aphids have a larger percentage of unsaturated and shorter-chain fatty acids (especially myristoleic)[76] than those in mature individuals; this may be a compensation for a volume/surface effect or for less effective chitin insulation, causing a lower body temperature in the juveniles.

B. Pigments.—Although investigations by L'Helias[79] suggested the presence of a number of pterins in the eyes of aphids, which were regarded as intermediate photoreceptors facilitating the synthesis of hormones which regulated the complex sexual and morphological changes during the aphids' yearly cycles, this conclusion has been cast in doubt by recent work showing a complete absence of detectable pteridines in Aphidoidea or Coccoidea.[80] The 'pterins' detected by L'Helias were reidentified as aphid glycosides (see below) with deceptively similar R_f values and fluorescence; the photoreceptors were suggested to be carotenes or still unidentified polar pigments.[80] Pteridines (leucopterin, erythropterin, xanthopterin and isoxanthopterin) were detected and identified, however, in Psyllids and Aleyrodids as well as various Auchenorrhyncha,[80]* perhaps indicating that these two families either do not belong to the Sternorrhyncha or are much more primitive than the aphids and scale insects.

Carotenes have been detected in small amounts in almost all species of aphid investigated.[73,80,81]† In one of the many species which demonstrate colour dimorphism, *Macrosiphum liriodendri* (Monell), the difference between the green and the pink forms was shown to be entirely due to the presence of differing and characteristic carotenoids.[82] The green phenotype was found to possess the blue-green aphinin (see below) and yellow carotenes with a γ-ionone ring [(43), (44)], while the pink morph produced red carotenoids bearing an open chain at one or both ends [(45a), (45b), (46a), and (46b)]. Both forms contained β,β-carotene, probably widely distributed in aphids.[73,80] The compounds (44), (45a), and (46a) had been previously isolated from micro-organisms, while (43) was new;[82] carotenes with the γ-ionene ring [(43), (44)] are so far known only from this aphid and a discomycete.

A number of carotenoids have also been isolated from *Aphis fabae*: β-carotene, diepoxy-β-carotene, lutein, flavaxanthin, and γ-carotene.[83] The first four were also present in the foodplant (*Vicia lutea*), while γ-carotene was apparently formed within the aphid.[83]

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* The green colour of the apple psyllid (*Psylla mali*) has been shown to be an 'insectoverdin' (combining yellow and blue components) of unknown structure, close to that found in true bugs (Hemiptera).[80]

† Carotenoid-like materials were detected but not isolated in two scale insects in the family Diaspididae, but were absent from other families investigated in the Coccoidea.[80]

[79] C. L'Helias, *Compt. rend.*, 1961, **253**, 1353; *Bull. Biol. France Belg.*, 1962, **96**, 187.

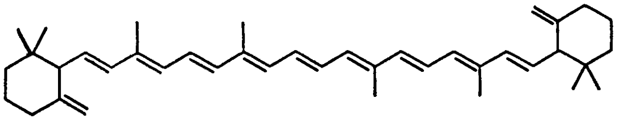
[80] H. J. Banks and D. W. Cameron, *Insect Biochem.*, 1973, **3**, 139.

[81] J. H, Bowie, D. W. Cameron, J. A. Findlay, and J. A. K. Quartey, *Nature*, 1966, **210**, 395.

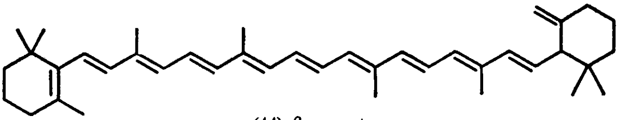
[82] K. H. Weisgraber, R. J. J. C. Lousberg and U. Weiss, *Experientia*, 1971, **27**, 1017; A. G. Andrewes, H. Kjøsen, S. Liaaen-Jensen, K. H. Weisgraber, R. J. J. C. Lousberg, and U. Weiss, *Acta Chim. Scand.*, 1971, **25**, 3878.

[83] L. R. G. Valadon and R. S. Mummery, *Comp. Biochem. Physiol.*, 1973, 46B, 427.

