Quinone/Hydroquinone Sesquiterpenes

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Abstract: The quinone/hydroquinone sesquiterpenes of drimane or rearranged drimane skeletons constitute a wide and diverse group of secondary metabolites of mixed biogenesis. These compounds are mainly of marine origin and their interest is not only for the variety of isolated structure but for the interesting biological activities that they present.

In this paper a series of quinone/hydroquinone sesquiterpenes of natural origin that have been reported to date is presented. The structures of these compounds are gathered into eight groups with reference to their biological activities and compounds synthesised.

Keywords: Sesquiterpenes quinone/hydroquinone, drimane, rearranged drimane.

Sesquiterpene quinones/hydroquinones having a normal drimane skeleton or a rearranged drimane skeleton, represent a prominent class of mixed biogenesis metabolites that incorporate a bicyclic sesquiterpene unit coupled to a quinone or quinol [1]. Those compounds have attracted the attention of researchers both through the abundance of structural variants and the wide range of remarkable biological properties ascribed to specific samples [2]. Although most sesquiterpene quinones/hydroquinones have been isolated from sponges, some of them have been reported from brown algae [3] and at least three compounds were described from a fungus [4-6].

We present herein a compilation of the naturally occurring sesquiterpene quinones/hydroquinones, whose terpenoid unit is bicyclic, that have been isolated to date. The following collection comprises a listing of structures, along with tables that include the source of isolation, biological activities and the literature source. Some compounds have also been synthesised and these are marked with an asterisk.

• Listing of Structures

In the first part of this review all the structures are shown. Each one is accompanied with its trivial name and is numbered. The compounds are presented in an order reflecting biogenetic pathways.

All the sesquiterpene quinones/hydroquinones presented in the review possess a drimane or rearranged drimane skeleton (Fig. **1**). We propose the name avarane and aureane for the rearranged skeletons considering the first compound isolated in each group (avarol/avarone [7] and aureol [8] respectively). Aureane and avarane skeletons arise from 1,2 rearrangements of the drimane skeleton. Within the avaranes two groups have been established owing to the fact that there is a large number of this class of compounds. The first one includes the avaranes Δ^3 and the second one the avaranes $\Delta^{4(13)}$ (*trans* fusion in decalin system) or $\Delta^{4(14)}$ (*cis* fusion in decalin system).

Compounds within this review have been organized in eight groups according to the sesquiterpene skeleton. Groups one to four are classified in accordance with their biogenetic evolution from the drimane skeleton:

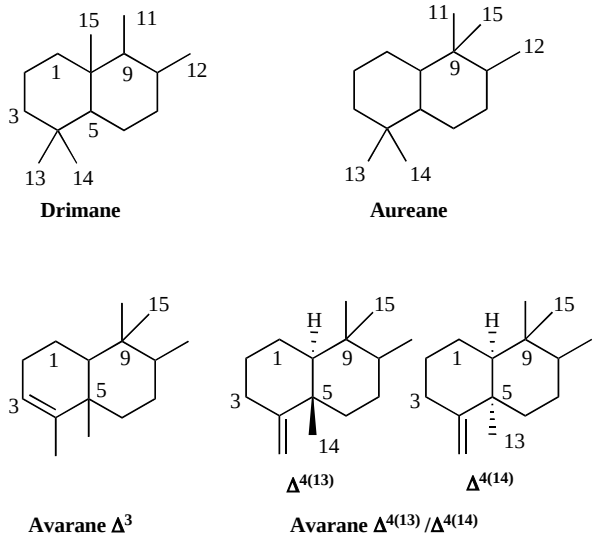

Fig. (1). Sesquiterpene skeletons.

- **Drimanes (Fig. 2)**
- **Aureanes (Fig. 3)**
- **Avaranes Δ^3 (Fig. 4)**
- **Avaranes $\Delta^{4(13)}/\Delta^{4(14)}$ (Fig. 5)**

Tetracarbocyclics (Fig. **6**). In this group are collected compounds with two C-C bonds between the sesquiterpene terpenoid and the quinone/quinol ring.

Norsesquiterpenes quinone/hydroquinone (Fig. **7**). Compounds in this group not only posses one less carbon than sesquiterpenes quinone/hydroquinone, but also have tetracarbocyclic skeletons and a furan ring annelated to rings A and B.

Other rearranged skeletons (Fig. **8**). Compounds in which the rearrangement of the sesquiterpene skeleton is unusual or because the ring B is expanded.

Dimers and related compounds (Fig. **9**). compounds that comprise two molecules of a quinoid moiety each linked to a rearranged drimane sesquiterpene and connected by an amino group, ether or C-C bond.

Within the drimanes, aureanes and avaranes (Δ^3 and $\Delta^{4(13)}/\Delta^{4(14)}$), structures possessing a quinone ring and a hydroqui-

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none ring have been distinguished in two different subgroups and every effort has been made, wherever possible, to present the aromatic subunits in increasing order of substitution. After the structure diagrams, one table for each group, is presented (Tables **1-8**), giving the trivial names and numbers of along with the natural source of isolation, the biological activity. In the third part of the review those sesquiterpene quinones/hydroquinones that have been synthesized are given together with the starting material for the synthesis of each one (Fig. (**10**)).

Quinones

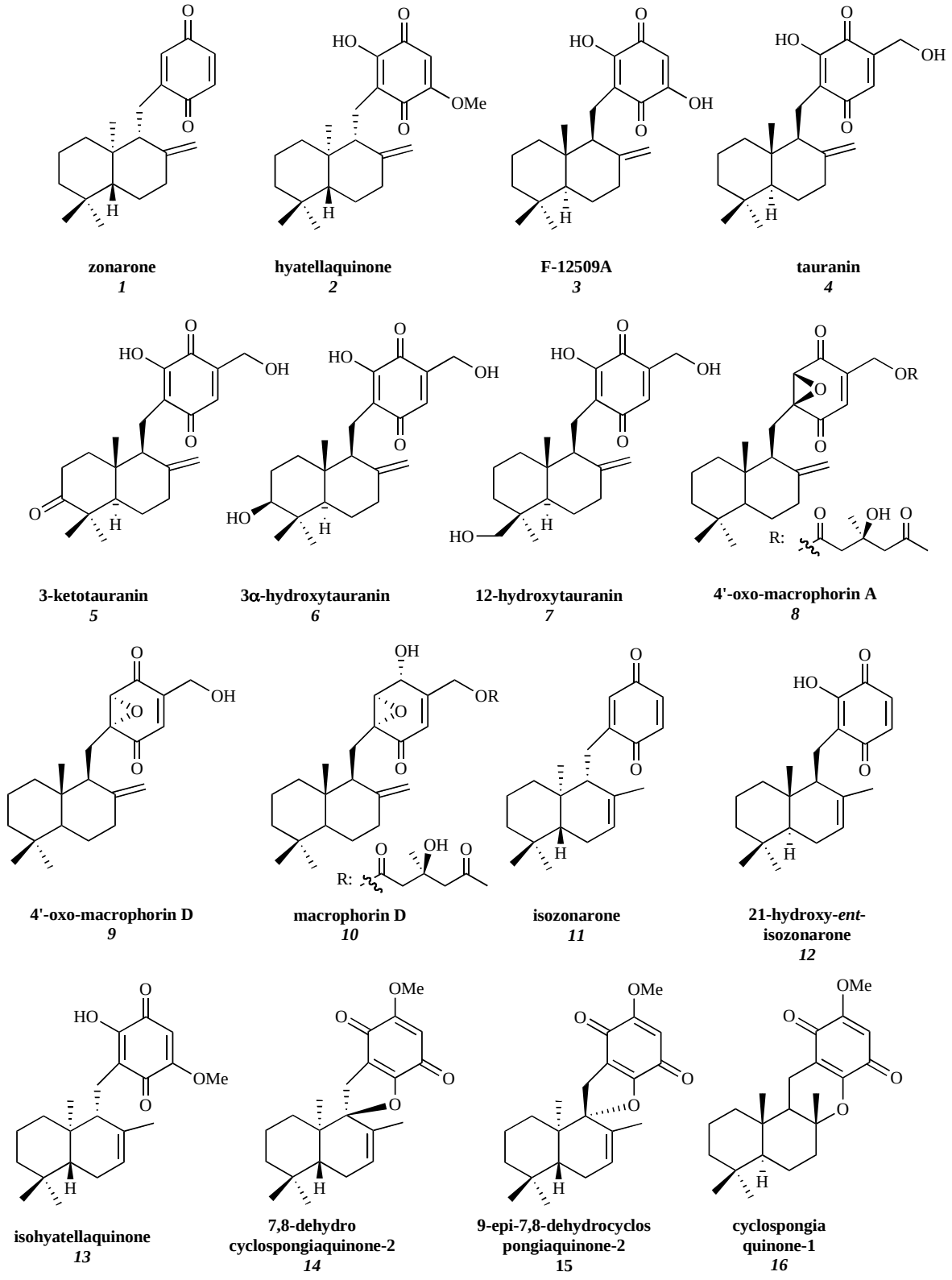
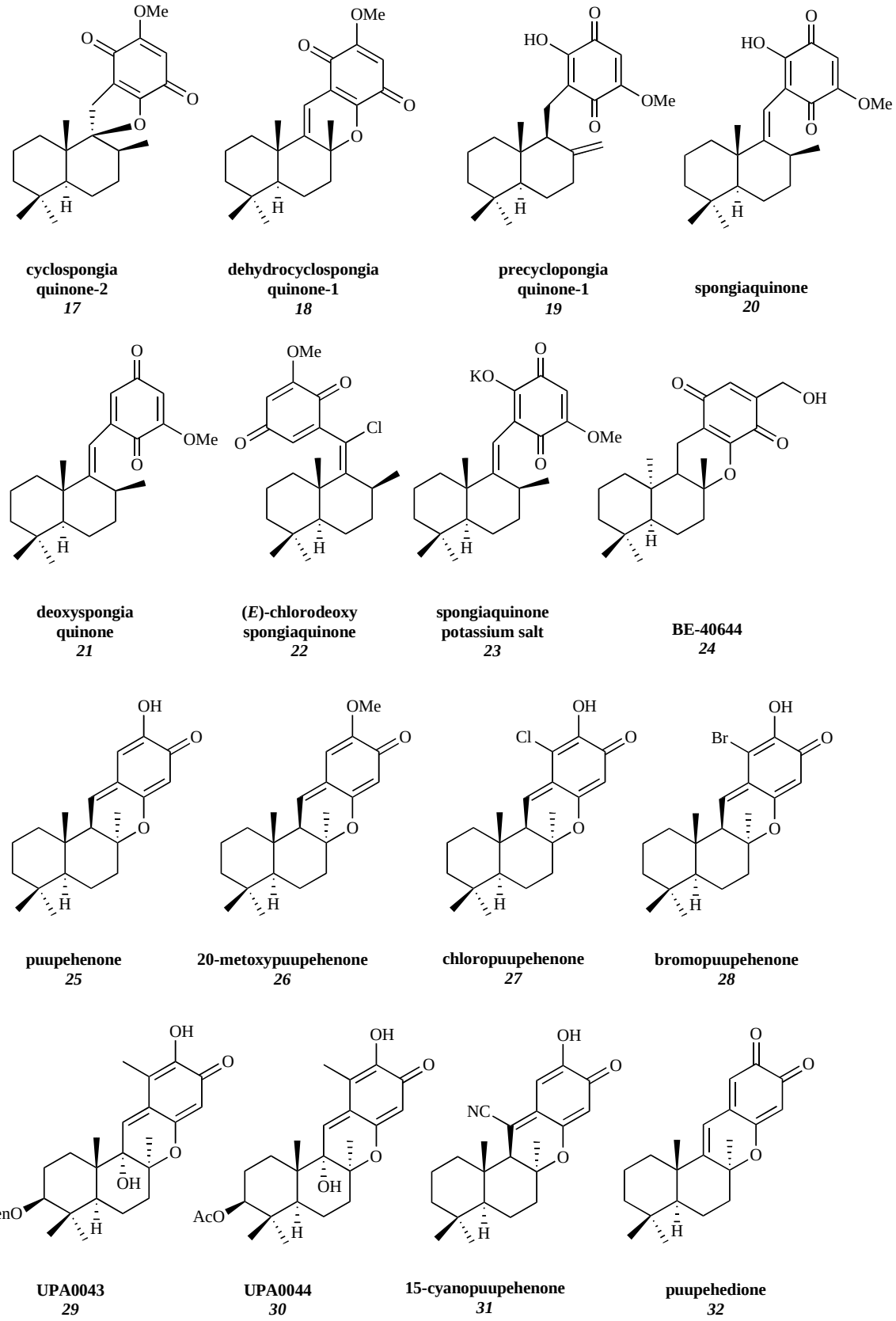


