Marine Mollusks from Australia and New Zealand: Chemical and Ecological Studies

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Abstract. Marine mollusks contain structurally diverse terpenes, polyketides, polypropionates and nitrogenous metabolites that may confer an ecological advantage on the host organism. From a chemical perspective, the most studied Australian taxa include representatives of the nudibranchs and sea hares, which are characterised by terpenes acquired from their specialised diets of sponges and algae, respectively. In contrast, siphonariid limpets that are prevalent on temperate seashores carry out *de novo* biosynthesis of polypropionate metabolites. Nitrogenous compounds isolated from Australian marine mollusks include precursors to the first commercially significant marine bioproduct, Tyrian purple, and metabolites that are characteristic of ingested cyanobacteria.

7.1 Introduction

Over the past 30 years, there has been a rich tradition of marine natural products chemistry in both Australia and New Zealand. Within Australia, work in this interdisciplinary research field was initiated in the 1960s by Maurice Sutherland and his (then) Ph.D. student Joe Baker at The University of Queensland. Subsequently, Baker became Director of the Roche Research Institute for Marine Pharmacology (RRIMP; 1974–1981). During the 1980s, a number of university research groups were active in Australia, while the Australian Institute of Marine Science developed a substantial marine biodiscovery program under first Peter Murphy and later Chris Battershill. For over 10 years, AstraZeneca have funded a major natural products discovery initiative, led by Ron Quinn at Griffith University, while more recently a Centre for Molecular Biodiscovery has been established at The University of Queensland. Meanwhile in New Zealand, over 20 years of marine natural products research has been led by John Blunt and Murray Munro. Together with Brent Copp, Peter Northcote and Michelle Prinsep, they now write the annual updates on marine natural products that were first initiated by the late John Faulkner (Faulkner 2001; Blunt et al. 2004).

The research from Australasian groups initially targeted algae that could be collected in quantity and then bioactive sponge and ascidian metabolites, because of the industry links that could be harnessed

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through identifying the pharmaceutical potential of these sessile invertebrates. Scientific research on mollusks requires a specialised collection strategy. Even though chemical ecology studies reveal that mollusks assimilate biologically active metabolites (for reviews, see Karuso 1987; Paul 1992; Cimino et al. 1999), there have been few chemical studies on Australian and New Zealand marine mollusks. For example, despite a prolific publication record on algal and sponge metabolites, there are no publications on mollusks arising out of RRIMP activities in the primary literature. In this chapter, the published chemistry from Australian and New Zealand mollusks is reviewed, and the chemical ecology and biosynthesis of selected metabolites that are of interest to the author are described.

7.2
Polyketide and Polypropionate Metabolites

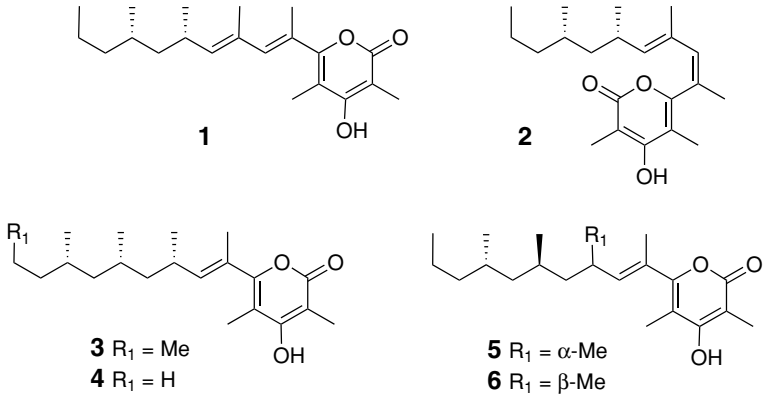
7.2.1
Polypropionate Metabolites in Australian and New Zealand Mollusks

A recent review considered the structures, stereochemistry and synthesis of polypropionates from siphonariid mollusks or sacoglossans (Davies-Coleman and Garson 1998).

Pulmonates of the genus *Siphonaria* are air-breathing, intertidal mollusks commonly found in temperate zones. From an evolutionary perspective, these mollusks are significant since they may represent an evolutionary link between marine and terrestrial gastropods. Although siphonariid limpets feed by moving around rock platforms and pools, grazing on algae at low tides, there is no evidence that they assimilate algal metabolites from their food. Instead, the chemistry of this genus is characterised by the presence of polypropionate metabolites that are now known to be products of *de novo* synthesis.

The first polypropionates reported from an Australian siphonariid mollusk were isolated from *Siphonaria diemenensis* collected at Phillip Island and near Mallacoota, in Victoria. The diemenensins A (**1**) and B (**2**), both containing an α-pyrone ring and differing only in the configuration of the Δ6,7 double bond, show modest antibiotic activity and inhibit cell division in a sea urchin egg assay (Hochlowski and Faulkner 1983). Pectinatone (**3**) and norpectinatone (**4**) are α-pyrones that were isolated from *S. pectinata* collected at Wollongong, NSW (Garson et al. 1990), but which were first isolated from *S. pectinata* (Florida) and *S. lessoni* (Chile), respectively (Biskupiak and Ireland 1983; Capon and Faulkner 1984). The relative stereochemistry of these

two metabolites was shown to be incorrect when the alleged structure of norpectinatone (**5**) and the C-9 epimer (**6**) were synthesised (Oppolzer et al. 1986). Subsequently, the structure of pectinatone was corrected by two independent X-ray studies (Garson et al. 1990; Norte et al. 1990). A recent total synthesis of pectinatone used SAMP-hydrazone methodology to introduce the methyl stereocentres (Birkbeck and Enders 1998).



