

## SOME RECENT DEVELOPMENTS IN THE CHEMISTRY OF ALCYONACEANS†

BERNARD TURSCH

Collectif de Bio-Ecologie, Université Libre de Bruxelles, Brussels, Belgium

**Abstract**—Sesquiterpenes, diterpenes and sterols found in Alcyonaceans are briefly reviewed. Their biogenetical origin, their distribution and their biological significance are discussed.

Coral reefs are scattered in tropical shallow waters covering about 190,000,000 km<sup>2</sup>. It has been estimated that the area of the reefs themselves is comparable to that of all cultivated land on earth.<sup>1,2</sup> The primary productivity of the reefs varies from 1500 to 3500 g of carbon/m<sup>2</sup>/yr: this is a hundred times more than that of the surrounding seas and eight times more than that of the most productive regions of temperate seas.<sup>3,4</sup> A striking characteristic of the reefs is their diversity: they contain many more species than any other marine biotope. Coral reefs thus constitute a potentially very important natural asset. They are still practically untapped to this day but it can be safely predicted that they will be systematically exploited in years to come. It can only be hoped that massive exploitation will be delayed until reliable conservation rules are worked out through progress in reef ecology, a very complex field which is still in its prime infancy.

The reef environment ideally fulfills the needs of the marine natural products chemist. A maximum diversity of species provides the opportunity for practically unlimited chemical prospection. Furthermore, since reefs are necessarily located in clear, shallow waters, collecting can generally be effected without the need of very sophisticated equipment. These conditions certainly favour the pursuit of classical activities such as detection and study of potentially useful physiologically active compounds or the more academic search for structural novelties. Furthermore one should emphasize that many reef species seem to be strongly interdependent: the study of chemical interactions between these species constitutes a most challenging field of investigations.

Reefs are built by hermatypic corals (mainly Coelenterata, Hexacorallia) and calcareous algae. These provide the ecological niches that are occupied by a multitude of reef dweller species, forming one of the richest and most complex living communities on the planet. The reef-building hermatypic corals generally dominate in volume and in numbers but not necessarily in biomass, calcium carbonate being by very far their main production. Prominent amongst the sessile reef-dwellers is another group of coelenterates, the subclass Octocorallia. The most conspicuous of these are the familiar gorgonians or sea-fans (Order Gorgonacea), of world-wide distribution but whose metropolis is the Caribbean region,<sup>5</sup> and the alcyonaceans or soft corals (Order Alcyonacea) which are abundant in the Indo-Pacific region. In contrast to the hermatypic corals, possessing massive inorganic skeletons surrounded by a thin layer of living tissues, alcyonaceans have a skeleton consisting of minute calcareous spicules,

and their bulky, fleshy colonies yield large proportions of extractable organic matter. Indeed, alcyonaceans seem to be the largest single contributors to the biomass of many Indo-Pacific reefs, a view supported by recent careful reef transect studies.<sup>6</sup>

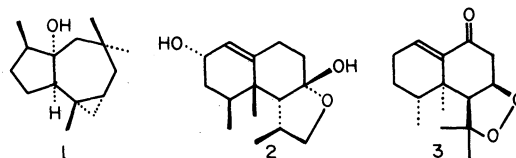
In addition to their ponderal importance, Octocorallia are remarkable by their ability to ward off algal and microbial growth and to prevent the settlement of larvae.<sup>7,8</sup> Alcyonaceans are submitted only to negligible grazing by large predators and all crude soft coral extracts tested so far were indeed highly unpalatable to a variety of reef fishes. The existence of such a set of diversified and effective chemical defenses having been surmised many years ago, it is not surprising that Octocorals have been one of the first marine groups to be the target of systematical chemical scrutiny.

Gorgonians, being within easy reach of well-established chemical laboratories, were naturally studied first. Within a few years they yielded a rich crop of novel and interesting compounds<sup>9</sup> including sterols,<sup>10</sup> prostaglandins,<sup>11</sup> butenolides,<sup>12</sup> sesquiterpenoid hydrocarbons,<sup>13</sup> cembranolide<sup>9,14</sup> and other<sup>15</sup> diterpenoids. Since a very large number of gorgonian species still remain to be investigated one can assume that these impressive results, in great part due to the group of the University of Oklahoma, are yet a *hors d'oeuvre* for other exciting findings to come.