Fig. (2). Drimanes . ***Quinones***. Compounds **1** to **16**.

Fig. (2). contd...

Quinones



cyclospongia quinone-2 ***17***

dehydrocyclospongia quinone-1 ***18***

precyclopongia quinone-1 ***19***

spongiaquinone ***20***

deoxyspongia quinone ***21***

(*E*)-chlorodeoxy spongiaquinone ***22***

spongiaquinone potassium salt ***23***

BE-40644 ***24***

puupehenone ***25***

20-metoxypuupehenone ***26***

chloropuupehenone ***27***

bromopuupehenone ***28***

UPA0043 ***29***

UPA0044 ***30***

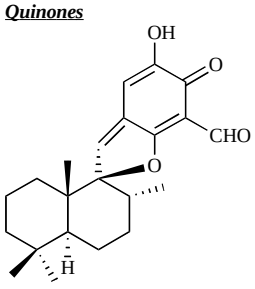
15-cyanopuupehenone ***31***

puupehedione ***32***

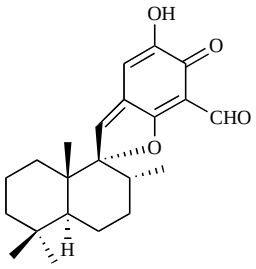
Fig. (2). Drimanes . ***Quinones***. Compounds **17** to **32**.

Fig. (2). contd...

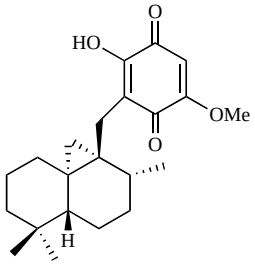
Quinones



corallidictyal A
33



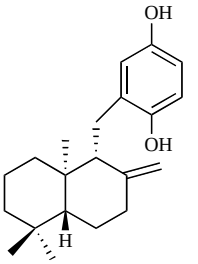
corallidictyal B
34



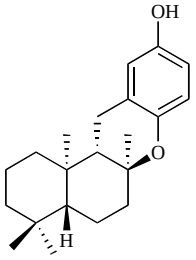
dictyoceratidaquinone
35

Fig. (2). Drimanes . ***Quinones***. Compounds **33** to **35**.

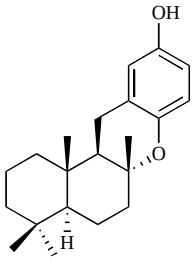
Hydroquinones



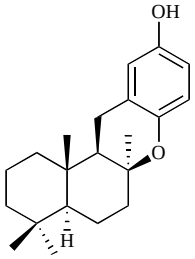
zonarol
36



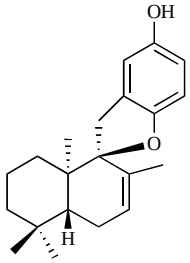
chromazonarol
37



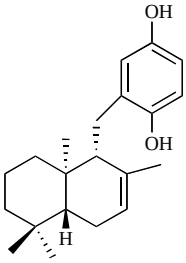
***ent*-chromazonarol**
38



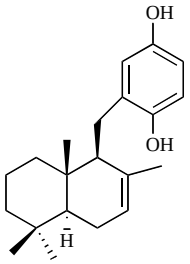
8-epi-chromazonarol
39



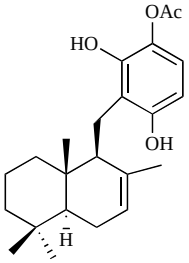
isochromazonarol
40



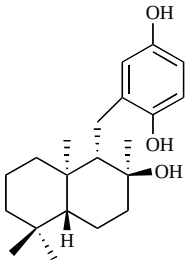
isozonarol
41



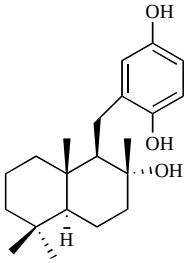
***ent*-isozonarol**
42



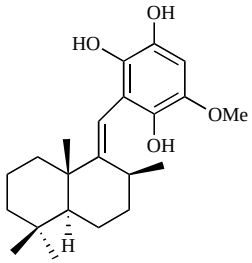
20-O-acetyl-21-hydroxy-*ent*-isozonarol
43



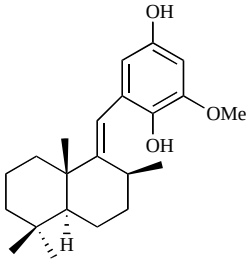
yahazunol
44



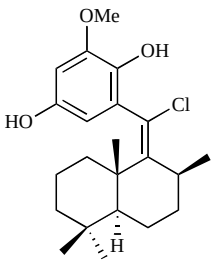
***ent*-yahazunol**
45



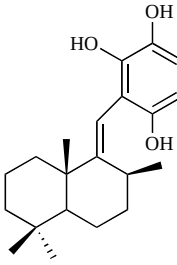
spongiaquinol
46



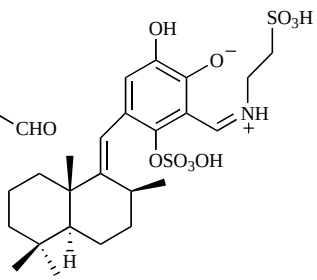
deoxyspongiaquinol
47



(*E*)-chlorodeoxy spongiaquinol
48



siphonodictyal-B
49

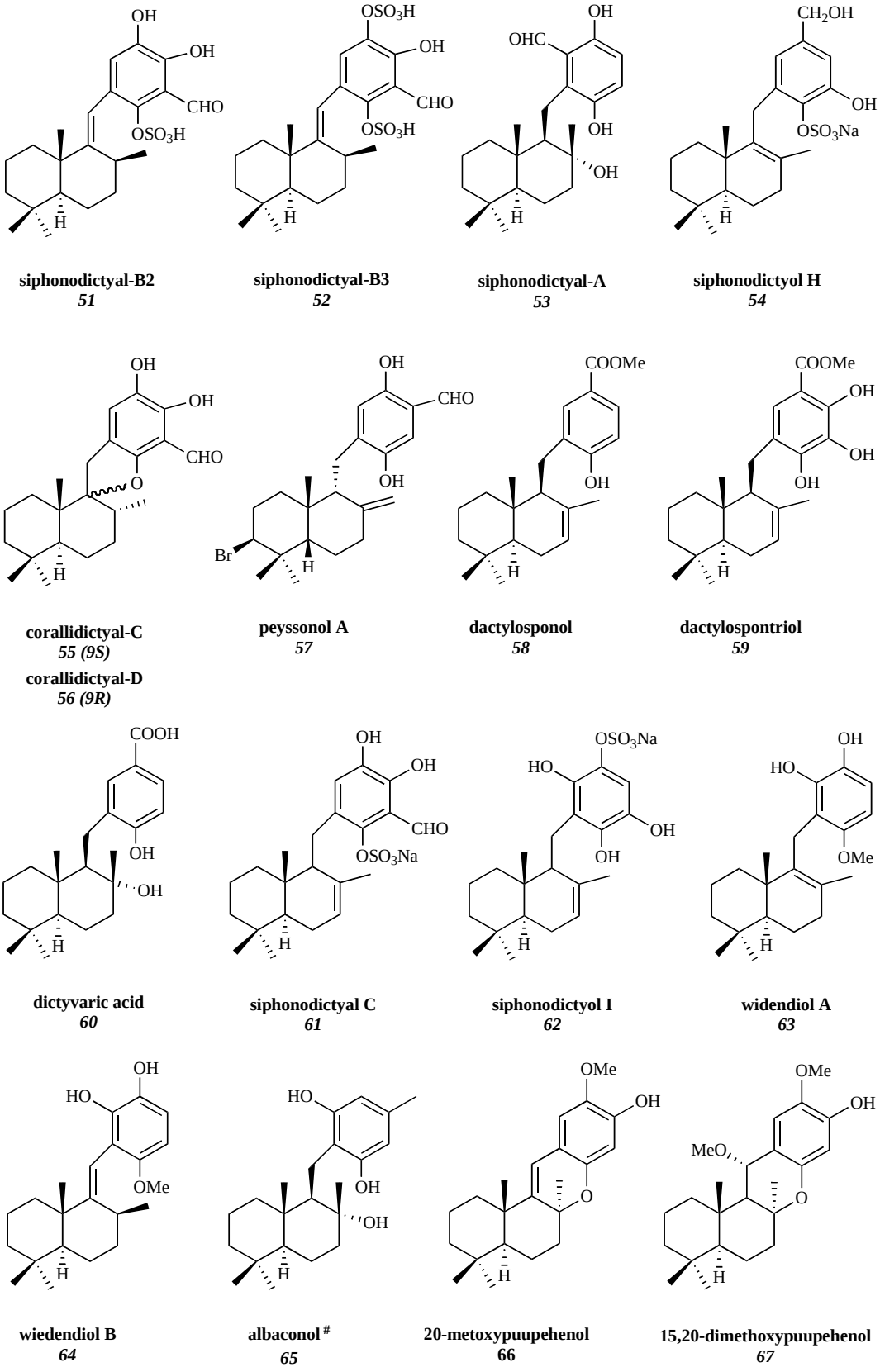


siphonodictyal-B1
50

Fig. (2). Drimanes . ***Hydroquinones***. Compounds **36** to **50**.