The siphonarins A (**7**) and B (**8**) are hemiacetal metabolites also containing a γ-pyrone unit that were first reported from *S. zelandica* collected in several parts of the Indo-Pacific. One collection was made from Bottle and Glass Rocks in Sydney Harbour, NSW, by the late John Faulkner while in Australia as a Queens Fellow in Marine Science. The relative stereochemistry of siphonarin A was deduced by single crystal X-ray analysis (Hochlowski et al. 1984), and the absolute stereochemistry deduced by X-ray analysis of a boronic acid derivative (Garson et al. 1994b) and by total synthesis of the γ-pyrone subunit (Paterson and Franklin 1994). The baconipyrones A–D (**9**–**12**) were isolated from *S. baconi* collected at Sorrento, Victoria, and are γ-pyrones that possess an unusual non-contiguous polypropionate structure (Manker et al. 1989). Although it was recognised that these metabolites originated from their siphonarin co-metabolites (Fig. 7.1), their isolation is now believed to represent post-collection chemistry rather than an enzymatic process (Brecknell et al. 2000). A total synthesis of (–)-baconipyrone C (**12**) established the absolute configuration of this series (Paterson et al. 2000), while asymmetric synthesis of the cyclohexanone subunit of baconipyrones A (**10**) and B (**9**) has been achieved (Turks et al. 2004).

Many siphonariid metabolites contain a hemiacetal ring. The denticulatins A (**13**) and B (**14**) (Fig. 7.2) are toxic hemiacetal metabolites first isolated from *S. denticulata* collected in Coledale or Eden, NSW, and differing from each other only in stereochemistry at C-10. The structure

of denticulatin B was confirmed by single crystal X-ray analysis (Hochlowski et al. 1983). Several total syntheses of these metabolites have been reported (Ziegler and Becker 1990; Andersen et al. 1991a,b; Paterson and Perkins 1992, 1996; Oppolzer et al. 1995; De Brabander and Oppolzer 1997). Specimens of *S. australis* collected near Auckland were found to contain the hemiacetal **15** and a related ketoester **16** (Fig. 7.3) (Hochlowski and Faulkner 1984), whose absolute stereochemistry was later confirmed by total synthesis (Sundram and Albizati 1992). When the rearranged ester **17** was isolated from denticulatin A during an attempt to derivatise this compound using Sharpless dihydroxylation, it became further apparent that polypropionate esters (e.g. **9–12, 16**) are artefacts that can be generated by mild basic treatment of hemiketal metabolites (Fig. 7.2) (Brecknell et al. 2000).

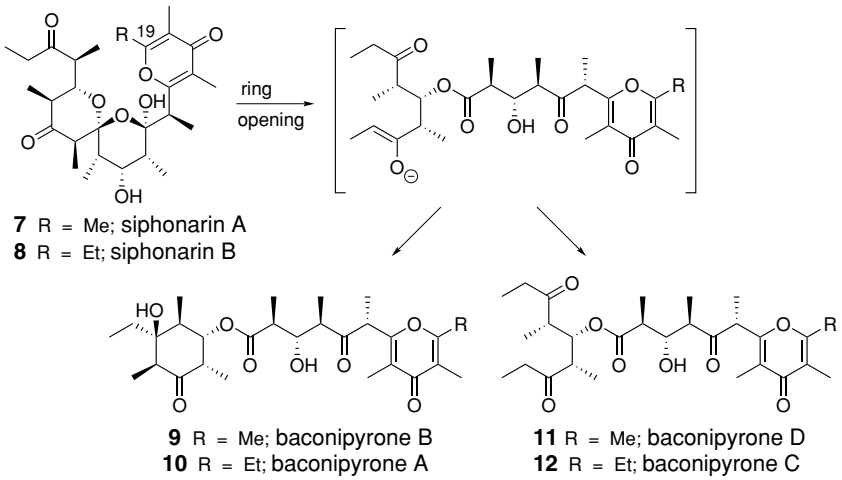


Fig. 7.1. Proposed conversion of siphonarins A and B into baconipyrones A–D in *Siphonaria zelandica*

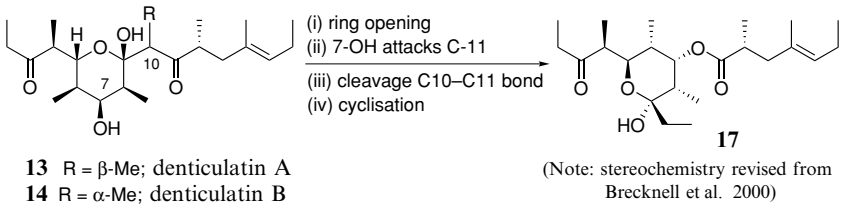
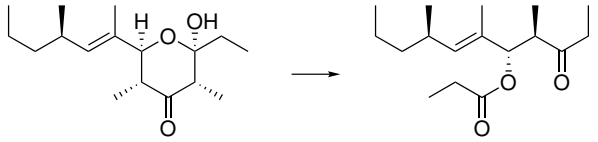


Fig. 7.2. Proposed conversion of denticulatin metabolites into polypropionate esters in *Siphonaria denticulata*

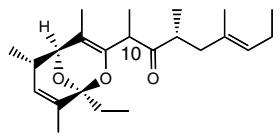


15 **16**

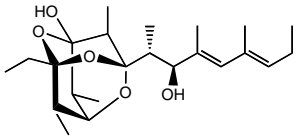
Fig. 7.3. Proposed conversion of a spiroacetal metabolite into a polypropionate ester in *Siphonaria australis*

Funiculatins A (**18**) and B (**19**) are polypropionates from *S. funiculata* collected on the Sunshine Coast of south-east Queensland that are structurally closely related to the denticulatins (Blanchfield et al. 1994). Two tricyclic polypropionate ketals have so far been identified, namely muamvatin (**20**) from a Fijian siphonariid (Roll 1986) and caloundrin B (**21**) from *S. zelandica* collected in south-east Queensland (Blanchfield et al. 1994), in which the unusual trioxaadamantyl moiety results from cyclisation of acyclic precursors (Blanchfield et al. 1994; Garson et al. 1994a).

The aposematically coloured sacoglossan *Cyerce nigricans* contains structurally related α– and γ-pyrones (**22**) and (**23**), related to metabolites of the cyercene family. The pyrones **22** and **23** were not responsible for the ichthyodeterrent properties of the whole-animal extract (Roussis et al. 1990). The original structure proposed for compound **23** has been revised to that shown here (Vardaro et al. 1992); and the structure suggested for pyrone **22** warrants further investigation.