Alcyonaceans are rather closely related to the Gorgonaceans and one could speculate that they would possibly yield their share of interesting molecules. The first results have not been discouraging and it is the purpose of this paper to report on the current situation in this field. In order to review present events it has been deemed necessary to mention a few compounds whose structures, although quite convincing, have not yet been established by unambiguous proof.

### SESQUITERPENES

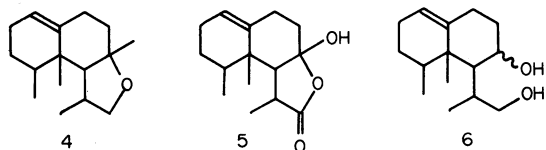
Africanol, C<sub>15</sub>H<sub>26</sub>O, has been isolated from *Lemnalia africana* collected at the island of Tanimbar, Southern Moluccas. It is the first representative of a novel sesquiterpene skeleton. Its structure (1) and absolute configuration were established by X-ray diffraction analysis.<sup>16</sup> Africanol has also been isolated from the related species *Lemnalia nitida*, also from Tanimbar.



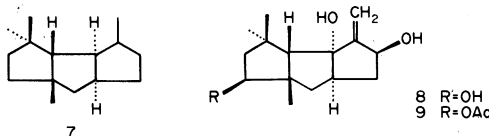
†Paper XV in the series: Chemical Studies of Marine Invertebrates. For paper XIV, see Ref. 21.

*Lamnalia carnosa*, collected at Leti Island, Southern Moluccas, yielded the novel sesquiterpene lemnacarnol,  $C_{15}H_{24}O_3$ , whose structure (2) and absolute configuration were also determined by X-ray diffraction.<sup>17</sup> Its carbon skeleton is antipodal to that of the known plant sesquiterpene nardosinone (3),<sup>18</sup> thus confirming the remarkable observation that "each of the sesquiterpenes isolated from marine coelenterates is the optical antipode of the form found, where known, in terrestrial plants".<sup>9</sup>

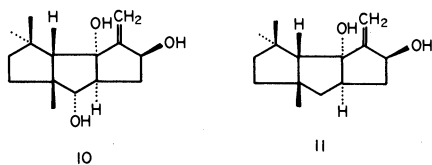
*Paralemnalia thyrsoides* from Tanimbar afforded two closely related compounds, 2-desoxylemnacarnol,  $C_{15}H_{24}O_2$  (4) and 2-desoxy-12-oxo-lemnacarnol,  $C_{15}H_{22}O_3$  (5) (also found in *Lemnalia africana* from Tanimbar). The structures of these compounds rest on chemical and spectral evidence. Compounds (4 and 5), upon treatment with lithium-aluminum hydride afford the same mixture of epimeric diols (6).<sup>19</sup>



*Capnella imbricata* contains an interesting mixture of polyhydroxylated sesquiterpenoids, all based upon the novel skeleton capnellane (7). The structure of  $\Delta^{9(12)}$ -capnellene-3 $\beta$ ,8 $\beta$ ,10 $\alpha$ -triol (8) was deduced from chemical and spectral evidence. It was independently established by single-crystal X-ray diffraction analysis, which also gave its stereochemistry and absolute configuration.<sup>20</sup> The structure proof of its naturally occurring 3-acetate (9) was quite straightforward.



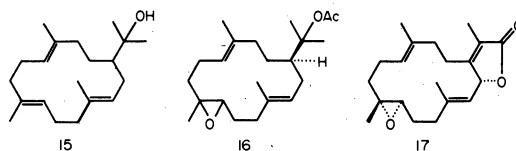
The structures of  $\Delta^{9(12)}$ -capnellene-5 $\alpha$ ,8 $\beta$ ,10 $\alpha$ -triol (10)  $\Delta^{9(12)}$ -capnellene-8 $\beta$ ,10 $\alpha$ -diol (11) and  $\Delta^{9(12)}$ -capnellene-2 $\xi$ ,8 $\beta$ ,10 $\alpha$ -triol (12) were deduced mainly from spectral evidence and confirmed by chemical correlation.<sup>21</sup> The main lines of the correlation were the obtention of the key intermediate (13) in seven steps from compound (8), four steps from compound (11) and seven steps from compound (10). A tetrol (14), whose spectral data indicate it is compound (8) with an additional primary hydroxyl group has also been isolated. Its structure has not yet been completely demonstrated. Our samples of *Capnella imbricata* come from the islands of Lakor, Masela, Sermata, Tanimbar and Leti, all in the Indo-Malay archipelago, and from Laing Island, Papua-New Guinea. All contain compound (11) but the presence and relative amounts of the other capnellane sesquiterpenoids have been found to vary considerably from population to population.