Fig. (2). contd...

Hydroquinones



siphonodictyal-B2
51

siphonodictyal-B3
52

siphonodictyal-A
53

siphonodictyol H
54

corallidictyal-C
55 (9S)

corallidictyal-D
56 (9R)

peyssonol A
57

dactylosponol
58

dactylospontriol
59

dictyvaric acid
60

siphonodictyal C
61

siphonodictyol I
62

widendiol A
63

wiedendiol B
64

albaconol [#]
65

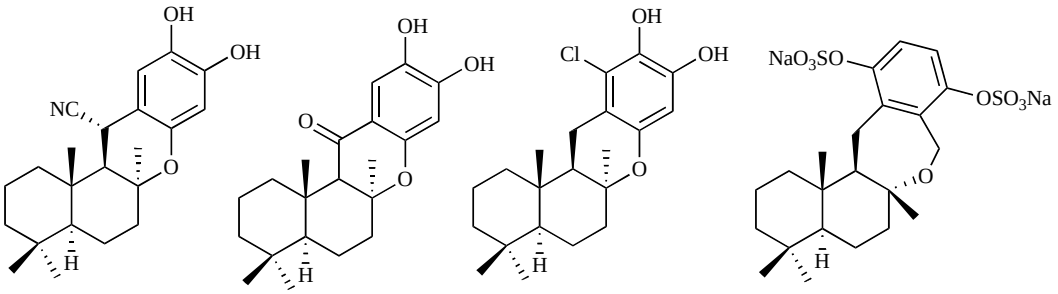
20-metoxypuupehenol
66

15,20-dimethoxypuupehenol
67

Fig. (2). Drimanes . ***Hydroquinones***. Compounds **51** to **67**.

Fig. (2). contd...

Hydroquinones



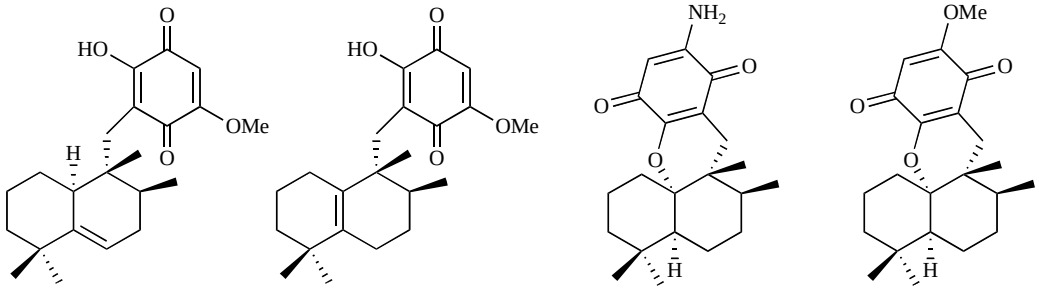
15-cyanopuupehenol
68

15-oxopuupehenol
69

21- chloropuupehenol
70

***bis*(sulfate)-cyclosiphonodictyol A**
71

Fig. (2). Drimanes. ***Hydroquinones***. Compounds **68** to **71**.



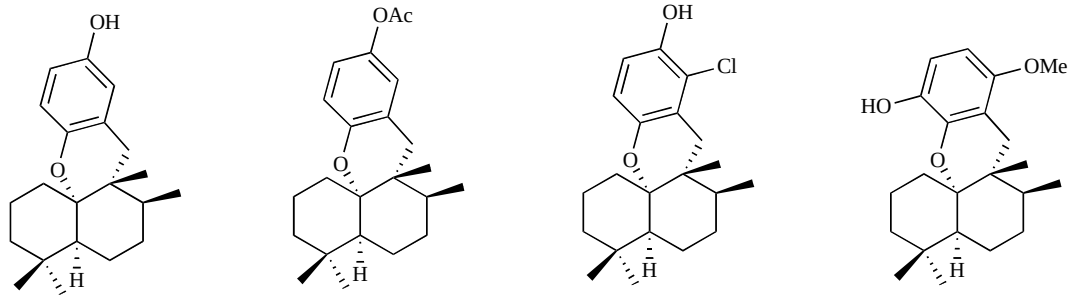
(-)-mamanuthaquinone
72

neomamanuthaquinone
73

cyclosmenospongine
74

smenoqualone
75

Fig. (3). Aureanes. ***Quinones***. Compounds **72** to **75**.

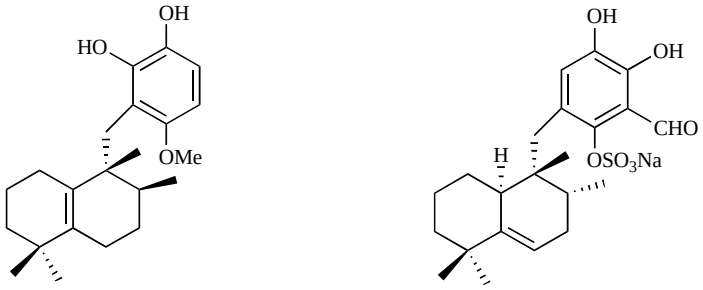


aureol
76

aureol acetate
77

6'-chloroaureol
78

strongylin A
79



sesquiterpene hydroquinone
80

siphonodictyal D
81

Fig. (3). Aureanes. ***Hydroquinones***. Compounds **76** to **81**.

Quinones

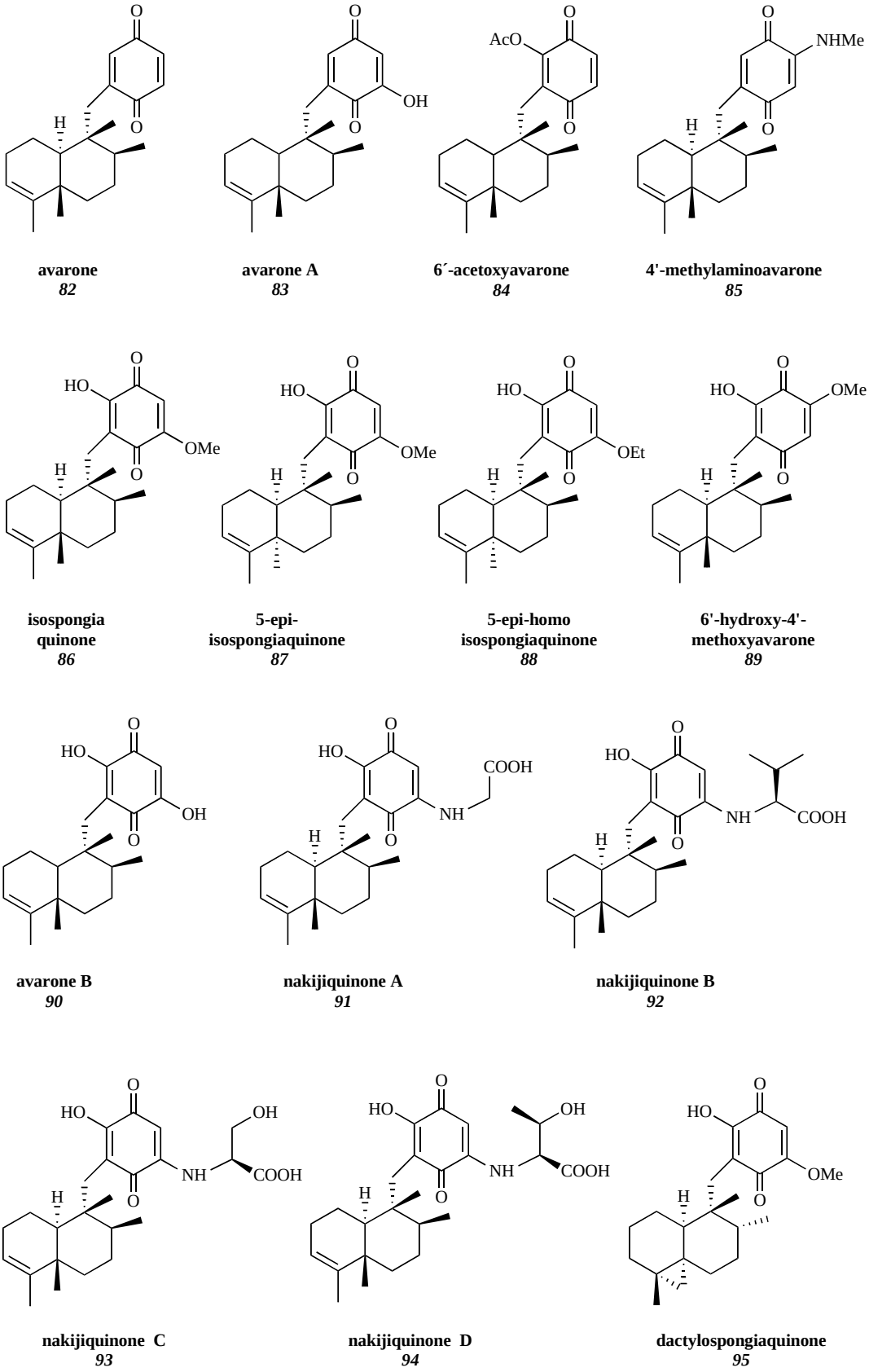
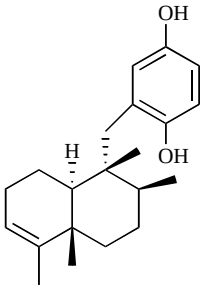


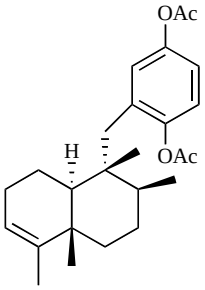
Fig. (4). Avaranes Δ^3. *Quinones*. Compounds **82** to **95**.