Green Aphids

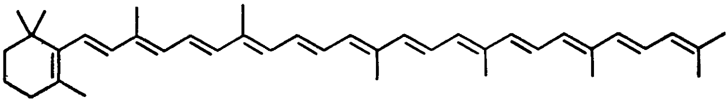


(43) γ,γ-carotene

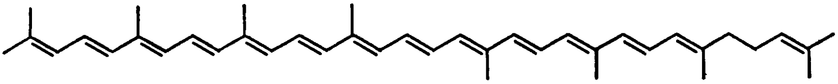


(44) β,γ-carotene

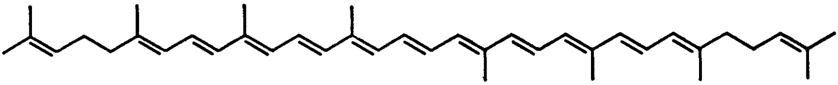
Pink Aphids



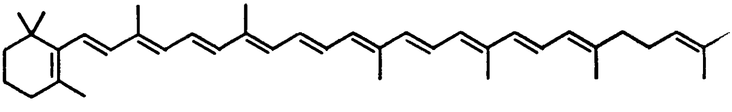
(45a) torulene (dehydro-β,ψ-carotene)



(46a) 3,4-dehydro-ψ,ψ-carotene



(46b) lycopene (ψ,ψ-carotene)



(45b) β,ψ-carotene (="γ-carotene")

The aphins or aphid glycosides are characteristic, biogenetically unified but structurally diversified pigments found in all aphids so far investigated. They have been excellently reviewed several times in recent years.[81,84–86] Only the newer developments and more interesting reactions and structures will be highlighted in this review. The known natural compounds, with principal biosynthetic