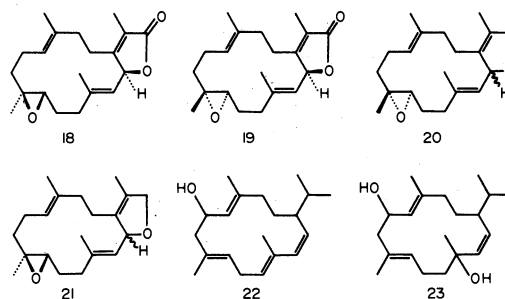
Another yet undescribed sesquiterpene has been obtained from the Xeniid *Cespitularia viridis*, collected in the Seychelles Islands. It is an isomer of africanol (1) and also contains a three membered carbon ring.

#### DITERPENES

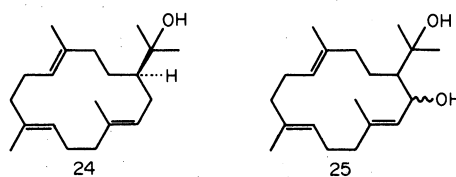
Schmitz, Vanderah and Ciereszko<sup>22</sup> have reported the structures of nephteno (15) and epoxynephtenol acetate (16) obtained from a *Nephtea* sp. collected at Eniwetok.



The cembranolide diterpene sarcophine (17) has been isolated by Israeli workers from *Sarcophyllum glaucum*, collected in the Red Sea. Its structure was established by X-ray diffraction analysis.<sup>23</sup> Sarcophine is a toxic material and its physiological action has been reported.<sup>24</sup> Mainly on the basis of spectral data, the same research group reported structures (18-23) for six additional diterpenes isolated from the same source, structure (23) being tentative.<sup>25</sup>

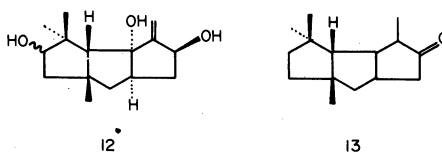


Nephtenol (15) has also been obtained from *Litophyton viridis*, collected at Leti Island, Southern Moluccas. In this instance, its absolute configuration was determined: it is (-)-nephtenol, depicted in structure (24). It is accompanied by 2-hydroxynephtenol  $C_{20}H_{34}O_2$  (25), whose structure rests on chemical and spectral evidence.<sup>26</sup>

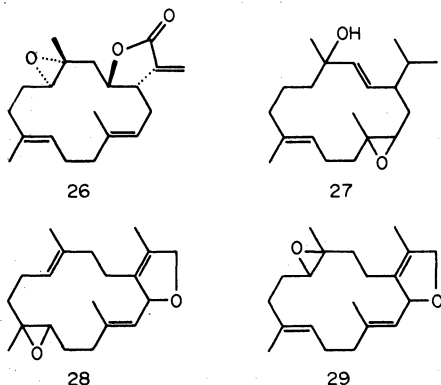


*Lobophyllum cristagalli*, also from Leti Island, yielded lobophytolide  $C_{20}H_{34}O_3$  (26), whose structure was established by chemical and spectral data. Its stereochemistry was obtained by X-ray diffraction analysis.<sup>27</sup>

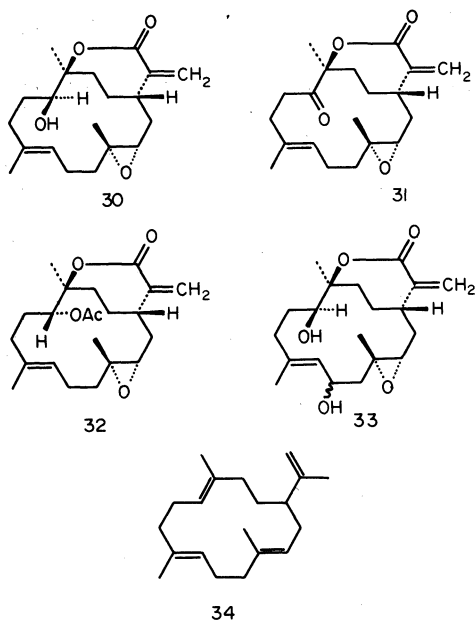
Colonies of *Sarcophyton trocheliophorum* collected in