18, 19; epimers at C-10



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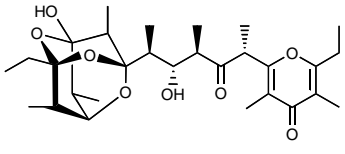

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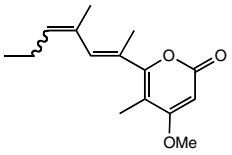

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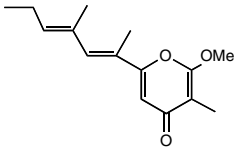

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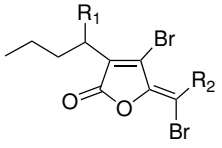
7.2.2 Polyketides

In Sydney, the sea hare *Aplysia parvula* selectively accumulates some fimbrolide metabolites (**24–27**) from the red alga *Delisea pulchra* at levels that are higher than in plant tissue (De Nys et al. 1996). The ecological role of dietary-derived metabolites sequestered by sea hares has been

questioned, since these metabolites are frequently stored in the digestive gland rather than in skin tissue. Other functions that have been suggested include protection against infection, a role in chemical camouflage, or storage as part of a detoxification process (Pennings et al. 1999). For *A. parvula*, the major furanone **26** is concentrated in the digestive gland and is also present in skin tissue at concentrations that deter predators. However, the metabolite is not present in significant quantities in the opaline or ink secretions of this animal (De Nys et al. 1996; Rogers et al. 2000). Tasmanian specimens of *A. parvula* accumulate furanone **24** from a *Delisea* sp. (Jongaramruong et al. 2002). These brominated furanones have been intensively studied for their antifouling potential (Steinberg et al. 1998), but few studies on their synthesis have been reported in the primary literature (Beecham and Sims 1979; Manny et al. 1997).



24 R_1 = H; R_2 = Br
25 R_1 = R_2 = Br
26 R_1 = OAc; R_2 = H
27 R_1 = OH; R_2 = Br

7.2.3 Biosynthetic Studies

The first studies on marine polypropionate biosynthesis investigated metabolites from siphonariid limpets and confirmed the operation of a polypropionate pathway, rather than an acetate–methionine route. The denticulatins A and B, **13** and **14**, were found to incorporate a radioactive label after a 6-day incubation period when [1-^{14}C] propionate was injected into specimens of *Siphonaria denticulata*. In contrast, incorporation of [1-^{14}C] acetate into these animals did not provide significantly labelled denticulatins. These data were consistent with a propionate-derived biosynthesis rather than the alternative addition of methyl groups from C_1-tetrahydrofolate metabolism onto a polyacetate backbone. Kuhn–Roth degradation revealed that only the carbons anticipated to originate from C-1 of propionate were labelled, but these data did not demonstrate a uniform distribution of ^{14}C label along the carbon chain. In an alternative incorporation protocol, the precursor was added directly to the aquarium water, from where it was absorbed directly through the skin tissue (Manker et al. 1988). Injection of [1-^{14}C] propionate into the foot tissue of *S. zelandica* followed by a 4-day incubation gave radiolabelled siphonarins A and B **7** and **8**, confirming their propionate origin (Garson et al. 1994b). The lower homologue, siphonarin A **7**, was shown to be assembled from an acetate chain starter unit with nine propionate-derived chain-building units, by determining that C-19 was not labelled

by [1-^{14}C] propionate. The selective isolation of C-19 plus attached methyl carbon (as *p*-bromophenacyl acetate) was achieved by ozonolysis, hydrolysis of the ensuing anhydride and derivatisation (Garson et al. 1994b). Furthermore, acetate was utilised by *S. zelandica* for synthesis of **7**. The role of succinate in furnishing propionate units is consistent with the presence of a functioning methylmalonyl mutase in these mollusk.