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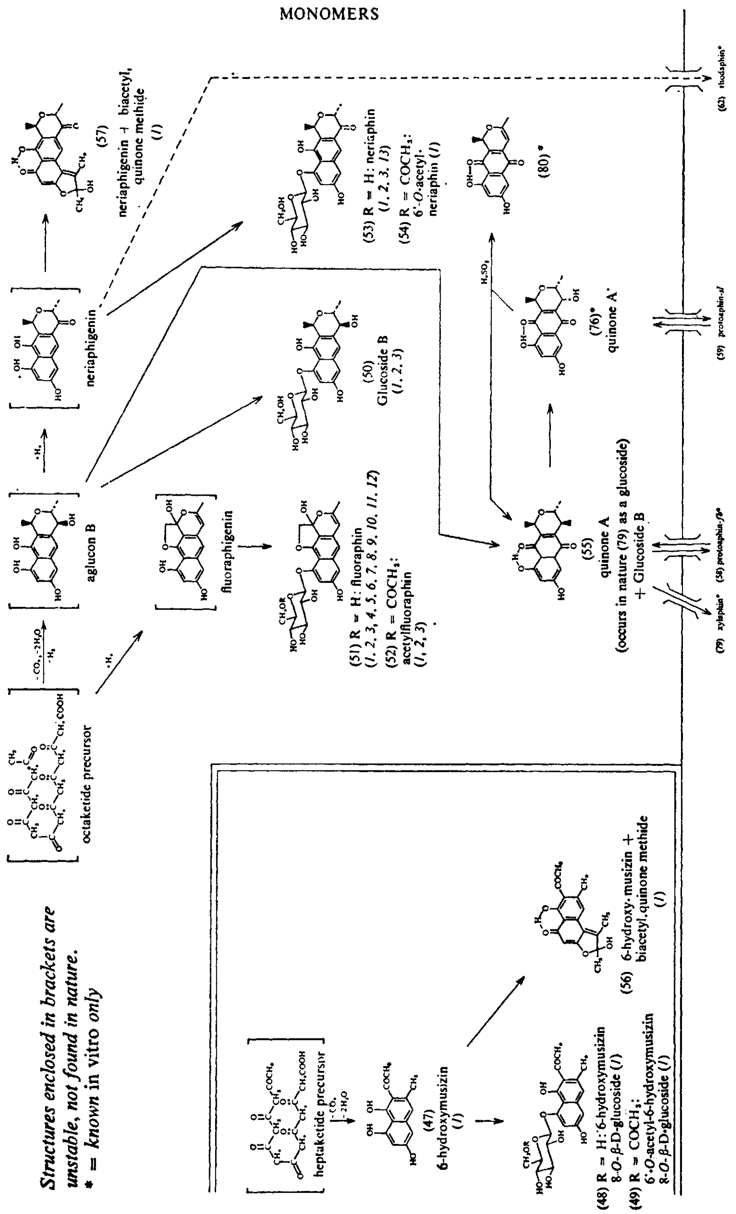
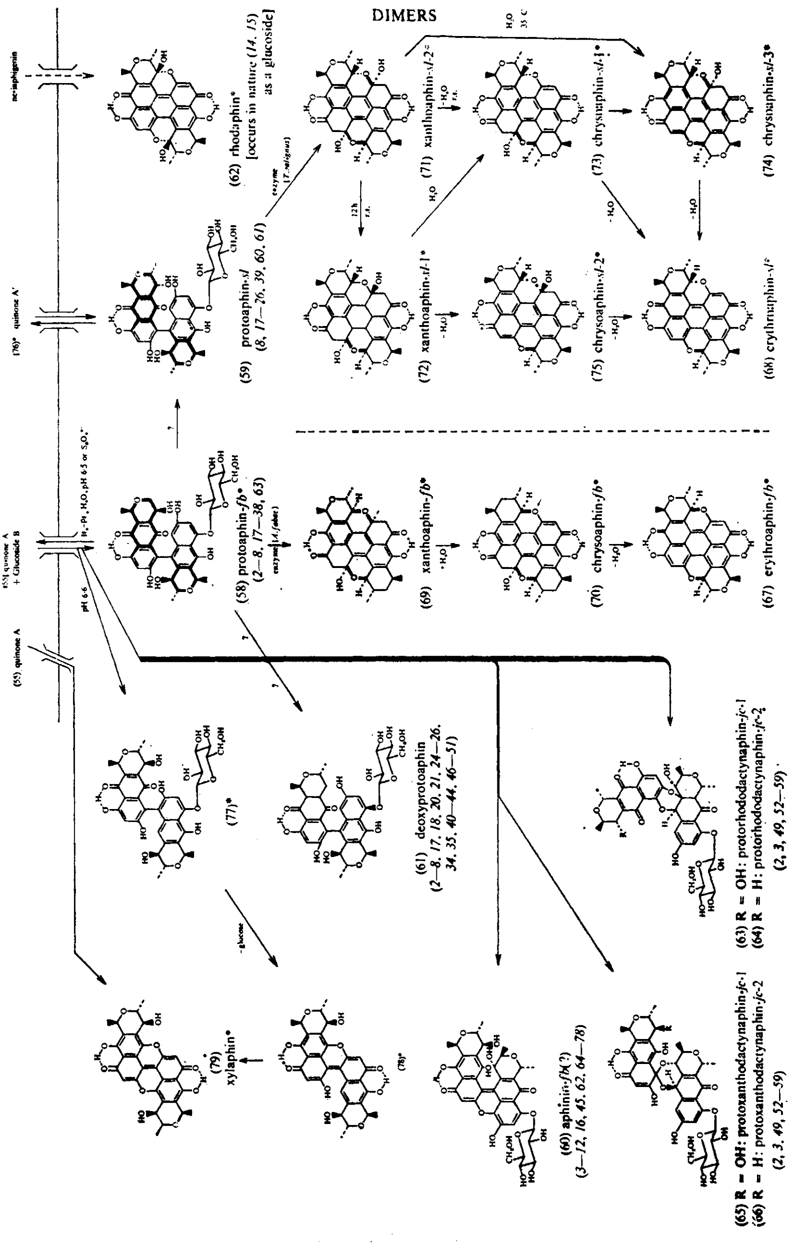
[84] Lord Todd, *Chem. in Britain*, 1966, **2**, 428.

[85] Ref. 29, pp. 597—623.

[86] D. W. Cameron and Lord Todd, in 'Oxidative Coupling of Phenols', ed. W. I. Taylor and A. R. Battersby, Marcel Dekker, New York, 1967, pp. 203—241.


MONOMERS
Structures enclosed in brackets are unstable, not found in nature.
* = known in vitro only
octaketide precursor
-CO₂, -2H₂O
-H₂
aglucon B
-H₂
neriaphigenin
(57) neriaphigenin + biacetyl, quinone methide (1)
-H₂
fluoraphigenin
(51) R = H: fluoraphin (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12)
(52) R = COCH₃: acetylfluoraphin (1, 2, 3)
(50) Glucoside B (1, 2, 3)
(53) R = H: neriaphin (1, 2, 3, 13)
(54) R = COCH₃: 6'-O-acetyl-neriaphin (1)
(55) quinone A (occurs in nature (79) as a glucoside) + Glucoside B
(76)* quinone A'
H₂SO₄
(80)*
(79) xylaphin*
(58) protoaphin-fb*
(59) protoaphin-sl
(62) rhodaphin*
heptaketide precursor
-CO₂, -2H₂O
(47) 6-hydroxymusizin (1)
(48) R = H: 6-hydroxymusizin 8-O-β-D-glucoside (1)
(49) R = COCH₃: 6'-O-acetyl-6-hydroxymusizin 8-O-β-D-glucoside (1)
(56) 6-hydroxy-musizin + biacetyl, quinone methide (1)