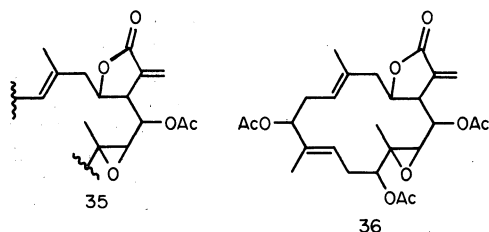
the Seychelles Islands contained the diterpene trocheliophorol  $C_{20}H_{34}O_2$  (27). Its structure was deduced from chemical and spectral evidence. This compound was not detected in specimens collected at Leti (Indonesia), which afforded two other compounds, sarcophytoxide  $C_{20}H_{30}O_2$  (28) (stereoisomer of (20 and 21)) and isosarcophytoxide  $C_{20}H_{30}O_2$  (29).<sup>28</sup> The structure of these compounds still await unambiguous demonstration.



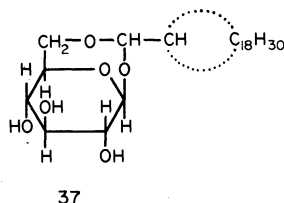
A series of close related cembranolides was isolated from *Sinularia flexibilis* collected at the islands of Leti and Kissar, in the Southern Moluccas. The structure of sinulariolide  $C_{20}H_{30}O_4$  (30) was obtained by chemical degradation and spectral data. It was independently established by X-ray diffraction analysis, which also yielded its stereochemistry and absolute configuration.<sup>29</sup> Sinulariolide is accompanied by 5-dehydrosinulariide (31), 5-episinulariide acetate (32) and 10 $\xi$ -hydroxy-sinulariide (33). A diterpene hydrocarbon that on the basis of its i.r., NMR and mass spectra appears to be cembrene-A (34)<sup>30</sup> has also been isolated from the same source.<sup>31</sup>



The highly oxygenated diterpene crassolide  $C_{26}H_{34}O_9$  has been isolated from *Lobophytum crassum*, collected at Leti Island. Its partial structure (35) has been established mainly by NMR decoupling experiments. All data in our possession point at structure (36) for crassolide.<sup>32</sup>



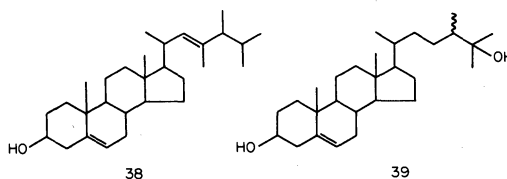
Only preliminary data are yet available for lemnalialoside  $C_{26}H_{42}O_6$ , obtained from *Lemnalia digitata*, collected at Tanimbar Kei, Indonesia. Hydrolysis indicates it consists of an aldehyde  $C_{20}H_{32}O$  attached to D-glucose by a rather unusual ketal linkage. NMR spectra of lemnalialoside and its derivatives indicate it is a  $\beta$ -glucoside with the partial structure (37). The aldehyde aglycone contains two double bonds, each substituted by a methyl group and is thus necessarily bicyclic. Lemnalialoside is the first example of an alcyonacean diterpene that does not belong to the cembrane group.<sup>33</sup>



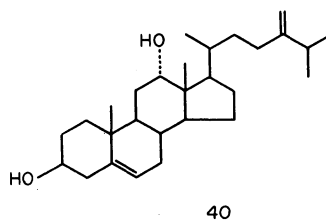
#### STEROLS

All alcyonaceans studied so far contain more or less complex mixtures of monohydroxysterols such as cholesterol, 24-methylcholesterol, 24-methylenecholesterol, brassicasterol, gorgosterol and other common marine sterols. They are often accompanied by minor compounds amongst which one could expect novel structures to be found. For instance 23,24-dimethylcholesta-5,22-dien-3 $\beta$ -ol (38) has recently been obtained by Japanese workers from *Sarcophyton elegans*.<sup>34</sup>