Fig. (4). contd...

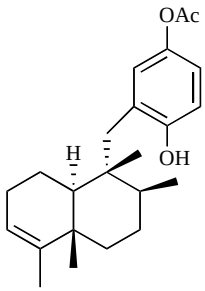
Hydroquinones



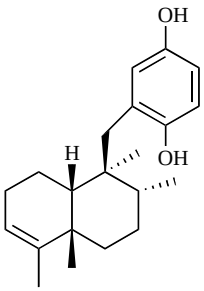
avarol
96



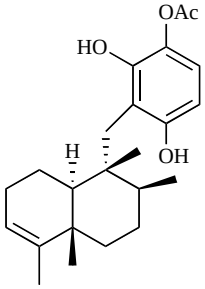
diacetylavarol
97



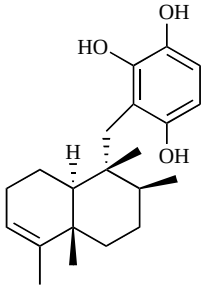
20-*O*-acetylavarol
98



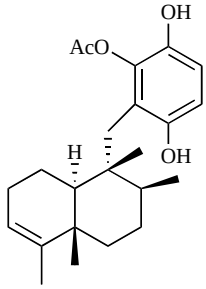
isoarenarol
99



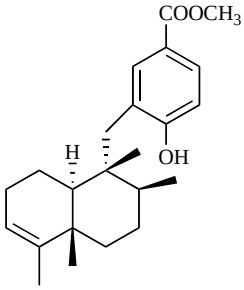
6'-hydroxy-5'-acetylavarol
100



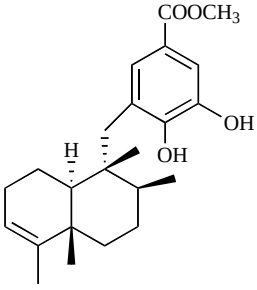
6´-hydroxyavarol
101



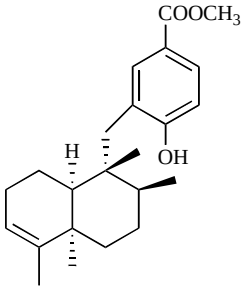
6´-acetoxyavarol
102



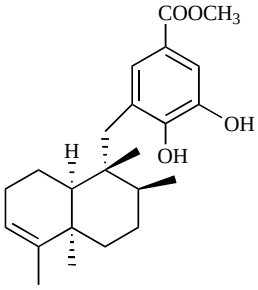
hyrtiophenol [#]
103



18-hydroxyhyrtiophenol
104



5-epi-hyrtiophenol [#]
105



18-hydroxy-5-epi-hyrtiophenol
106

Fig. (4). Avaranes Δ^3. *Hydroquinones*. Compounds **96** to **106**.

[#] Compounds that although are not strictly sesquiterpene quinones/hydroquinones are included in the review due to their structural similarity with the main class.

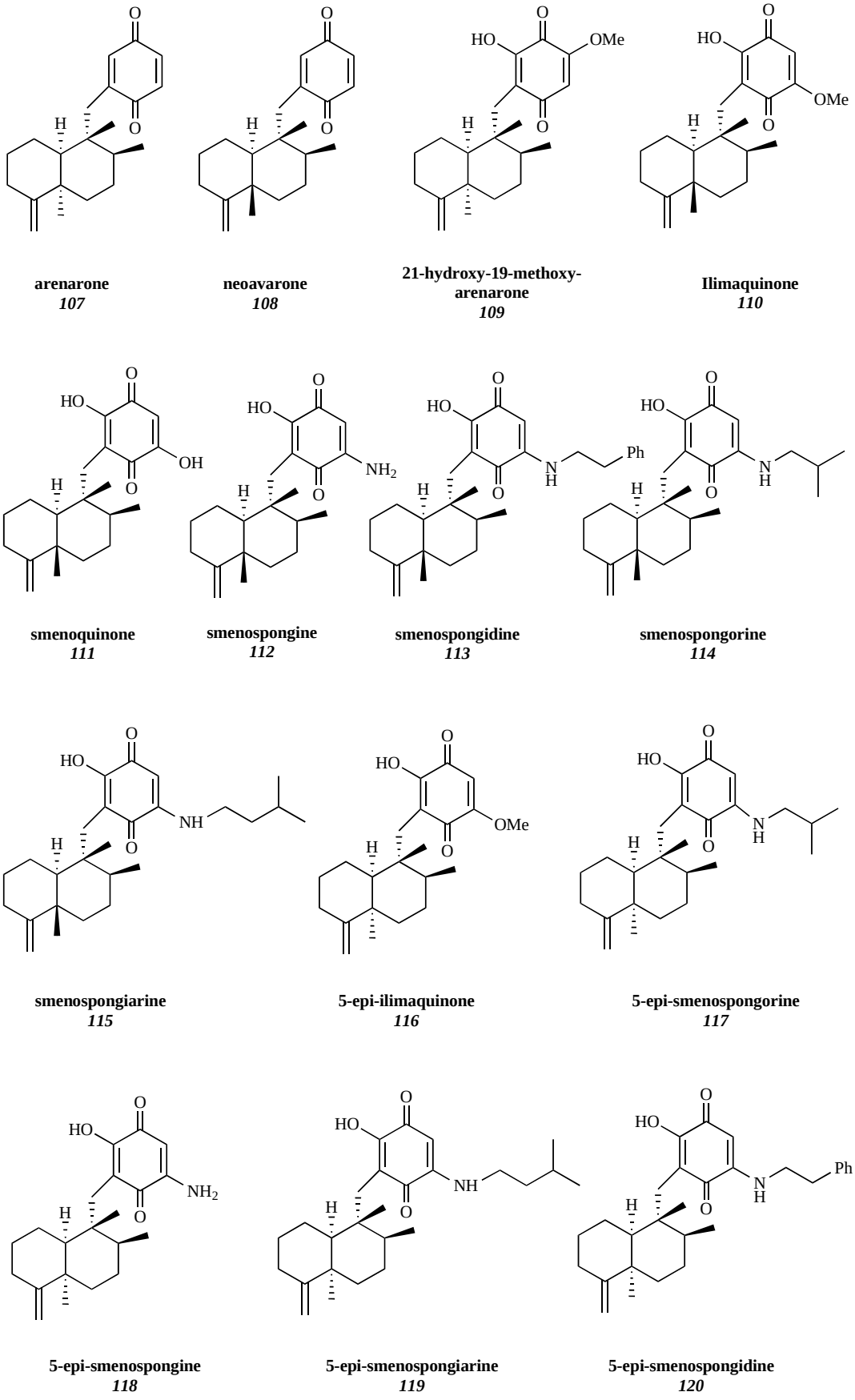
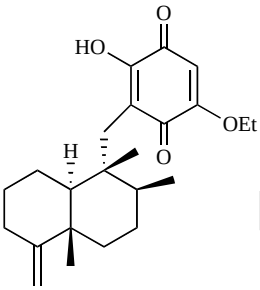


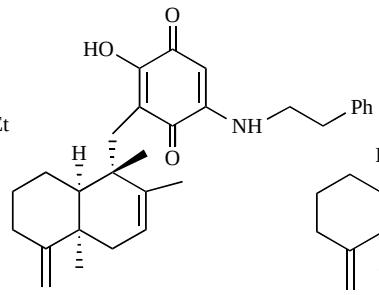
Fig. (5). Avaranes $\Delta^{4(14)}$/ $\Delta^{4(13)}$. *Quinones*. Compounds **107** to **120**.

Fig. 5). contd...

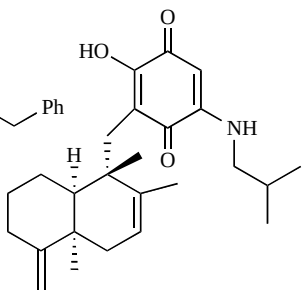
Quinones



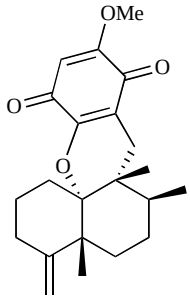
smenorthoquinone
121



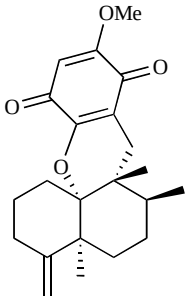
episменospongidine
122



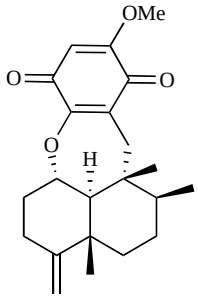
episменospongiarine
123



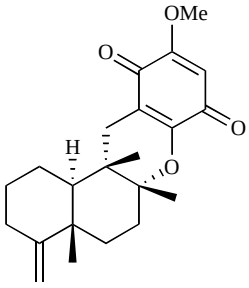
dactyloquinone A
124



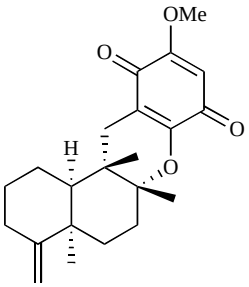
dactyloquinone B
125



dactyloquinone C
126



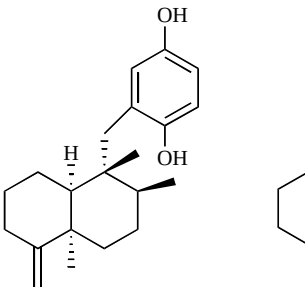
dactyloquinone D
127



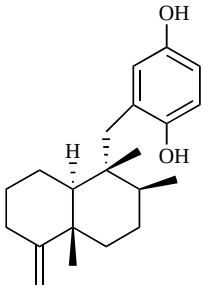
dactyloquinone E
128

Fig. (5). Avaranes $\Delta^{4(14)}$/ $\Delta^{4(13)}$. ***Quinones***. Compounds **121** to **128**.