Scheme 5 Polyketide Aphid Pigments (Aphins) (*1, 2 . . .*) = *sources (see Table)*

Table *List of aphid species investigated*; source numbers for Scheme 5*

1 Aphis nerii Fonscolombe
2 Dactynotus cirsii (L.)
3 Dactynotus jaceae (L.)
4 Aphis fabae Scopoli
5 Aphis rumicis L.
6 Aphis sambuci L.
7 Aphis farinosa Gmelin
8 Aphis corniella H.R.L.
9 Brevicoryne brassicae (L.)
10 Hyalopterus prunii (Geoffr.)
11 Macrosiphoniella artemisiae (Fonsc.)
12 Megoura viciae Buckton
13 Periphyllus testudinaceus (Fernie)
14 Hormaphis betulina (Horvath)
15 Hormaphis spinosus (Shimer)
16 Macrosiphum rosae (L.)
17 Aphis epilobii Kltb.
18 Aphis craccivora Koch
19 Aphis cytisorum Hartig
20 Aphis sarothamni Franssen
21 Aphis taraxacicola (Börner)
22 Dysaphis crataegi (Kltb.)
23 Dysaphis devecta (Walker)
24 Dysaphis plantaginea (Pass.)
25 Dysaphis pyri (Fonsc.)
26 Cinara pilicornis (Hartig)
27 Aphis philadelphi Börner
28 Aphis viburni Scopoli
29 Aphis evonymi Fabr.
30 Aphis hederae Kltb.
31 Aphis ilicis Kltb.
32 Brachycaudus klugkisti (Börner)
33 Brachycaudus rociadae (Cockerell)
34 Eriosoma lanigerum (Hausmann)
35 Schizoneura ulmi (L.)
36 Myzus cerasi (F.)
37 Rhopalosiphum nymphaeae (L.)
38 Schizolachnus pineti (F.)
39 Tuberolachnus salignus (Gmelin)
40 Pterocomma populium (Kltb.)
41 Aphis acanthi Schrank
42 Aphis armata Hausmann
43 Aphis newtoni Theobald
44 Aphis epilobiaria Theobald
45 Symydobius oblongus (V. Heyd.)
46 Aphis grossulariae Kltb.
47 Aphis lamiorum Börner
48 Aphis thalictri Koch
49 Macrosiphoniella sanborni (Gillette)
50 Thelaxes dryophila (Schrank)
51 Tetraneura ulmi (L.)
52 Macrosiphoniella absinthii (L.)
53 Dactynotus rudbeckiae (Fitch)
54 Dactynotus taraxaci (Kltb.)
55 Dactynotus tanaceti (L.)
56 Dactynotus ambrosiae Thomas
57 Dactynotus nigrotuberculatus Th. Olive
58 Dactynotus cichorii (Koch)
59 Dactynotus sonchi (L.)
60 Pineus strobi (Hartig)
61 Pineus pini (Gmelin)
62 Macrosiphum liriodendri (Monell)
63 Aphis cognatella M. G. Jones
64 Aphis urticata F.
65 Chaitophorus populicola Thomas
66 Cryptomyzus ribis (L.)
67 Drepanosiphum platanoides (Schrank)
68 Hyadaphis foeniculi Pass.
69 Hyalopterus arundinus (F.)
70 Liosomaphis berberidis (Kltb.)
71 Macrosiphum gei (Koch)
72 Macrosiphum albifrons Essig.
73 Microlophium carnosum Buckton
74 Myzaphis rosarum (Kltb.)
75 Nasonovia ribis-nigri Mosley
76 Periphyllus acericola (L.)
77 Paraprociphilus tessellata (Fitch)
78 Dysaphis viburnicolum Gillette
79 Rhopalosiponinus calthae (Koch)†

* Mostly from the older literature; updated in thesis and manuscripts of H. J. Banks.
† H. J. Banks, personal communication.