Di- and polyhydroxysterols are quite frequently encountered in soft corals, 25-hydroxy-24 $\xi$ -methylcholesterol (39) was isolated from *Sinularia mayi*, collected at Nias Island, near Sumatra.<sup>35</sup>

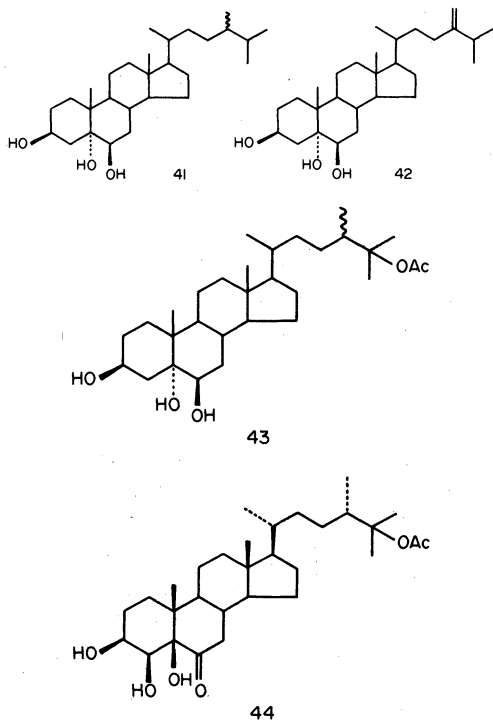


Another dihydroxysterol is 12 $\alpha$ -hydroxy-24-methylenecholesterol (40) obtained from *Litophyton viridis*, collected at Leti.<sup>36</sup>



Two triols, 24 $\xi$ -methylcholestane-3 $\beta$ ,5 $\alpha$ ,6 $\beta$ -triol (41) and 24-methylenecholestane-3 $\beta$ ,5 $\alpha$ ,6 $\beta$ -triol (42), each accompanied by its 6-monoacetate, were isolated from *Sinularia dissecta*, collected at Leti Island. Their structures have been established mainly by chemical correlation.<sup>37</sup> These compounds are closely related to 24 $\xi$ -methylcholestane-3 $\beta$ ,5 $\alpha$ ,6 $\beta$ ,25-tetrol 25-monoacetate (43), previously obtained from *Sarcophyton elegans* (collected in the Seychelles Islands) and whose structure was demonstrated by chemical and spectral arguments.<sup>38</sup>

A still further stage of sterol oxidation was found in lobsterol (44) obtained from *Lobophytum pauciflorum*, collected in the Seychelles. Its structure and absolute configuration were established by X-ray diffraction analysis.<sup>39</sup>



Alcyonaceans certainly constitute a rich source for polyhydroxysterols: many more compounds have been isolated and are at present under study.

#### DISTRIBUTION

So far, the occurrence of terpenoids in various alcyonacean genera can be summarized as in Table 1.

Some genera, like *Lemnalia*, contain representatives possessing either sesquiterpenes or diterpenes, but these two families of terpenoids have never yet been encountered together in the same species. Sesquiterpenes have been isolated only from the families Nephtheidae and Xenidiidae. These data should be interpreted only as preliminary indications since less than a hundred species have been subjected even to preliminary evaluation. Furthermore it is felt that only some of the most stable and most obvious compounds have been so far isolated. Many of the alcyonacean terpenoids are notoriously unstable and number of promising and abundant compounds have vanished between routine TLC screening on the reef and reception of the samples in the laboratory. Obvious artefacts have been isolated in some instances; they have not been mentioned in this text.

#### ORIGIN AND IMPLICATIONS

Like many coelenterates (in particular hermatypic corals, gorgonians and sea-anemones) most reef-dwelling alcyonaceans live in symbiosis with intracellular dinoflagellate algae known as zooxanthellae. This association is not passive and the existence of important chemical exchanges between the partners have been demonstrated.<sup>40</sup> Zooxanthellae play a prominent part in the ecology of a coral reef<sup>2,41</sup> and it appears that it is the availability of light that restricts the reefs to clear, shallow waters. At the depth limit, called compensation depth, illumination is such that the photosynthetic activity of the algae exactly compensates their respiratory activity.<sup>42</sup> The molecular aspects of such a symbiosis certainly constitute a most tantalizing field of research.