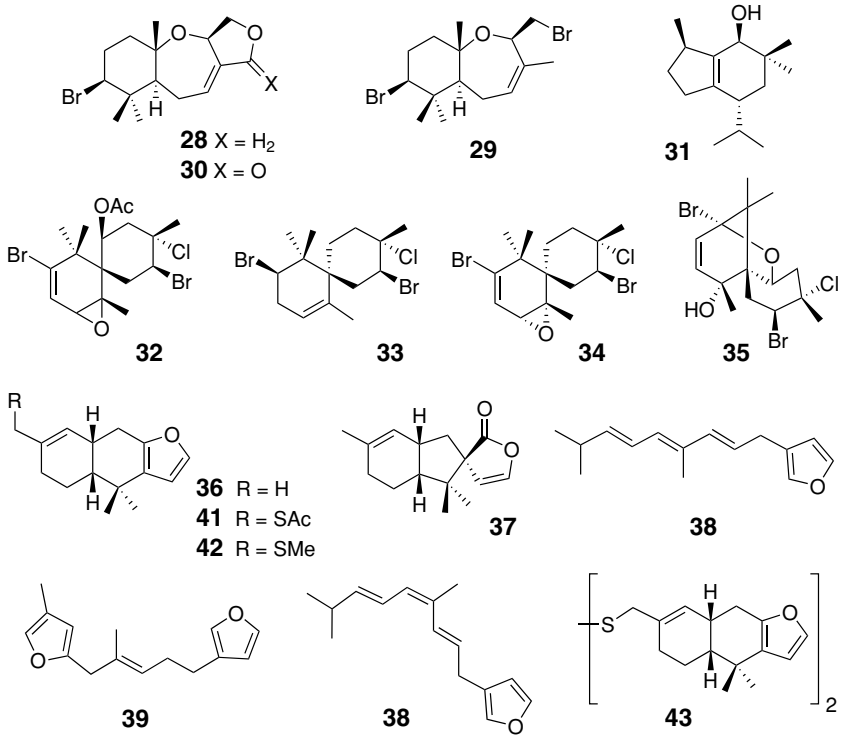
7.3 Terpenes

7.3.1 Terpene Metabolites from Australian and New Zealand Mollusks

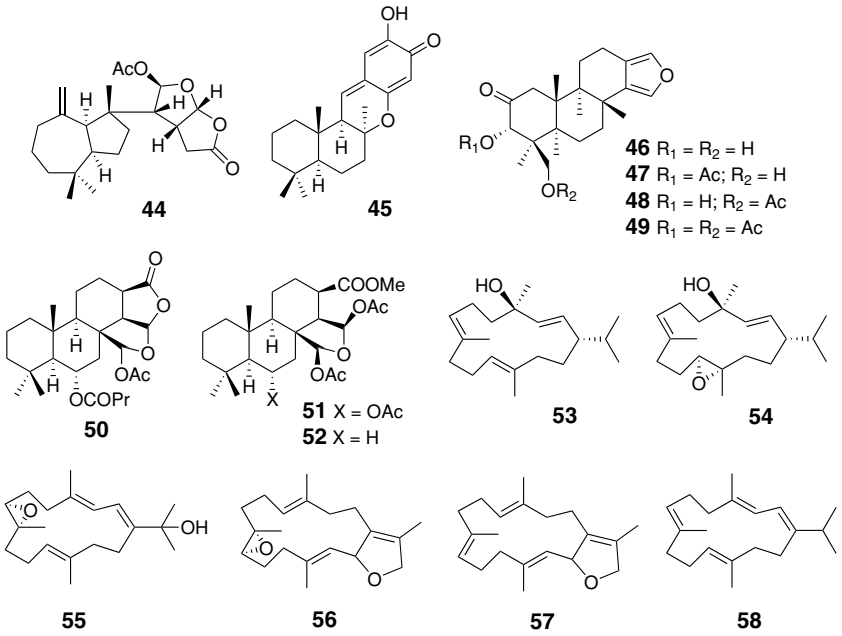
Several studies have explored the chemical relationships between Australian sea hares and the algal diets that contain sesquiterpenes. Studies on *A. parvula* from Sydney, NSW revealed that it accumulates *Laurencia obtusa* metabolites, such as the palisadins A **28** and B **29**, aplysistatin **30** and brasilenol **31**. Metabolite **28** is excreted in the mucous and opaline secretions of this animal consistent with a defensive role. The sea hare *A. dactylomela* also feeds on the same alga and stores low quantities of metabolites **28**, **29** and **30**. When fed on a diet of *L. obtusa* in laboratory experiments, the sea hare also accumulates brasilenol **31**, but this compound was never found in field-collected *A. dactylomela* (Rogers et al. 2000). Tasmanian specimens of *A. parvula* acquire the chamigrenes **32** and **33** and the pacifenols **34** and **35** from *L. filiformis* (Jongaramruong et al. 2002).

Nudibranchs frequently feed on terpene-containing sponges. A *Hypselodoris* sp. from south-east Queensland contains the well-known furanosesquiterpenes furodysinin **36** and dehydroherbadysidolide **37** (Garson 2004). Six sesquiterpene furans **38**–**43** have been reported from *Chromodoris epicuria* (previously named *Ceratosoma brevicaudatum*; Ksebati and Schmitz 1988). Furodysinin has also been isolated from *Asteronotus cespitosus* (Fahey and Garson 2002). All of these metabolites are characteristic of sponges of the genus *Lamellodysidea*, previously placed within the genus *Dysidea* (Cook and Bergquist 2002). A specimen of *Chromodoris coi* from Heron Island contained dendrillolide A **44** (Garson et al., unpublished data) while in south-east Queensland *C. elisabethina* consistently feeds on a grey-purple dictyoceratid sponge, as yet of unknown taxonomy, from which it sequesters the strongly cytotoxic terpene quinone metabolite puupehenone **45** (Garson 2004). The mollusk *Glossodoris atromarginata* collected at Mooloolaba, south-east Queensland, contains spongiane metabolites such as spongiadiol (**46**) and the acetate derivatives (**47**) and (**48**). On dissection, the mantle

dermal formations contained spongiadiol-3α, 19-diacetate (**49**) (Garson et al., unpublished data). Nine spongiane diterpenes, including **50–52**, have been isolated from *C. epicuria* from Adelaide, South Australia (Ksebati and Schmitz 1987).



Soft corals can also be eaten by mollusks. On the Great Barrier Reef, the aeolid nudibranch *Phyllodesmium longicirra* feeds on the soft coral *Sarcophyton trocheliophorum* and accumulates diterpenes such as thunbergol **53**, trocheliophorol **54** and the epoxyalcohol **55** (Coll et al. 1985). The prosobranch mollusk *Ovula ovum* feeds on a *Sarcophyton* sp. and may detoxify ingested sarcophytoxide **56** by converting it into the deoxy derivative **57** prior to excretion in the faeces (Coll et al. 1983). The chemistry of the clam *Tridachna maxima* has been investigated and has yielded the sequiterpene germacrene C (**58**), previously isolated from a soft coral. This is suggestive of a zooxanthellar origin for the metabolite in both animals (Bowden et al. 1980).



7.3.2
Chemical and Biosynthetic Studies on Phyllidid Nudibranchs

Nudibranchs from the genus *Phyllidia* consistently form associations with marine sponges that contain nitrogenous terpene metabolites. A N_1–C_1 functional group such as –NC, –NCS, or –NHCHO is common, but also found are the rarer –NCO, –SCN and –N=CCl_2 groups (Garson and Simpson 2004). Great Barrier Reef specimens of *Phyllidiella pustulosa* feed on the sponge *Acanthella cavernosa* from which they acquire terpene isocyanide and isothiocyanate metabolites (**59**–**62**) (Fig. 7.4). In aquaria, sponge samples converted ^{14}C-cyanide or -thiocyanate into the metabolites axisonitrile-3 (**59**) and axisothiocyanate-3 (**60**), while the mollusks, when injected with these precursors, were incapable of de novo synthesis. Mollusks were then allowed to feed on "labelled" sponges and subsequently contained radioactive metabolites that could only have come from the sponge (Dumdei et al. 1997). A useful chemical comparison is provided by the Fijian *P. pustulosa*, which accumulates axisonitrile-3 (**59**) and the isocyanide/isothiocyanate pair **63** and **64** from the sponge *Phakellia* (syn. *Acanthella*) *carduus* (Wright 2003).