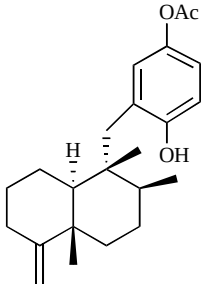
Hydroquinones



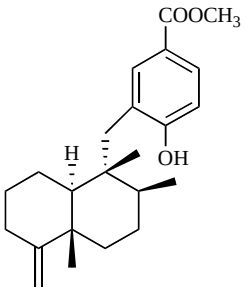
arenarol
129



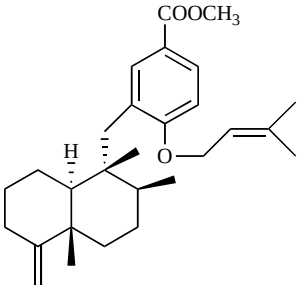
neoavarol
130



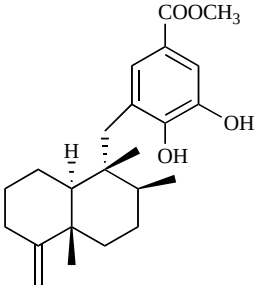
20-*O*-acetyl-neoavarol
131



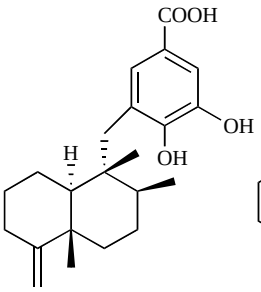
dictyoceratin C [#]
132



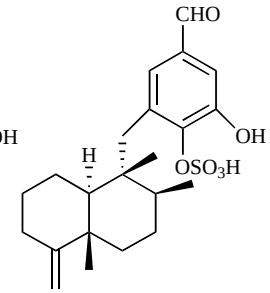
***O*-isoprenyl dictyoceratin C** [#]
133



smenospondiol o dictyoceratin A
134

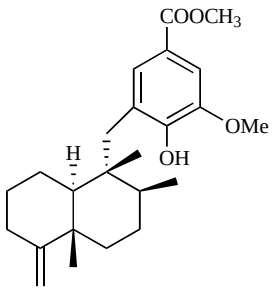


syphonodictyoic acid
135

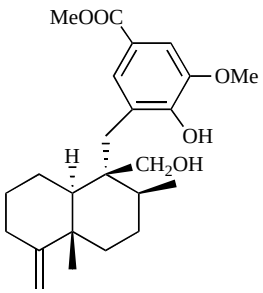


siphonodictyal G
136

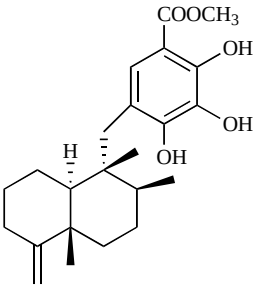
Fig. (5). contd...



polyfibrospongol A
137



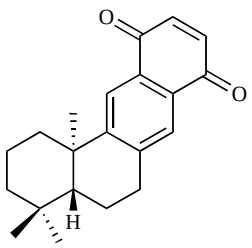
polyfibrospongol B
138



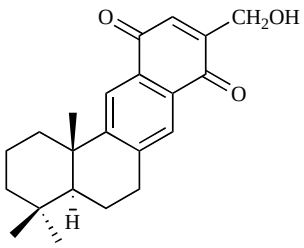
dictyoceratin B
139

Fig. (5). Avaranes $\Delta^{4(14)}$/ $\Delta^{4(13)}$. *Hydroquinones*. Compounds **129** to **139**.

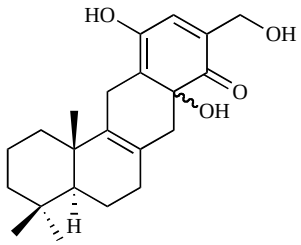
[#] Compounds that although are not strictly sesquiterpene quinones/hydroquinones are included in the review due to their structural similarity with the main class.



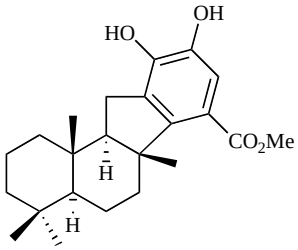
cyclozonarone
140



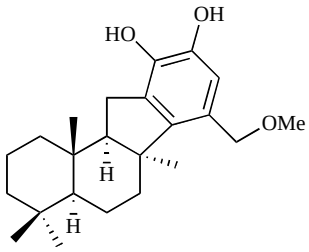
(+)-(5*S*,10*S*)-4'-hydroxy methylcyclozonarone
141



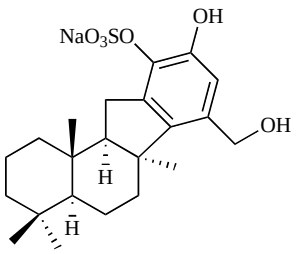
phyllospinarone
142



pelorol
143

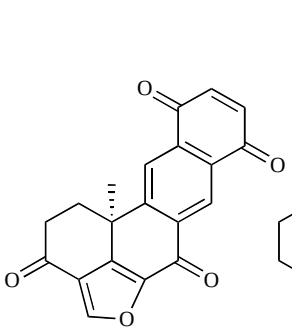


akaol A
144

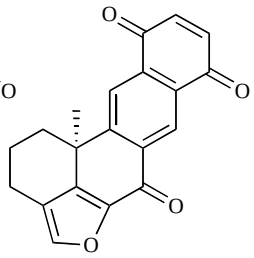


akaol B
145

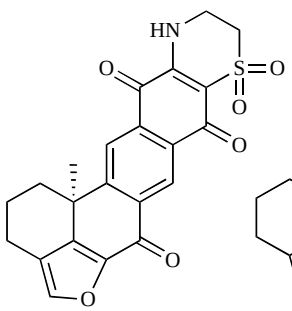
Fig. (6). Tetracarbocyclic. Compounds **140** to **145**.



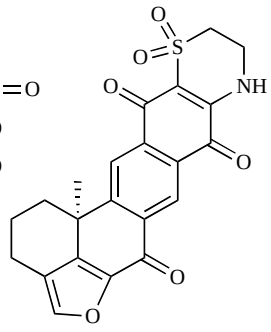
halenaquinone
146



xestoquinone
147

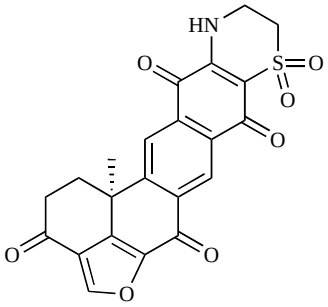


adociaquinone A
148

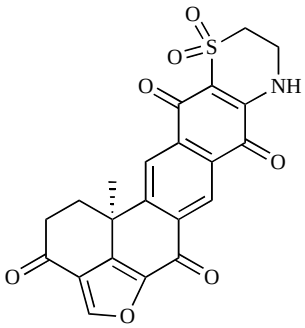


adociaquinone B
149

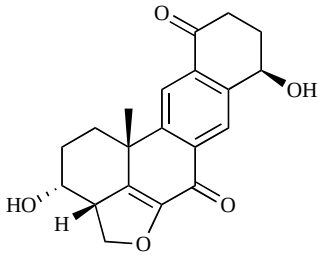
Fig. (7). contd...



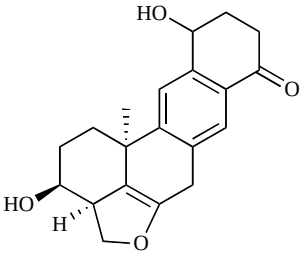
3-ketoadociaquinone A
150



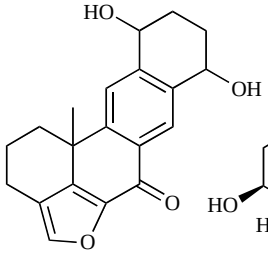
3-ketoadociaquinone B
151



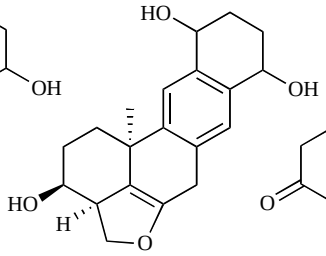
3,13-dideoxo-1,2,14,15-tetrahydro-3,13-dihydroxy-halenaquinone
152



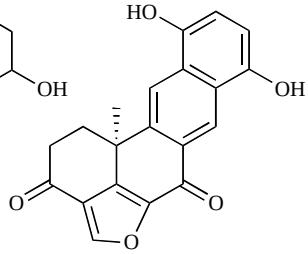
xestosaprol A
153



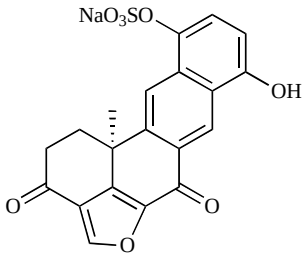
13,14,15,16-tetrahydroxestoquinol
154



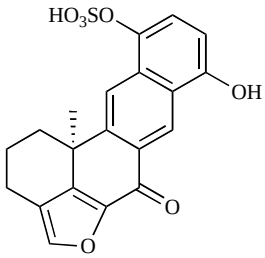
xestosaprol B
155



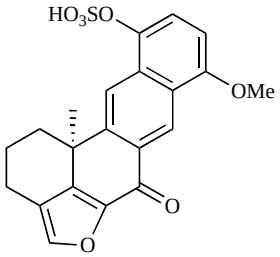
halenaquinol
156



halenaquinol sulfate
157

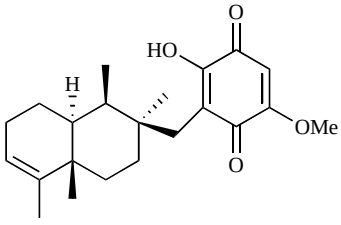


xestoquinol sulfate
158

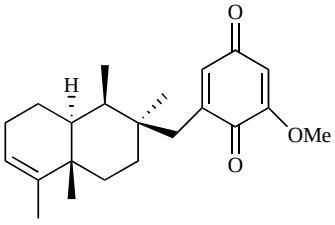


13-*O*-methyl xestoquinol sulfate
159

Fig. (7). Norsesquiterpene quinones/hydroquinone. Compounds **146** to **159**.



bolinaquinone
160



21-dehydroxybolinaquinone
161

Fig. (8). contd...