precursors and chemical transformation products, are represented in Scheme 5.* The natural pigments range in colour from very light yellow through oranges and reds to deep blue-green; all aglycons are apparently derived from cyclization of hepta- or octa-ketide precursors. They may be preliminarily divided into two classes, monomers (C_{13} or C_{15}) and dimers (C_{30}). The monomeric pigments, of recent discovery, fall into three subclasses: (i) heptaketide-derived compounds [6-hydroxymusizin (47), possibly an artefact, and its glycosidic derivatives (48) and (49)], known only from *Aphis nerii*;[73,87,88] (ii) octaketide-derived compounds [glucoside B (50);[73,88–90] fluoraphin (51) and acetylfluoraphin (52),[73,81,87,88,90] very widely distributed and easily detected through their intense yellow-white fluorescence; neriaphin (53),[73,90] the principal pigment of *Aphis nerii*, and its acetyl derivative (54);[88] and quinone A (55) glucoside[89,91*]; and (iii) the biacetyl methides (56) and (57),[88,92] of problematical biogenetic origin. The dimeric pigments include the widely distributed and epimeric protoaphins-*fb* (58) and -*sl* (59);[89,90] the blue-green aphinin (60)[81,82,85,86] of near-general occurrence (as both *fb*- and *sl*-isomers) but still uncertain structure; the recently discovered deoxyprotoaphin (61);[90] rhodoaphin (62);[93] and the dactynaphins (63)—(66).[90,94] The last are among the most complex natural products known; (65) and (66) contain a theoretically aromatizable but sterically fixed cyclohexadienone ring, and a quinone acetal. The two series (63)—(64) and (65)—(66) are interconvertible by simple equilibration in aqueous or methanolic solution.[90,94]

The protoaphins undergo a characteristic series of transformations[95] when the glucosyl group is removed by the aphid's own enzymes or other β-glucosidases,[96] terminating in two isomeric perylenequinones, erythroaphins-*fb* (67) and -*sl* (68).[97] The *fb*-reaction series is straightforward, as the first intermediate,

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[*] Much additional information on more than 40 aphid pigments and allied colourless materials is presented in 'Glycosides from the Aphidoidea,' the Ph.D. thesis of H. J. Banks, Cambridge, 1969, and in manuscripts in preparation by Dr. Banks (Canberra) and Prof. D. W. Cameron (Melbourne). A full account of their newer and very significant work will be left for description in their forthcoming publications. The Banks thesis also presents a lucid discussion summarizing much experimental evidence for the synthesis of aphin pigments by endosymbiotes.

[87] K. S. Brown, jun. and U. Weiss, *Anais Acad. Bras. Ciências*, 1971, **42**, Supplement, 205.

[88] K. S. Brown, jun. and U. Weiss, *Tetrahedron Letters*, 1971, 3501.

[89] D. W. Cameron, R. I. T. Cromartie, D. G. I. Kingston, and Lord Todd, *J. Chem. Soc.*, 1964, 51.

[90] H. J. Banks and D. W. Cameron, *Austral. J. Chem.*, 1972, **25**, 2199.

[91] D. W. Cameron, personal communication; D. W. Cameron, D. G. I. Kingston, N. Sheppard, and Lord Todd, *J. Chem. Soc.*, 1964, 98.

[92] K. S. Brown, jun. and P. M. Baker, *Tetrahedron Letters*, 1971, 3505; A. T. Henriques, J. A. Rabi, P. M. Baker, and K. S. Brown, jun., in preparation.

[93] S. F. MacDonald, *J. Chem. Soc.*, 1954, 2378; J. H. Bowie and D. W. Cameron, *J. Chem. Soc. (C)*, 1967, 704.

[94] U. Weiss and H. W. Altland, *Nature*, 1965, **207**, 1295; J. H. Bowie and D. W. Cameron, *J. Chem. Soc. (C)*, 1967, 708, 712, 720.

[95] A. Calderbank, D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, E. Haslam, D. G. I. Kingston, Lord Todd, and J. C. Watkins, *J. Chem. Soc.*, 1964, 80; H. J. Banks, D. W. Cameron, and J. C. A. Craik, *J. Chem. Soc. (C)*, 1969, 627.

[96] D. W. Cameron and J. C. A. Craik, *J. Chem. Soc. (C)*, 1968, 3068.