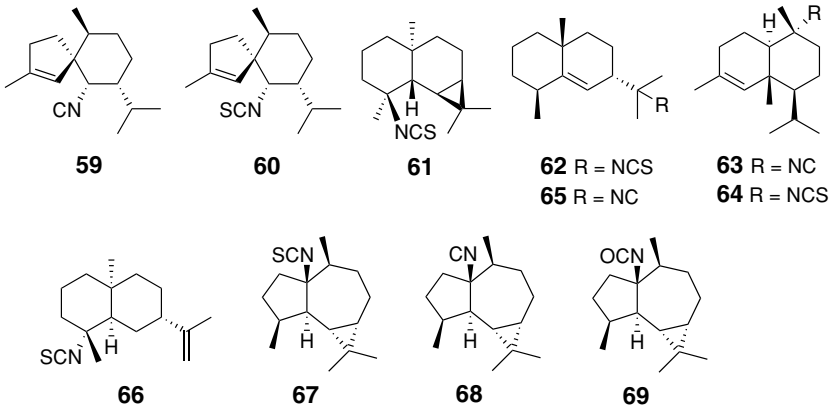


Fig. 7.4. Terpene metabolites isolated both from Phyllidid nudibranchs collected in Queensland, Australia, and in Fiji, and from their dietary sponge *Acanthella cavernosa*

Collections of "isocyanide" sponges and their associated phyllidid mollusks from south-east Queensland have provided great structural diversity. Specimens of *A. cavernosa* collected at Mooloolaba contained the known sesquiterpenes **59–60** and **62–69** (Fig. 7.4), three of which (**59**, **62**, **67**) were also found in the nudibranch *Phyllidia ocellata* that feeds on this sponge.

The rare isocyanate (**69**; Braekman et al. 1989) was found in trace quantities in the sponge (Stapleton 2002). Collections of *P. ocellata* from Rottnest Island in Western Australia have yielded isocyanides and isothiocyanate sesquiterpenes (e.g. **59**, **61**, **65**) that are again typical of an *A. cavernosa* diet (Stapleton 2002).

Study of the mollusk *P. varicosa* and its sponge prey *Axinyssa* n.sp. from south-east Queensland reveals that this mollusk also concentrates a range of sesquiterpene metabolites typical of its diet. Compounds isolated include tricyclic (**70–74**) and bicyclic (**75–76**) metabolites (Fig. 7.5) (Simpson et al. 1997; Stapleton 2002). Notably the metabolite, 9-thiocyanatopupukeanane (**71**), first reported together with its 9-epimer from Indonesian specimens of *P. varicosa* and its sponge source *A. aculeata*, (Yasman et al. 2003) was isolated from the Australian nudibranch, but has not yet been found in the sponge diet (Stapleton 2002). When tested in an ascidian larval assay (Degnan et al. 1996), the various sponge sesquiterpene fractions inhibited larval development, although individual *Acanthella* or *Axinyssa* metabolites were not effective inhibitors (Stapleton 2002). The reasons why the phyllidid mollusks selectively accumulate certain sponge chemicals, and the ecological implications of these specific sponge–nudibranch associations, require further study.

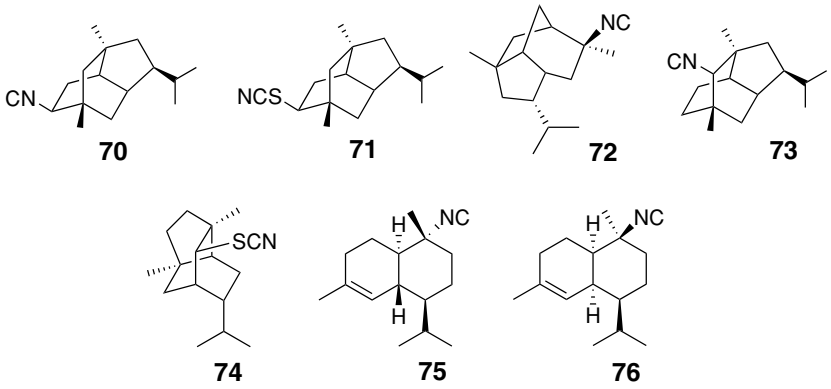
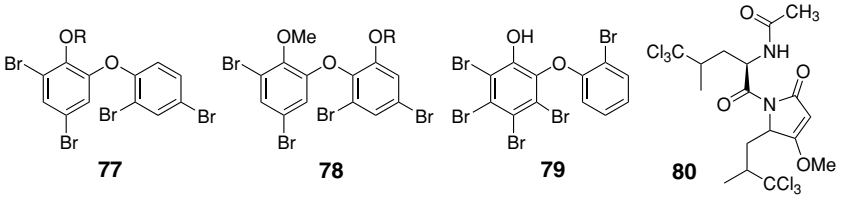


Fig. 7.5. Chemistry of *Phyllidiella varicosa* and its dietary sponge *Axinyssa* n.sp. from Mooloolaba, south-east Queensland. *Note*: compounds **75** and **76** have not been reported previously from this sponge

7.4 Miscellaneous Metabolites

In Sect. 7.3.1, the association of the tropical nudibranch *Asteronotus cespitosus* with the sponge *Lamellodysidea* (syn. *Dysidea*) *herbacea* was discussed. Further evidence of this dietary association is provided by the isolation of halogenated metabolites that are characteristic of this sponge. The bromophenols **77**, **78** and **79** have been isolated from Great Barrier Reef and West Australian samples of the mollusk, while a specimen collected under permit in the Philippines contained the chloropeptide **80** in addition to bromophenol metabolites (Fahey and Garson 2002).



Mollusks of the families Muricidae and Thaisidae are sources of the purple dye Tyrian purple (**81**) that has been used since antiquity. The early chemical work of Baker with Sutherland (Baker and Sutherland 1968) and Duke (Baker and Duke 1973, 1976), which revealed the role of bromoindole sulphates (Fig. 7.6) in dye formation, has been reviewed (Baker et al, 1974; Benkendorff et al, 2000). A recent study revealed that fresh egg masses of the muricid *Dicathais orbita* are protected by the

presence of tyrindoleninone (**82**). As the eggs mature and hatch into larvae, the monomer 6-bromoisatin (**83**) and the dimer tyriverdin (**84**) are formed. The antimicrobial or pathogenic properties of metabolites **82–84** appear to guard the eggs against infection during the ripening process (Benkendorff et al. 2000).