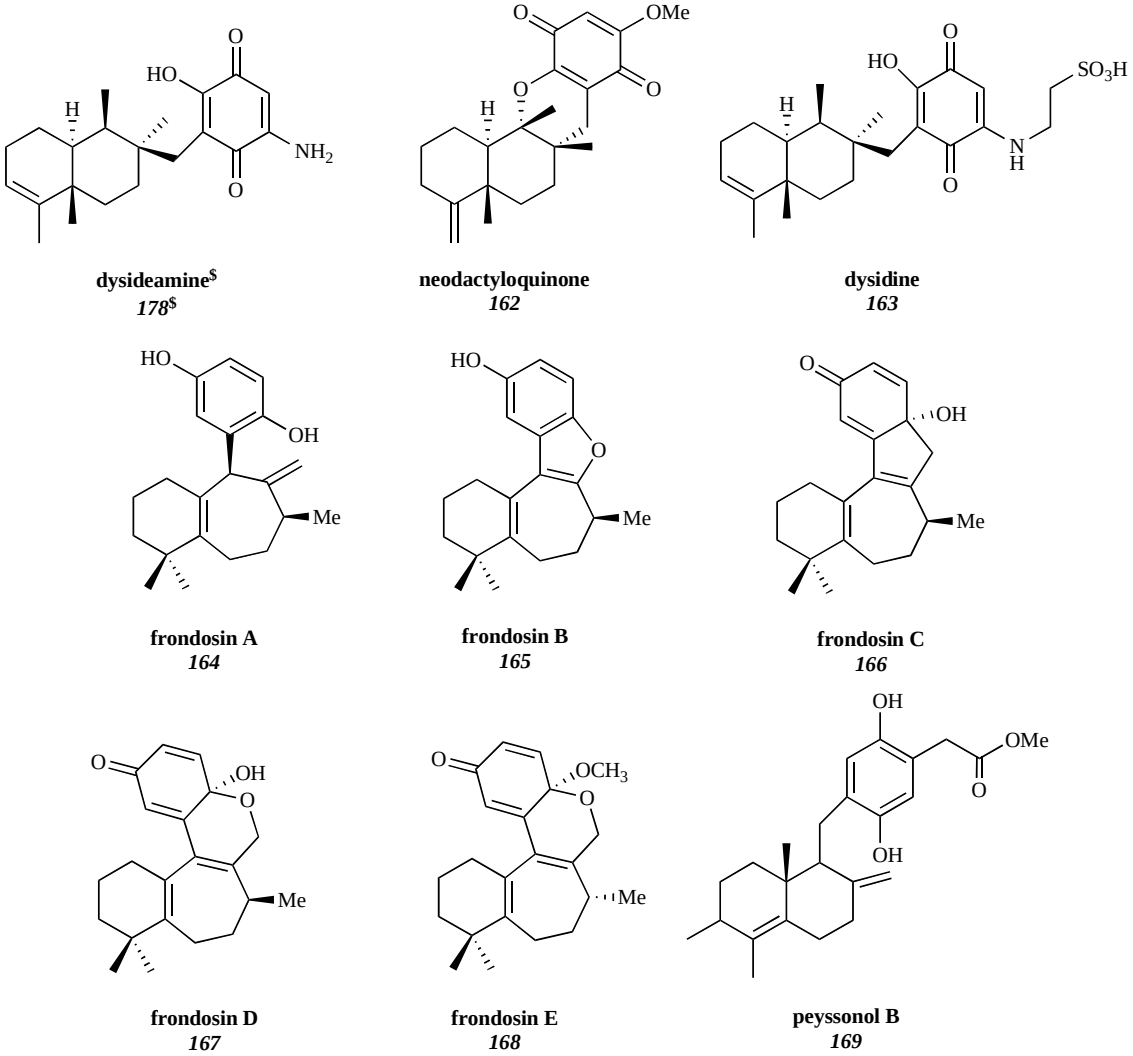


Fig. (8). Other rearranged skeleta. Compounds **160** to **169**.

$ Compound **178** was isolated during the preparation of this paper. For this reason it appears with a number out of the order both in the structure listing and in the tables.

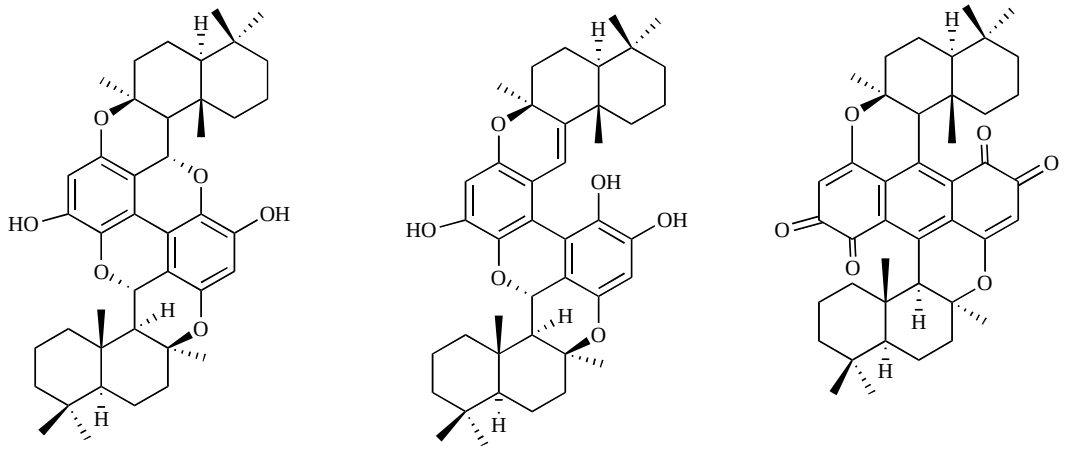
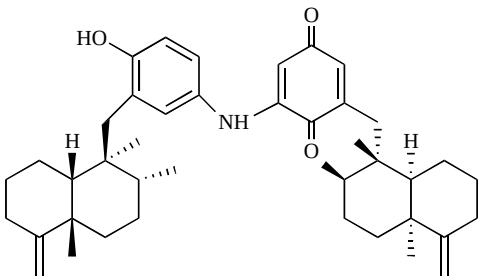
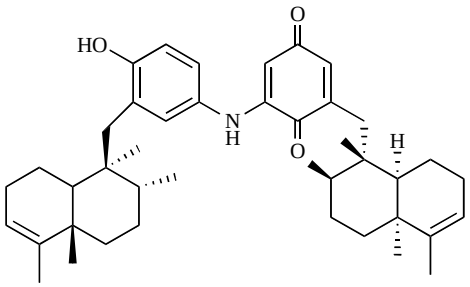


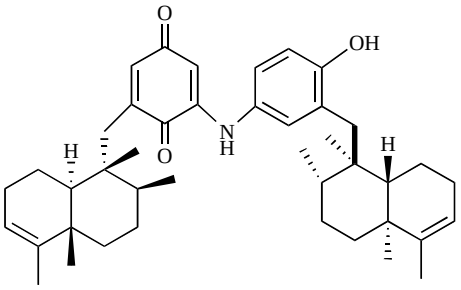
Fig. (9). contd...



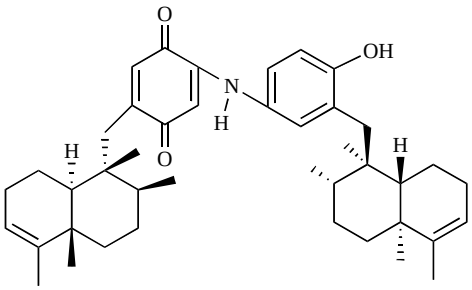
popolohuanone A
173



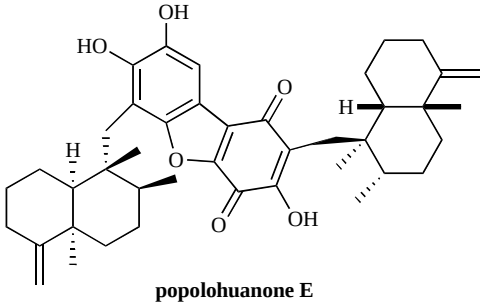
popolohuanone B
174



popolohuanone C
175



popolohuanone D
176



popolohuanone E
177

Fig. (9). Dimers and related compounds. Compounds **170** to **177**.