A growing body of evidence indicates that the xanthellae (alone or in conjunction with the coelenterate tissues) are responsible for the synthesis of the terpenoids encountered in the Alcyonaria.<sup>9,43</sup> Attempts to detect terpenoids in alcyonaceans that are devoid of xanthellae (such as the European *Alcyonium digitatum*) have consistently failed. The gorgonian *Eunicella stricta* which afforded the diterpene eunicelline<sup>15</sup> has a deep water form *Eunicella stricta aphyta* that is devoid of zooxanthellae.<sup>44</sup> Very careful examination of the form *aphyta* failed to detect the presence of eunicelline, although the chemical content of both forms appeared otherwise quite similar.<sup>45</sup>

If, as it would seem, xanthellae are indispensable for the production of terpenoids, then the study of these compounds might be quite irrelevant to the taxonomy of alcyonaceans but most important for the systematics of the symbiotic zooxanthellae themselves, a field which is today practically non-existent. Since the very existence of the coral reef ecosystem appears to rest on the association

Table 1. Distribution of terpenoids in alcyonaceans

	Sesquiterpenes	Diterpenes	Polyhydroxysterols
Fam. Alcyoniidae			
gen. <i>Lobophytum</i>		+	+
<i>Sarcophyton</i>		+	+
<i>Sinularia</i>		+	+
Fam. Nephtheidae			
gen. <i>Capnella</i>	+		
<i>Lemnalia</i>	+	+	
<i>Litophyton</i>		+	+
<i>Nephtea</i>		+	
<i>Paralemnalia</i>	+		
Fam. Xenidiidae			
gen. <i>Cespitularia</i>	+		

of xanthellae with coelenterate hosts, several questions do immediately come to the mind. Are there one or many species of xanthellae? If many, are the associations specific? If specific, are the associations exclusive? Unless one postulates a quite unprecedented biochemical plasticity, the great variety of terpenoids encountered so far pleads in favour of the existence of numerous species of xanthellae. Furthermore, the regularity of occurrence of given compounds in given alcyonacean species would indicate that the associations are specific, in agreement with the general principle that "two species with the same ecology cannot coexist".<sup>46</sup>

It has been commonly observed that alcyonaceans of the same species but from different localities contain different (but closely related) terpenoids. A compound can even be dominant in a given population and conspicuously absent from another. This could indicate that the same coelenterate host might accommodate several related varieties of xanthellae and that the associations are not necessarily exclusive. In the absence of firm premises, these views should yet be regarded as strictly speculative.

#### BIOLOGICAL SIGNIFICANCE

The obvious protection of Alcyonaceans towards large predators such as fish can be justified by the presence of toxic terpenoids. The LD<sub>50</sub> of sarcophine (17) for *Gambusia affinis* has been reported to be 3 mg/l.<sup>24</sup> Lethality tests on *Lebistes reticulatus* have shown that africanol (1) has a LD<sub>50</sub> of 4 mg/l, crassolide (36) a LD<sub>50</sub> of 7 mg/l and lobophytolide (26) a LD<sub>50</sub> of 12 mg/l.<sup>47</sup> Since feeding deterrent action would probably take place below lethal concentrations, alcyonaceans could be effectively protected by terpenoids occurring at concentrations below 0.001% and thus generally escaping routine isolation techniques.

No acute toxicity could be established for some abundant terpenoids such as the capnellenes (10 and 11), sinulariolide (30) and lemmalialoside (37). In contrast, these compounds have been shown to be powerful inhibitors of algal growth, minute concentrations completely preventing the growth of the unicellular algae *Chaetoceros septentrionalis*, *Asterionella japonica*, *Thalassiosira excentricus*, *Protocentrum micans* and *Amphidinium carterae*. The same activity was observed for africanol (1).<sup>48</sup> It is tempting to speculate that such compounds could be used to protect the specificity of the coelenterate-zooxanthellae associations.