The nudibranch *Notodoris gardineri* is commonly found on sponges such as *Leucetta* sp. and *Pericharax* sp. in the northern Great Barrier Reef. Specimens of *N. gardineri* from Flynn Reef (Carroll et al. 1993) and from Lizard Island (Garson et al., unpublished data) contain the imidazole alkaloid clathridine **85**.

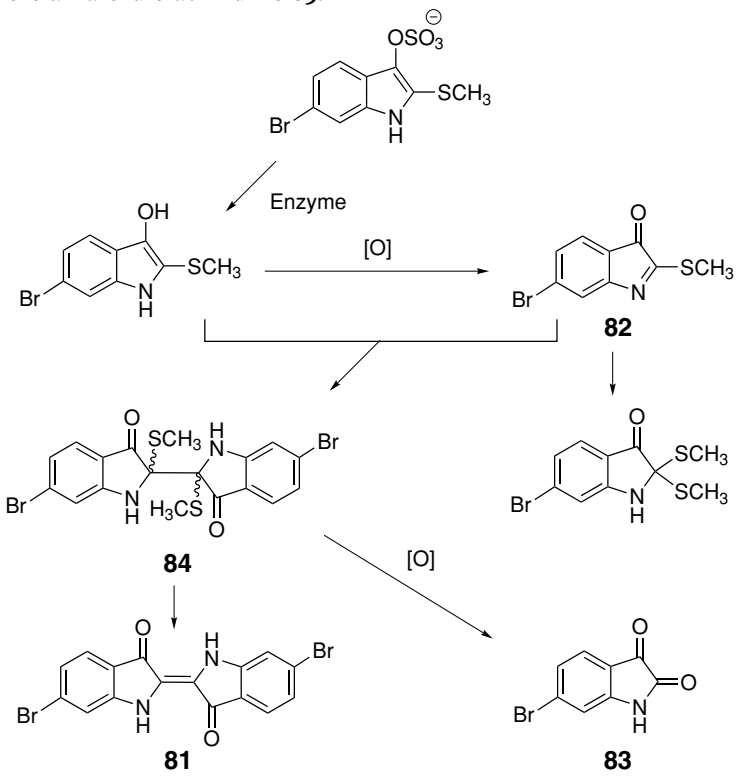
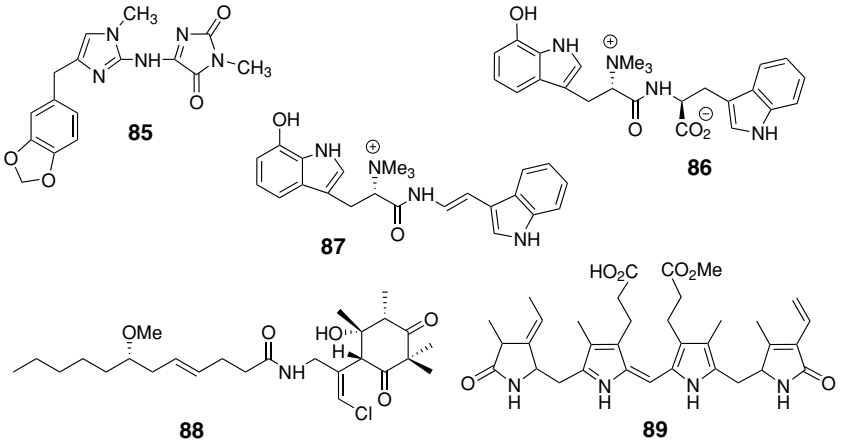


Fig. 7.6. The formation of Tyrian purple in *Dicathais orbita* (from Benkendorff et al. 2000)

Nitrogenous metabolites have also been isolated from New Zealand mollusks. The sea hare *Aplysia dactylomela* was shown to contain the tryptophan dipeptides **86** and **87** (Appleton et al. 2001), while *Bursatella leachii* contains a new biologically active malyngamide **88** (Appleton et al. 2002). These metabolites are likely to be of dietary origin, since the feeding preference of sea hares for chemically defended algae is well established. The isolation of the purple pigment aplysioviolin **89**, whose structure resembles the photosynthetic pigment phycoerythrin (Pennings et al. 1999), from a Tasmanian collection of the sea hare *A. parvula* in Tasmania must be related to its red algal diet (Jongaramruong et al. 2002).



7.5 Conclusions

The survey above indicates that there continues to be much scope for chemical study of Australian and New Zealand mollusks. Although this group has received extensive taxonomic attention, current understanding of their natural products chemistry is limited. In contrast, there is a rich and diverse literature on the chemistry of Australian and New Zealand marine invertebrates (soft corals, sponges, ascidians) and algae (for a general overview, see Volkman 1999).

Experimental attention has focused largely on two classes of mollusk metabolites (i) the polypropionate metabolites of the *Siphonaria* and selected sacoglossans, (ii) the sesquiterpene metabolites from nudibranch mollusks and their dietary sources. The dietary associations between sea hares and algae have also been studied. The biosynthetic processes that lead to the metabolites, and an understanding of their natural biological roles, deserve detailed study.

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References

Andersen MW, Hildebrandt B, Dahmann G, Hoffmann RW (1991a) Stereoselective total synthesis of the denticulatins. Chem Ber 124:2127–2139

Andersen MW, Hildebrandt B, Hoffmann RW (1991b) Efficient stereoselective total synthesis of denticulatins A and B. Angew Chem Int Ed Engl 30:97–99

Appleton DR, Babcock RC, Copp BR (2001) Novel tryptophan-derived dipeptides and bioactive metabolites from the sea hare *Aplysia dactylomela*. Tetrahedron 57:10181–10189

Appleton DR, Sewell MA, Berridge MV, Copp BR (2002) A new biologically-active malyngamide from a New Zealand collection of the sea hare *Bursatella leachii*. J Nat Prod 65:630–631

Baker JT (1974) Tyrian purple: ancient dye, modern problem. Endeavour 33:11–17

Baker JT, Duke CC (1973) Chemistry of the indolenines. II. Isolation from the hypobrancial gland of marine molluscs of 6-bromo-2,2-dimethylthioindolin-3-one and 6-bromo-2-methylthioindoleninone as alternative precursors to Tyrian purple. Aust J Chem 26:2153–2157

Baker JT, Duke CC (1976) Isolation of choline and choline ester salts of tyrindoxyl sulphate from the marine molluscs *Dicathais orbita* and *Mancinella keineri*. Tetrahedron Lett 1976:1233–1234