Table 1. Drimanes

Sesquiterpene-Quinone	Marine Source	Activity	References
Quinones			
zonarone, ***1*** *	*Dictyoperis undulada*	Antiinflammatory	[9-14]
hyatellaquinone, ***2*** *	*Hyatella intestinalis* *Dactylospongia elegans* *Peyssonnelia sp.* *Spongia sp.*	Anti HIV Cytostatic Cytotoxic Antiproliferative Antiinflammatory	[12, 15-21]
F-12509A, ***3*** *	*Trichopezizella barbata*	Sphingosine Kinase inhibitor	[2, 6, 22, 23]
tauranin, ***4***	*Phyllosticta spinarum*	Antitumour Inhibits cholesterol biosynthesis	[17, 24]
3-ketotauranin, ***5***	*Phyllosticta spinarum*		[24]
3α-hydroxytauranin, ***6***	*Phyllosticta spinarum*		[24]
12-hydroxytauranin, ***7***	*Phyllosticta spinarum*		[24]
4'-oxo-macrophorin A, ***8***	*Eupenicillium crustaceum*	Immunosuppressive	[4, 25]
4'-oxo-macrophorin D, ***9***	*Eupenicillium crustaceum*	Immunosuppressive	[4, 25]
macrophorin D, ***10***	*Eupenicillium crustaceum*		[25]

Table 1. Contd…

Sesquiterpene-Quinone	Marine Source	Activity	References
isozonarone, ***11*** *	*Dictyoperis undulada*	Antiinflammatory	[9-14]
21-hydroxy-*ent*-isozonarone, ***12***	*Dysidea cf.Cristagalli*	Antiinflammatory Inhibits superoxide production by human neutrophils	[26-28]
isohyatellaquinone, ***13***	*Dactylospongia* *Dactylospongia elegans*		[16]
7,8-dehydrocyclospongiaquinone-2, ***14***	*Dactylospongia elegans*		[16]
9-epi-7,8-dehydrocyclospongiaquinone-2, ***15***	*Dactylospongia elegans*		[16]
cyclospongiaquinone-1, ***16***	*Stelospongia conulata* *Dactylospongia sp.* *Dactylospongia elegans*		[29-32]
cyclospongiaquinone-2, ***17***	*Stelospongia conulata* *Dactylospongia sp.*		[16, 29, 30]
dehydrocyclospongiaquinone-1, ***18***	*Stelospongia conulata* *Southern Australian spongia sp.* *Dactylospongia sp.*		[16, 29, 30]
precyclospongiaquinone-1, ***19***	*Spongia sp.*		[1]
spongiaquinone, ***20*** *	*Stelospongia conulata* *Southern Australian spongia sp.* *Dactylospongia sp.*	Cytostatic Cytotoxic Antiproliferative Antiinflammatory	[12, 16, 21, 29, 30, 33]
deoxyspongiaquinone, ***21***	*Euryspongia*		[34-36]
(*E*)-chlorodeoxyspongiaquinone, ***22***	*Euryspongia*		[34-36]
spongiaquinone potassium salt, ***23***	*Spongia sp.*		[19]
BE-40644, ***24***	*Actinoplanes sp.*	Inhibitor of the human thieredoxin system	[34]
puupehenone, ***25*** *	*Sponge order Verongida* *Dysidea*	Antitumour Antiviral Antimalarial Antibiotic Immuno modular Antituberculosis	[14, 17, 19, 20, 32, 35, 37-44]
20-methoxypuupehenone, ***26***	*Hyrtios sp.*		[32, 33]
chloropuupehenone, ***27***	*Sponge order Verongida*	Antitumour Antiviral Antimalarial Antibiotic Inmuno modular	[17, 19, 38, 39]
bromopuupehenone, ***28***		Antitumour Antiviral Antimalarial Antibiotic Inmuno modular	[17, 39]
UPA 0043, ***29***		Antibiotic	[176]
UPA 0044, ***30***		Antibiotic	[176]
15-cyanopuupehenone, ***31***	*Sponge order Verongida*		[17, 19, 42]
puupehedione, ***32*** *	*Sponge order Verongida*		[17, 19, 45]
corallidictyal A, ***33***	*Aka coralliphagum*		[46, 47]
corallidictyal B, ***34***	*Aka coralliphagum*		[46, 47]
dictyoceratidaquinone, ***35***	*Dictyoceratid sponge* *Dactylospongia elegans*		[16]
Hydroquinones			
zonarol, ***36***	*Dictyopteris undulada* *Dictyopteris zonaroides*	Antiinflammatory	[9-15, 48]
chromazonarol, ***37***	*Dictyopteris undulada*		[13]
ent-chromazonarol, ***38*** *	*Dysidea pallescens*		[20, 49, 50]

Table 1. Contd…

Sesquiterpene-Quinone	Marine Source	Activity	References
8-epi-chromazonarol, ***39***	*Dysidea pallescens*		[1]
isochromazonarol, ***40***	*Dysidea sp.*		[16, 182]
isozonarol, ***41*** *	*Dictyopteris undulada* *Dictyopteris zonaroides* *Dysidea*	Antiinflammatory	[9, 10, 11, 12, 13, 48]
ent-isozonarol, ***42*** *	*Dysidea*	Antitumour	[49, 51]
20-O-acetyl-21-hydroxy-*ent*-isozonarol, ***43***	*Dysidea cf.cristagalli* *Dysidea* genus	Antiinflammatory Cytotoxic	[26, 27, 28]
yahazunol, ***44*** *	*Dictyoperis undulada*		[9, 10, 14, 27, 52, 53]
ent-yahazunol, ***45***	*Dysidea* genus		[27, 28, 51]
spongiaquinol, ***46***	*Euryspongia*		[34, 36]
deoxispongiaquinol, ***47***	*Euryspongia*		[34, 35, 36]
(*E*)-chloro-deoxyspongiaquinol, ***48***	*Euryspongia*		[34, 35, 36]
siphonodictyal-B, ***49***	*Siphonodictyon coralliphagum*	Antimicrobial	[54, 55, 56, 177]
siphonodictyal-B1, ***50***	*Aka coralliphagum*		[2, 47]
siphonodictyal-B2, ***51***	*Aka coralliphagum*		[2, 47]
siphonodictyal-B3, ***52***	*Aka coralliphagum*		[2, 47]
siphonodictyal-A, ***53***	*Siphonodictyon coralliphagum*		[54, 57]
siphonodictyol H, ***54***	*Aka sp.*		[1, 56, 57]
corallidictyal C, ***55***	*Aka coralliphagum*		[2, 47]
corallidictyal D, ***56***	*Aka coralliphagum*		[2, 47]
peyssonol A, ***57***	*Peyssonnelia sp.* *Hyatella intestinalis*		[15, 18]
dactylosponol, ***58***	*Dactylospongia elegans*	Cytotoxic	[58, 59]
dactylospontriol, ***59***	*Dactylospongia elegans*	Cytotoxic	[58, 59]
dictyvaric acid, ***60***	*Dictyopteris divaricada*		[60, 61]
siphonodictyal C, ***61*** *	*Siphonodictyon coralliphagum*	Antimicrobial	[12, 33, 54, 56, 57]
siphonodictyol I, ***62***	*Aka sp.*		[33, 57]
wiedendiol A, ***63*** *	*Xestospongia wiedemayeri*	Cholesteryl ester transport protein inhibitor	[2, 12, 49, 62-68]
wiedendiol B, ***64*** *	*Xestospongia wiedemayeri*	Cholesteryl ester transport protein inhibitor Antiinflammatory Cyclooxiganase 2 inhibitor	[12, 37, 49, 62-66, 69, 177]
albaconol, ***65***	*Albatrellus confluens*		[5, 25]
20-methoxypuupehenol, ***66***	*Hyrtios sp.*		[32, 33]
15,20-dimethoxypuupehenol, ***67***	*Hyrtios sp.*		[32, 33]
15-cyanopuupehenol, ***68***	Sponge genus *Hyrtios*	Antitumour Antiviral Antimalarial Antibiotic Inmuno modular	[17, 39, 42]
15-oxopuupehenol, ***69*** *	Sponge genus *Hyrtios*	Antitumour Antimalarial Antiviral Antibiotic Inmuno modular	[17, 27, 39, 42, 62, 64, 70]
21-chloropuuphehenol, ***70***	*Hyrtios* genus	Antitumour Antimalarial	[42, 64]
bis(sulfate)-cyclosiphonodictyol, ***71***	*Siphonodictyon coralliphagum*	Antiinflammatory	[71]

Table 2. Aureanes

Sesquiterpene-Quinone	Marine Source	Activity	References
Quinones			
(-)-mamanuthaquinone, ***72***	*Dactylospongia elegans*		[16, 72, 74, 75]
neomamanuthaquinone, ***73***	*Dactylospongia*	Antiinflammatory Cytotoxic Antiproliferative	[12, 16, 73, 76, 77]
cyclosmenospongine, ***74***	*Spongia* sp.	Antimicrobial Cytotoxic Antitumour	[33, 77, 78]
smenoqualone, ***75***	*Smenospongia* sp.		[58, 77, 79]
Hydroquinones			
aureol, ***76*** *	*Smenospongia aurea*	Cytotoxic against A549 non small cell lung cancer cell Anti-influenza A virus	[8, 14, 73, 80-88, 183]
aureol acetate, ***77***	*Smenospongia aurea*		[14, 86]
6'-chloroaureol, ***78***	*Smenospongia aurea*	Antimicrobial	[14, 19, 86]
strongylin A, ***79***	*Strongyliphora hartmani*		[65, 89]
sesquiterpene hydroquinone, ***80***			[12]
siphonodictyal D, ***81***	*Siphonodictyon coralliphagum*	Antimicrobial	[56]

Table 3. Avaranes Δ^3

Sesquiterpene-Quinone	Marine Source	Activity	References
Quinones			
avarone, ***82*** *	*Dysidea avara* *Dysidea cf.cristagalli*	Antiviral Anti HIV I Antiinflamaatory Antileukemic	[7, 20, 26, 34, 35, 49, 55, 59, 84, 90-99, 181]
avarone A, ***83***	*Dysidea cinerea*	Anti- HIV I	[100, 101]
6´-acetoxiavarone, ***84***	*Dysidea cinerea*	Anti- HIV I	[100]
4'-methylaminoavarone, ***85***	*Dysidea avara*		[63]
isospongiaquinone, ***86*** *	*Stelospongia conulata* *Hyrtios tubulatus*		[16, 29, 30, 59, 77, 102, 103, 104]
5-epi-isospongiaquinone, ***87***	*Spongia hispida*	Antibiotic	[30, 58, 73, 105]
5-epi-homoisospongia quinone, ***88***	*Spongia hispida*		[105]
6'-hydroxy-4'-methoxyavarone, ***89***	*Dysidea cinerea*		[100, 101]
avarone B, ***90***	*Dysidea cinerea*		[100, 101]
nakijiquinone A, ***91*** *	*Spongiidae*	Antifungal Antiviral Cytotoxic	[18, 75, 106, 179]
nakijiquinone B, ***92*** *	*Spongiidae*	Antifungal Antiviral Cytotoxic	[18, 75, 179]
nakijiquinone C, ***93*** *	*Spongiidae*	Inhibitory activity against c-erbB-2 kinase Inhibitory activity of Her-2/Neu protooncogen Antiviral Cytotoxic	[20, 62, 64, 75, 104, 178]
nakijiquinone D, ***94*** *	*Spongiidae*	Inhibitory activity against c-erbB-2 kinase Antiviral Cytotoxic	[62, 64, 75, 178]