[97] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 62; D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, N. Sheppard, and Lord Todd, *ibid.*, p. 90.

xanthoaphin-*fb* (69), is symmetrical, giving a single chrysoaphin-*fb* (70) by elimination of water from either side of the molecule. Removal of an additional mole of water gives erythroaphin-*fb* (67). The initially formed and analogous xanthoaphin-*sl*-2 (71) is highly strained and unstable, rapidly being converted into xanthoaphin-*sl*-1 (72) and chrysoaphin-*sl*-1 (73) at room temperature, or chrysoaphin-*sl*-3 (74) at −35 °C. The stable but unsymmetrical xanthoaphin-*sl*-1 (72) can undergo dehydration in two different manners, giving chrysoaphin-*sl*-1 (73) and -*sl*-2 (75). All three chrysoaphins-*sl* give the single erythroaphin-*sl* (68) upon loss of a further molecule of water.[95]

Enzymic hydrolysis of deoxyprotoaphin (61) led directly to a deoxychrysoaphin, as (70) but with an enolic hydroxy-group in place of the enol ether arrowed.[90]

The dimeric protoaphins could be cleaved by mild reduction *in vitro* to give glucoside B (50) and quinone A (55) (from protoaphin-*fb*) or A′ (76) (from protoaphin-*sl*).[89] Conversely, simple incubation of a mixture of the glucoside with either quinone at pH 6.6 produced a small amount of the respective protoaphin and a major product (77) from symmetrical condensation. The latter could be converted by hydrolysis into a compound (78) having a chromophore very similar to that of aphinin (60), and easily oxidized to xylaphin (79).[98] The last compound was also produced directly and in high yield by heat-induced self-coupling of quinone A at pH 6.2.[99]

Solution of either quinone A or A′ in concentrated sulphuric acid produced the same brown entity (λ_{max} 851 nm) with a strong e.s.r. signal. Dilution of the mixture resulted in the precipitation of an anhydro-compound (80).[100] Similar ion-radical formation was observed for erythroaphins and derivatives, and attributed to protonation at the quinone carbonyl.[100]

C. Other Secondary Compounds.—Among the various other compounds reported from aphids, a few are worthy of special mention. The bright orange aphid, *Aphis nerii*, is apparently aposematic (warningly coloured), and is almost always found on plants containing poisonous cardenolides. Analysis of populations feeding on oleanders (*Nerium oleander* L.) and tropical milkweeds (*Asclepias curassavica* L.) revealed the presence of cardenolides in the tissues of the aphid: strospeside, odoroside-H, and adynerin* (but no oleandrin) in oleander-feeding, and calotropin and proceroside (but no calactin) in milkweed-feeding aphids.[10] The three oleander glycosides were also present in large quantities in the honeydew of oleander-fed *A. nerii*, although the phloem sap contained none of these.[101] The plants on which the aphids were collected were not completely analysed, and it is not established whether the differences in composition between the aphids and the reported cardenolide mixtures for leaves of these plants are due to

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* These same three compounds were found in a scale insect, *Aspidiotus nerii* Bouché, feeding on *N. oleander* (ref. 10).

[98] D. W. Cameron and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1825.

[99] G. M. Blackburn, D. W. Cameron, and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1836.

[100] D. W. Cameron, H. W.-S. Chan, and M. R. Thoseby, *J. Chem. Soc.* (*C*), 1969, 631.

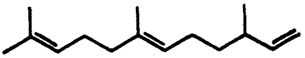
[101] R. T. Aplin and M. P. Bailey, manuscript in preparation.

seasonal or populational variations in the plants, selective occurrence of cardenolides in the phloem ingested by the aphids, or selective metabolism by the aphids.[10] As no large quantities of cardenolides are stored by the aphids[73] (as is done by many other *Asclepias*- and *Nerium*-feeding aposematic insects),[10] the exact role of the cardenolides in protection of *A. nerii* is still somewhat uncertain. Some invertebrate predators of *A. nerii* (*Chrysopa* sp. larva, *Coccinella undecempunctata* L.) contained cardenolides sequestered from their prey, while others (*Coccinella septempunctata* L. and a Syrphidae larva) did not.[10]

The aphid *Megoura viciae* was shown to be very toxic to some coccinellid larvae, but a systematic investigation of its chemical constituents failed to reveal any basis for this character; the chloroform extract contained a number of waxes and hydrocarbons, in addition to triglycerides.[102] Other aphids which feed on poisonous plants have been observed to cause illness and/or death in, or be avoided by, many species of coccinellid.[103]

D. Pheromones.—The presence of sex pheromones, released by complex 'scent plaques' located on the hind tibiae, has been reported for oviparous females of *Schizaphis borealis* Tambs-Lyche,[104] *Brevicoryne brassicae*,[105] and *Megoura viciae*;[106] although some biological and isolational work has been undertaken on these pheromones, no chemical structures are yet known. Because of the complex life cycles and dispersal ability of aphids, it is not sure how useful such compounds would be in their control.