Baker JT, Sutherland MD (1968) Pigments of marine animals VIII. Precursors of 6,6′-dibromoindigotin (Tyrian purple) from the marine mollusc *Dicathais orbita* (Gmelin). Tetrahedron Lett 1968:43–46

Beecham CM, Sims JJ (1979) The first synthesis of fimbrolides, a novel class of halogenated lactone occuring in the red seaweed *Delisia fimbriata*. Tetrahedron Lett 1979:1649–1652

Benkendorff K, Davis AR, Bremner JB (2000) Tyrian purple precursors in the egg masses of the Australian muricid *Dicathais orbita*: a possible defense role. J Chem Ecol 26:1037–1050

Birkbeck AA, Enders D (1998) The total synthesis of (+)-pectinatone: an iterative alkylation approach based on the SAMP-hydrazone method. Tetrahedron Lett 39:7823–7826

Biskupiak JE, Ireland CM (1983) Pectinatone, a new antibiotic from the mollusc *Siphonaria pectinata*. Tetrahedron Lett 24:3055–3058

Blanchfield JT, Brecknell DJ, Brereton IM, Garson MJ, Jones DD (1994) Caloundrin A and funiculatin B: new polypropionates from siphonariid limpets. Aust J Chem 50:2255–2269

Blunt JW, Copp BR, Munro MHG, Northcote PT, Prinsep MR (2004) Marine natural products. Nat Prod Rep 21:1–49

Bowden BF, Coll JC, Mitchell SJ (1980) Studies of Australian soft corals. XXI. A new sesquiterpene from *Nepthea chabrolii* and an investigation of the common clam *Tridacna maxima*. Aust J Chem 33:1833–1839

Braekman JC, Daloze D, Moussiaux B, Stoller C, Deneubourg F (1989) Sponge secondary metabolites: new results. Pure Appl Chem 61:509–512

Brecknell DJ, Collett LA, Davies-Coleman MT, Garson MJ, Jones DD (2000) New non-contiguous polypropionates from marine molluscs: a comment on their natural product status. Tetrahedron 56:2497–2502

Capon RJ, Faulkner DJ (1984) Metabolites of the pulmonate *Siphonaria lessoni*. J Org Chem 49:2506–2508

Carroll AR, Bowden BF, Coll JC (1993) New imidazole alkaloids from the sponge *Leucetta* sp. and the associated predatory nudibranch *Notodoris gardineri*. Aust J Chem 46:1229–1234

Cimino G, Fontana A, Gavagnin M (1999) Marine opistobranch molluscs: chemistry and ecology in sacoglossans and dorids. Curr Org Chem 3:327–372

Coll JC, Tapiolas DM, Bowden BF, Webb L, Marsh H (1983) Transformation of soft coral (Coelenterata: Octocorallia) (*Sarcophyton* sp.) terpenes by *Ovula ovum* (Mollusca: Prosobranchia). Mar Biol 74:35–40

Coll JC, Bowden BF, Tapiolas DM, Willis RH, Djura P, Streamer M, Trott L (1985) Studies of Australian soft corals – XXXV. The terpenoid chemistry of soft corals and its implications. Tetrahedron 41:1085–1092

Cook SC, Bergquist PR (2002) Family Dysideidae Gray 1876. In: Hooper JNA, Van Soest RWM (eds) Systema Porifera: a guide to the classification of sponges. Plenum, New York, pp. 1061–1066

Davies-Coleman MT, Garson MJ (1998) Marine polypropionates. Nat Prod Rep 15:477–512

De Brabander J, Oppolzer W (1997) Enantioselective total synthesis of (–)-denticulatins A and B using a novel group-selective aldolisation of a *meso* dialdehyde as a key step. Tetrahedron 53:9169–9202

De Nys R, Steinberg PD, Rogers CN, Charlton TS, Duncan MW (1996) Quantitative variation of secondary metabolites in the sea hare *A. parvula* and its host plant *Delisea pulchra*. Mar Ecol Prog Ser 130:135–146

Degnan BM, Rohde PR, Lavin MF (1996) Normal development and embryonic gene activity of the ascidian *Herdmania momus*. Mar Freshwater Res 47:543–551

Dumdei EJ, Flowers AE, Garson MJ, Moore CJ (1997) The biosynthesis of sesquiterpene isocyanides and isothiocyanates in the marine sponge *Acanthella cavernosa*: evidence for dietary transfer to the dorid nudibranch *Phyllidiella pustulosa*. Comp Biochem Physiol 118B:1385–1392

Fahey SJ, Garson MJ (2002) Geographic variation of natural products of the tropical nudibranch *Asteronotus cespitosus*. J Chem Ecol 28:1773–1785

Faulkner DJ (2001) Marine natural products. Nat Prod Rep 18:1–49

Garson MJ (2004) Chemical associations between Australian nudibranchs and their dietary sponges. Chem Aust 71:16–19

Garson MJ, Simpson JS (2004) Marine isocyanides and related natural product structures – structure, biosynthesis and ecology. Nat Prod Rep 21:164–179

Garson MJ, Small CJ, Skelton BW, Thinapong P, White AH (1990) Structural and stereochemical correlations of polypropionate metabolites from marine pulmonates: revision of relative stereochemistry of pectinatone by X-ray structure analysis. J Chem Soc Perkin Trans 1:805–807

Garson MJ, Goodman JM, Paterson I (1994a) A configurational model for siphonariid polypropionates derived from structural and biosynthetic considerations. Tetrahedron Lett 35:6929–6932

Garson MJ, Jones DD, Small CJ, Liang J, Clardy J (1994b) Biosynthetic studies on polypropionates: a stereochemical model for siphonarins A and B from the pulmonate limpet *Siphonaria zelandica*. Tetrahedron Lett 35:6291–6294

Hochlowski JE, Faulkner DJ (1983) Antibiotics from the marine pulmonate *Siphonaria diemenensis*. Tetrahedron Lett 24:1917–1920

Hochlowski JE, Faulkner DJ (1984) Metabolites of the pulmonate *Siphonaria australis*. J Org Chem 49:3838–3840