#### REFERENCES

- <sup>1</sup>J. V. Wells, *Treatise on marine ecology and paleoecology* (1957).
- <sup>2</sup>C. M. Yonge, *The biology of coral reefs*, in: *Advances in Marine Biology*. Vol. 1 (1963).
- <sup>3</sup>A. J. Kohn and P. Helfrich, *Limnol. Oceanogr.* **2**, 241 (1957).
- <sup>4</sup>J. W. Kanwisher and S. A. Wainwright, *Biol. Bull.* **133**, 378 (1967).
- <sup>5</sup>F. M. Bayer, *The Shallow-Water Octocorallia of the West Indian Region*. The Hague (1961).
- <sup>6</sup>H. Mergner and H. Schuhmacher, *Helgoländer wiss. Meeresunters.* **26**, 238 (1974).
- <sup>7</sup>P. Burkholder and L. M. Burkholder, *Science* **127**, 1173 (1958).
- <sup>8</sup>L. S. Ciereszko, *Trans. N.Y. Acad. Sci.* **24**(2), 502 (1962).
- <sup>9</sup>L. S. Ciereszko and T. K. B. Karns. Comparative biochemistry of coral reef coelenterates, in: *Biology and Geology of Coral Reefs*. Vol. 2 (1), p. 183 (1973).
- <sup>10</sup>R. L. Hale, J. Leclercq, B. Tursch, C. Djerassi, R. A. Gross, A. J. Weinheimer, K. Gupta and P. J. Scheuer, *J. Am. chem. Soc.* **92**, 2179 (1970); N. C. Ling, R. L. Hale and C. Djerassi, *Ibid.* **92**, 5281, (1970); F. J. Schmitz and T. Pattabhiraman, *Ibid.* **92**, 6073 (1970); E. L. Enwall, D. Van Der Helm, I. Nan Hsu, T. Pattabhiraman, F. J. Schmitz, R. L. Spraggins and A. J. Weinheimer, *Chem. Comm.* 215 (1972).
- <sup>11</sup>A. J. Weinheimer and R. L. Spraggins, *Tetrahedron Lett.* 5185 (1969); G. L. Bundy, E. G. Daniels, F. H. Lincoln and J. E. Pike, *J. Am. chem. Soc.* **94**, 2124 (1972); W. P. Schneider, R. D. Hamilton and L. E. Rhuland, *J. Am. chem. Soc.* **94**, 2122 (1972); R. J. Light and B. Samuelsson, *Europ. J. Biochem.* **28**, 232 (1972).
- <sup>12</sup>F. J. Schmitz, K. W. Kraus, L. S. Ciereszko, D. H. Sifford and A. J. Weinheimer, *Tetrahedron Lett.* 97 (1966); F. J. Schmitz, E. D. Lorance and L. S. Ciereszko, *J. Org. Chem.* **34**, 1989 (1969); F. J. Schmitz and E. D. Lorance, *Ibid.* **36**, 719 (1971).
- <sup>13</sup>A. J. Weinheimer and P. H. Washecheck, *Tetrahedron Lett.* 3315 (1969); A. J. Weinheimer, P. H. Washecheck, D. Van Der Helm and B. Hossain, *Chem. Comm.* 1070 (1968); A. J. Weinheimer, W. W. Youngblood, P. H. Washecheck, T. K. B. Karns and L. S. Ciereszko, *Tetrahedron Lett.* 497 (1971); P. W. Jeffs and L. T. Lytle, *Lloydia*, **37**(2), 315 (1974).
- <sup>14</sup>A. J. Weinheimer, R. E. Middlebrook, J. O. Bledsoe, W. E. Marsico and T. K. B. Karns, *Chem. Comm.* 384 (1968); M. B. Hossain, A. F. Nicholas and D. Van Der Helm, *Chem. Comm.* 385 (1968); M. B. Hossain and D. Van Der Helm, *J. Am. chem. Soc.* **90**, 6607 (1968).
- <sup>15</sup>O. Kennard, D. G. Watson, L. Riva Di Sanseverino, B. Tursch, R. Bosmans and C. Djerassi, *Tetrahedron Lett.* 2879 (1968).
- <sup>16</sup>B. Tursch, J. C. Braekman, D. Dalozé, P. Fritz, A. Kelecom, R. Karlsson and D. Losman, *Tetrahedron Lett.* **9**, 747 (1974).
- <sup>17</sup>B. Tursch, M. Colin, D. Dalozé, D. Losman and R. Karlsson, *Bull. Soc. Chim. Belg.* **84**, 81 (1975).