The supercooled cornicle secretion of many aphids contains, in addition to triglyceride, an alarm pheromone identified as *trans*-β-farnesene (81).[107] Of obvious utility to the aphids, this pheromone could also be of assistance in their control by man, causing feeding aphids to remove their stylets and walk over contact insecticides applied to the plants.[107]



(81) *trans*-β-farnesene

6 Summary and Perspective

All of the secondary substances reported for aphids and scales, with the exception of cardenolides, common carbohydrates and amino-acids, and possibly some wax constituents, are apparently produced within the insects. In the cases

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[102] A. F. G. Dixon, M. Martin-Smith, and G. Subramanian, *J. Chem. Soc.*, 1965, 1562.

[103] I. Hodek, 'Biology of Coccinellidae', Junk, The Hague, 1973, chapter 6.

[104] J. Pettersson, *Entomol. Scand.*, 1970, **1**, 63; 1971, **2**, 81.

[105] J. Pettersson, *Swedish J. Agric. Res.*, 1973, **3**, 95.

[106] D. Marsh, *Nature New Biology*, 1972, **238**, 31.

[107] C. J. Kislow and L. J. Edwards, *Nature*, 1972, **235**, 108; W. S. Bowers, L. R. Nault, R. E. Webb, and S. R. Dutky, *Science*, 1972, **177**, 1121; L. J. Edwards, J. B. Siddall, L. L. Dunham, P. Uden, and C. J. Kislow, *Nature*, 1973, **241**, 126; W. H. J. M. Wientjans, A. J. Lakwijk, and T. van der Marel, *Experientia*, 1973, **29**, 658.

where this has been investigated, the production of these species-specific compounds is also independent of the host-plants chosen by the homopterans.

This would not be so unusual, were it not for the large number of typical fungal metabolites known from these insects. Anthraquinone pigments, ophiobolin-type sesterterpenes, γ- and ψ-carotenoids, and polyketide naphthotriols are typical products of biosynthetic pathways of micro-organisms, known only very occasionally in higher plants and practically restricted to aphids and scales among the animals. Even the cedrene-type sesquiterpenes and the sorbic acid-containing triglycerides stretch the known limits of normal animal metabolic pathways. The interpretation which immediately suggests itself is the biosynthesis of these metabolites by the homopteran endosymbiotes.[12,73,80,82] At least with relation to the polyketide pigments, this suggestion is strongly supported by the colours observed in the mycetomes, which are often so tinged with red, yellow, or green as to be easily visible through the insect's body wall; some of these compounds have been shown to be synthesized from acetate within the insects.[74]

To investigate this hypothesis further, it will be necessary to expand to other components the sort of careful experiments conducted by Ehrhardt,[14,17] who demonstrated steroid synthesis from radioactive acetate in normal aphids (*Neomyzus circumflexus* Buckton, feeding on artificial medium) and lack of any incorporation in chlortetracycline-treated (aposymbiotic) colonies; and synthesis of methionine and cysteine from radioactive sulphate, absent in aureomycin-treated aphids. It is predictable that many aphids and scales will also be found to depend upon their symbiotes for synthesis and accumulation of many of the secondary compounds which characterize these insects. The aphids and scales may thus represent a new, barely opened chapter in the growing book of chemical ecology, in which the chemical interactions between species, at the level of secondary metabolism, take place and might be studied in the internal microcosm of the individual organism.

This paper was first outlined while the author was at the Centro de Pesquisas de Produtos Naturais of the Universidade Federal do Rio de Janeiro. Drs. Ulrich Weiss, D. W. Cameron, H. J. Banks, Y. Tamaki, T. R. Seshadri, K. Venkataraman, Sukh Dev, M. Jacobson, A. D. Lees, R. T. Aplin, M. Rothschild, V. F. Eastop, and W. B. Mors aided substantially in the preparation and revision of the manuscript at various stages.