Hochlowski JE, Faulkner DJ, Matsumoto GK, Clardy J (1983) The denticulatins, two polypropionate metabolites from the pulmonate *Siphonaria denticulata*. J Am Chem Soc 105:7413–7415

Hochlowski JE, Coll JC, Faulkner DJ, Biskupiak JE, Ireland CM, Qi-tai Z, Cun-heng H, Clardy J (1984) Novel metabolites of four *Siphonaria* species. J Am Chem Soc 106:6748–6750

Jongaramruong J, Blackman AJ, Skelton BW, White AH (2002) Chemical relationships between the sea hare *Aplysia parvula* and the red seaweed *Laurencia filiformis* from Tasmania. Aust J Chem 55:275–280

Karuso P (1987) Chemical ecology of the nudibranchs. In: Scheuer PJ (ed) Bioorganic marine chemistry. Springer, Berlin Heidelberg New York, pp. 31–60

Ksebati MB, Schmitz FJ (1987) New spongiane diterpenes from an Australian nudibranch. J Org Chem 52:3766–3773

Ksebati MB, Schmitz FJ (1988) Sesquiterpene furans and thiosesquiterpenes from the nudibranch *Ceratosoma brevicaudatum*. J Nat Prod 51:857–861

Manker DC, Garson MJ, Faulkner DJ (1988) De novo biosynthesis of polypropionate metabolites in the marine pulmonate *Siphonaria denticulata*. J Chem Soc Chem Commun 1061–1062

Manker DC, Faulkner DJ, Stout TJ, Clardy J (1989) The baconipyrones: novel polypropionates from the pulmonate *Siphonaria baconi*. J Org Chem 54:5371–5374
Manny AJ, Kjelleberg S, Kumar N, De Nys R, Read RW, Steinberg PD (1997) Reinvestigation of the sulfuric acid-catalysed cyclisation of brominated 2-alkyllevulinic acids to 3-alkyl-5-methylene-2(5*H*)-furanones. Tetrahedron 53:15813–15826
Norte M, Cataldo F, González AG, Rodríguez ML, Ruiz-Perez C (1990) New metabolites from the marine mollusc *Siphonaria grisea*. Tetrahedron 46:1669–1678
Oppolzer W, Moretti R, Bernadinelli G (1986) Enantioselective synthesis of the alleged structure of norpectinatone. Tetrahedron Lett 27:4713–4716
Oppolzer W, De Brabander J, Walther E, Bernadinelli G (1995) Asymmetric synthesis of (–)-denticulatins A and B via group-selective aldolization of a *meso* dialdehyde with a chiral *N*-propionylsultam. Tetrahedron Lett 36:4413–4416
Paterson I, Franklin AS (1994) Assignment of the absolute stereochemistry of the siphonarins and baconipyrones. Enantiocontrolled synthesis of a γ-pyrone unit. Tetrahedron Lett 35:6925–6928
Paterson I, Perkins MV (1992) Studies in polypropionate synthesis: stereoselective synthesis of (–)-denticulatins A and B. Tetrahedron Lett 33:801–804
Paterson I, Perkins MV (1996) Total synthesis of (–)-denticulatins A and B using efficient methods of acyclic stereocontrol. Tetrahedron 52:1811–1834
Paterson I, Chen DY-K, Aceña JL, Franklin AS (2000) Studies in marine polypropionate synthesis: total synthesis of (–)-baconipyrone C. Org Lett 2:1513–1516
Paul VJ (1992) Ecological roles of marine natural products. Comstock, Ithaca
Pennings SC, Paul VJ, Dunbar DC, Hamann MT, Lumbang WA, Novack B, Jacobs RS (1999) Unpalatable compounds in the marine gastropod *Dolabella auricularia*: distribution and effect of diet. J Chem Ecol 25:735–755
Rogers CN, De Nys R, Charlton TS, Steinberg PD (2000) Dynamics of algal secondary metabolites in two species of sea hare. J Chem Ecol 26:721–744
Roll DM, Biskupiak JE, Mayne CE, Ireland CM (1986) Muamvatin, a novel tricyclic spiro ketal from the Fijian mollusc *Siphonaria normalis*. J Am Chem Soc 108:6680–6682
Roussis V, Pawlik JE, Hay ME, Fenical W (1990) Secondary metabolites of the chemically rich ascoglossan *Cyerce nigricans*. Experientia 46:327–329
Simpson JS, Garson MJ, Hooper JNA, Cline EI, Angerhofer CK (1997) Terpene metabolites from the tropical marine sponge *Axinyssa* sp. Aust J Chem 50:1123–1127
Stapleton BL (2002) Structural studies of bioactive natural products from marine invertebrates. Ph.D. thesis, The University of Queensland, Brisbane
Steinberg PD, De Nys R, Kjelleberg S (1998) Chemical inhibition of epibiota by Australian seaweeds. Biofouling 12:227–244
Sundram UN, Albizati KF (1992) Synthesis and absolute configuration of polypropionate metabolites of *Siphonaria australis*. Tetrahedron Lett 33:437–440
Turks M, Murcia MC, Scopelliti R, Vogel P (2004) First asymmetric synthesis of the cyclohexanone subunit of baconipyrones A and B. Revision of its structure. Org Lett 6:3031–3034
Vardaro RR, Di Marzo V, Marin A, Cimino G (1992) α and γ-pyrone-polypropionates from the Mediterranean ascoglossan mollusc *Ercolania funerea*. Tetrahedron 48:9561–9566
Volkman JK (1999) Australasian research on marine natural products: chemistry, bioactivity and ecology. Mar Freshwater Res 50:761–779
Wright AD (2003) GC-MS and NMR analysis of *Phyllidiella pustulosa* and one of its dietary sources, the sponge *Phakellia carduus*. Comp Biochem Physiol 134A:307–313
Yasman, Edrada RA, Wray V, Proksch P (2003) New 9-thiocyanatopupukeanane sesquiterpenes from the nudibranch *Phyllidia varicosa* and its sponge prey *Axinyssa aculeata*. J Nat Prod 66:1512–1514
Ziegler FE, Becker MR (1990) Total synthesis of (–)-denticulatins A and B: marine polypropionates from *Siphonaria denticulata*. J Org Chem 55:2800–2805