- <sup>18</sup>G. Rücker, *Tetrahedron Lett.* 3615 (1968).
- <sup>19</sup>B. Tursch, P. Georget, J. C. Braekman and D. Dalozé, Unpublished data.
- <sup>20</sup>M. Kaisin, Y. M. Sheikh, L. J. Durham, C. Djerassi, B. Tursch, D. Dalozé, J. C. Braekman, D. Losman and R. Karlsson, *Tetrahedron Lett.* (26) 2239 (1974).
- <sup>21</sup>Y. M. Sheikh, G. Singy, M. Kaisin, H. Eggert, C. Djerassi, B. Tursch, D. Dalozé, J. C. Braekman, To be published.
- <sup>22</sup>F. J. Schmitz, D. J. Vanderah and L. S. Ciereszko, *Chem. Comm.* 407 (1974).
- <sup>23</sup>J. Bernstein, U. Schmeuli, E. Zadock, Y. Kashman and I. Neeman, *Tetrahedron* **30**, 2817 (1974).
- <sup>24</sup>I. Neeman, L. Fishelson and Y. Kashman, *Toxicon* **12**, 593 (1974).
- <sup>25</sup>Y. Kashman, E. Zadock and I. Neeman, *Tetrahedron* **30**, 3615 (1974).
- <sup>26</sup>B. Tursch, J. C. Braekman and D. Dalozé, *Bull. Soc. Chim. Belg.* **84** (7), 767 (1975).
- <sup>27</sup>B. Tursch, J. C. Braekman, D. Dalozé, M. Herin and R. Karlsson, *Tetrahedron Lett.* 3769 (1974).
- <sup>28</sup>B. Tursch, P. Cornet, J. C. Braekman and D. Dalozé, Unpublished data.
- <sup>29</sup>B. Tursch, J. C. Braekman, D. Dalozé, M. Herin, R. Karlsson and D. Losman, *Tetrahedron* **31**, 129 (1975).
- <sup>30</sup>V. D. Patil, U. R. Nayar and Sukh Dev, *Tetrahedron* **29**, 341 (1973).
- <sup>31</sup>B. Tursch and M. Herin, Unpublished data.
- <sup>32</sup>B. Tursch, J. C. Braekman, D. Dalozé and H. Dedeurwaerder, Unpublished data.
- <sup>33</sup>B. Tursch, J. C. Braekman, C. Charles, D. Dalozé, M. Herin, A. Kelecom and M. Van Haelen, Unpublished data.
- <sup>34</sup>A. Kanazawa, S. Teshima, T. Ando and S. Tomita, *Bull. Jap. Soc. Sci. Fish.* **40**(7), 729 (1974).
- <sup>35</sup>J. P. Engelbrecht, B. Tursch and C. Djerassi, *Steroids* **20**(1), 121 (1972).
- <sup>36</sup>B. Tursch, J. C. Braekman, D. Dalozé and P. Wautelet, Unpublished data.
- <sup>37</sup>B. Tursch, M. Bortolotto, J. C. Braekman and D. Dalozé, *Bull. Soc. Chim. Belg.* **85**, 27 (1976).
- <sup>38</sup>M. Moldowan, B. Tursch and C. Djerassi, *Steroids* **24**(3), 387 (1974).
- <sup>39</sup>C. Hootele, M. Kaisin, B. Tursch, D. Losman and R. Karlsson, To be published.
- <sup>40</sup>L. Muscatine, *Science*, **156**, 516 (1967); L. Muscatine and E.

- Cernichiari, *Biol. Bull.* **137**, 506 (1969); D. Smith, L. Muscatine and D. Lewis, *Biol. Rev.* **44**, 17 (1969); C. Von Holt and M. Von Holt, *Comp. Biochem. Physiol.* **24**, 73, 83 (1968).
- <sup>41</sup>T. F. Goreau, N. I. Goreau and C. M. Yonge, *Biol. Bull.* **141**, 247 (1971).
- <sup>42</sup>R. H. Ryther, *Deep Sea Res.* **2**, 134 (1954).
- <sup>43</sup>J. R. Rice, C. Papastephanou and D. Anderson, *Biol. Bull.* **138**, 334 (1970).
- <sup>44</sup>J. Theodor, *Vie et Milieu* **20** (3A), 635 (1969).
- <sup>45</sup>B. Tursch and M. Kaisin, Unpublished data.
- <sup>46</sup>A. Macfayden, *Animal Ecology*. p. 206. Pitman, New York (1963).
- <sup>47</sup>B. Tursch and M. Colin, Unpublished data.
- <sup>48</sup>B. Tursch and C. Van Beveren, Unpublished data.