Table 3. contd…

Sesquiterpene-Quinone	Marine source	Activity	References
dactylospongiaquinone, ***95***	*Dactylospongia sp.*		[2, 16, 30]
Hydroquinones			
avarol, ***96*** *	*Dysidea avara* *Dysidea cf.cristagalli*	Antiviral against HIV I Antiinflammatory Antitumour	[2, 7, 15, 20, 26, 34, 35, 51, 55, 73, 84, 90-97, 99, 103, 107, 108]
diacetylavarol, ***97***	*Dysidea avara*		[51, 64, 91]
20-*O*-acetylavarol, ***98***	*Dysidea avara*		[64, 96]
isoarenarol, ***99***	*Dysidea arenaria*	Protein kinase inhibitor	[33, 110]
6'-hydroxy-5'-acetyl-avarol, ***100***	*Dysidea avara*		[26, 91]
6´-hydroxyavarol, ***101***	*Dysidea cinerea*	Anti-HIV-I	[100]
6´-acetoxyavarol, ***102***	*Dysidea cinerea*	Anti-HIV-I	[26, 100]
hyrtiophenol, ***103***	*Hyrtios tubulatus* *Petrosiaspongia metachromia*		[22, 102, 111, 112]
18-hydroxy-hyrtiophenol, ***104***	*Hyrtios tubulatus* *Petrosiaspongia metachromia*		[22, 102, 111, 112]
5-epi-hyrtiophenol, ***105***	*Hyrtios tubulatus*		[22, 102, 112]
18-hydroxy-5-epi-hyrtiophenol, ***106***	*Hyrtios tubulatus*		[22, 102, 112]

Table 4. Avaranes $\Delta^{4(14)}/\Delta^{4(13)}$

Sesquiterpene-Quinone	Marine Source	Activity	References
Quinones			
arenarone, ***107***	*Dysidea arenaria*		[105, 109]
neoavarone, ***108*** *	*Dysidea genus*		[82, 84, 103, 105, 113]
21-hydroxy-19-methoxyarenarone, ***109***	*Hyrtios tubulatus*		[22, 102, 112]
ilimaquinone, ***110*** *	*Hippospongia metachromia* *Hyatella intestinales* *Dactylospongia elegans* *Hippospongia sp.* *Polyfibrospongia australis* *Petrosiaspongia metachromia* *Fenestraspongia sp.* *Smenospongia sp.*	Antitumour Differentiation-inducing activity of K562 cells into erythroblast	[14, 15, 16, 31, 55, 59, 63, 64, 72, 73, 76, 85, 92, 94, 103, 105, 106, 111, 114-124]
smenoquinone, ***111***	*Hippospongia sp.*		[1, 118]
smenospongine, ***112***	*Smenospongia sp.* *Dactylospongia elegans* *Hippospongia sp.*	Antitumour Differentiation-inducing activity of K562 cells into erythroblast	[31, 38, 59, 60, 115, 116, 118, 119, 125, 126, 127]
smenospongidine, ***113*** *	*Dactylospongia elegans* *Hippospongia sp.* *Smenospongia sp.*	Differentiation-inducing activity of K562 cells into erythroblast	[9, 59, 92, 115, 118]
smenospongorine, ***114***	*Dactylospongia elegans* *Hippospongia sp.*	Differentiation-inducing activity of K562 cells into erythroblast	[115, 116]
smenospongiarine, ***115***	*Smenospongia sp.*		[59, 116]
5-epi-ilimaquinone, ***116***	*Dactylospongia elegans* *Hippospongia sp.* *Polyfibrospongia australis* *Hyrtios tubulatus* *Petrosiaspongia metachromia* *Fenestraspongia sp.*	Antimicrobial Differentiation-inducing activity of K562 cells into erythroblast	[31, 59, 73, 76, 102, 105, 111, 115, 116, 117, 123]
5-epi-smenospongorine, ***117***	*Smenospongia sp.* *Dactylospongia elegans* *Hippospongia sp.*	Differentiation-inducing activity of K562 cells into erythroblast	[60, 115, 116, 118]
5-epi-smenospongine, ***118***	*Dactylospongia elegans* *Hippospongia sp.* *Petrosiaspongia metachromia*	Differentiation-inducing activity of K562 cells into erythroblast	[22, 111, 112, 115, 116]

Table 4. contd…

Sesquiterpene-Quinone	Marine Source	Activity	References
5-epi-smenospongiarine, ***119***	*Hippospongia sp.*	Antileukemic	[59, 116, 118]
5-epi-smenospongidine, ***120***	*Dactylospongia elegans* *Hippospongia sp.*	Differentiation-inducing activity of K562 cells into erythroblast	[59, 115, 116]
smenorthoquinone, ***121***	*Smenospongia sp* *Spongia hispida*		[105, 118]
epismenospongidine, ***122***	*Dactylospongia elegans*	Cytotoxic	[58]
epismenospongiarine, ***123***	*Dactylospongia elegans*	Cytotoxic	[58]
dactyloquinone A, ***124***	*Dactylospongia elegans*		[31, 128, 129]
dactyloquinone B, ***125***	*Dactylospongia elegans*		[31, 128, 129]
dactyloquinone C, ***126***	*Dactylospongia elegans*		[14, 31, 130]
dactyloquinone D, ***127***	*Dactylospongia elegans*		[14, 31, 130]
dactyloquinone E, ***128***	*Dactylospongia elegans*		[14, 31, 130]
Hydroquinones			
arenarol, ***129*** *	*Hyrtios tubulatus* *Dysidea arenaria*		[37, 63, 64, 73, 80, 81, 83, 102, 103, 105, 109, 131, 132, 176]
neoavarol, ***130*** *	*Dysidea genus*		[20, 51, 82, 84, 105, 113]
20-*O*-acetylneoavarol, ***131***	*Dysidea genus* *Dysidea cf.cristagalli*	Inhibited superoxide production by human neutrophils	[27, 28, 51]
dictyoceratin C, ***132***	*Dactylospongia elegans* *Petrosiaspongia metachromia*		[111, 115, 124]
O-isoprenyl-dictyoceratin, ***133***	*Spongia genus*	Inhibits the lyase activity of DNA polymerase	[38, 60, 124]
dictyoceratin A o smenospondiol, ***134*** *	*Polyfibrospongia australis* *Hippospongia sp.* *Dactylospongia elegans* *Smenospongia sp.*		[31, 59, 115, 117, 118, 123, 129, 133, 134]
siphonodictyoic acid, ***135***	*Aka coralliphagum*		[1, 56]
siphonodictyal G, ***136***	*Aka coralliphagum*		[2, 47, 56]
polyfibrospongol A, ***137***	*Polyfibrospongia australis*	Cytotoxic against KB-16, A-549 and murine P-388	[37, 117, 123]
polyfibrospongol B, ***138***	*Polyfibrospongia australis*	Cytotoxic against KB-16, A-549 and murine P-388.	[37, 117, 123]
dictyoceratin B, ***139***	*Hippospongia sp.*		[1, 134]

Table 5. Tetracarbocyclic

Sesquiterpene-Quinone	Marine Source	Activity	References
cyclozonarone, ***140*** *	*Dictyopteris undulada*	Inhibited the feeding of young abalone *Haliotis discus*	[9, 10, 13, 34, 35, 135, 136]
(+)-(5*S*,10*S*)-4'-hydroxymethylcyclozonarone, ***141***	*Phyllosticta spinarum*		[24]
phyllospinarone, ***142***	*Phyllosticta spinarum*		[24]
pelorol, ***143*** *	*Dactylospongia elegans* *Petrosaspongia metachromia*		[22, 31, 57, 111, 131, 137, 180]
akaol A, ***144***	*Aka sp.*		[33, 57]
akaol B, ***145***	*Aka sp.*		[1, 57]

Table 6. Norsesquiterpenes quinone/hydroquinone

Sesquiterpene-Quinone	Marine Source	Activity	References
halenaquinone, ***146*** *	*Xestospongia sapra* *Xestospongia exigua*	Inhibits protein tyrosine kinase, PI3 kinase and topoisomerase I. Inhibits the Ca^{2+} and K^{+} (AEDT) ATPase activities of myosin. Activates the ATPase of actomyosin. Cytotoxic against KB and P388 cell lines Cardiotonic activity	[1, 138-149]
xestoquinone, ***147*** *	*Xestospongia sapra* *Xestospongia exigua* *Adocia sp.*	Cardiotonic activity Inhibits the Ca^{2+} and K^{+} (AEDT) ATPase activities of myosin. Activates the ATPase of actomyosin. Inhibits protein tyrosine kinase, PI3 kinase and topoisomerase I. Antiplasmodial Antimalarial	[1, 138, 139, 142, 150-156]
adociaquinone A, ***148*** *	*Xestospongia* genus *Adocia sp.*	Cytotoxic against P388, HCT, KB16 and HEP-3B cell lines.	[1, 139, 142, 154]
adociaquinone B, ***149*** *	*Xestospongia* genus *Adocia sp.*	Cytotoxic against P388, HCT, KB16 and HEP-3B cell lines.	[1, 139, 142, 154]
3-ketoadociaquinone A, ***150***	*Xestospongia* genus *Adocia sp.*		[1, 139, 142]
3-ketoadociaquinone B, ***151***	*Xestospongia* genus		[1, 139]
3,13-dideoxo-1,2,14,15-tetrahydro-3,13-dihydroxy-halenaquinone, ***152***	*Adocia sp.*		[1, 139, 142, 149]
xestosaprol A, ***153***	*Xestospongia* genus *Xestospongia sapra*		[1, 139, 157]
13,14,15,16-tetrahydroxestoquinol, ***154***	*Adocia sp.*		[1, 149]
xestosaprol B, ***155***	*Xestospongia sapra*		[1, 157]
halenaquinol, ***156*** *	*Xestospongia sapra* *Xestospongia exigua*	Inhibits protein tyrosine kinase	[1, 138, 140, 144, 145, 146, 147, 148, 148]
halenaquinol sulfate, ***157***	*Xestospongia sapra* *Xestospongia exigua*	Inhibits the membrane fusion events of echinoderm gametes	[1, 138, 148, 149]
xestoquinol sulfate, ***158***	*Xestospongia sapra*		[1, 149, 157]
13-*O*-methyl xestoquinol sulfate, ***159***	*Xestospongia* genus		[1, 139]

Table 7. Other Rearranged Skeletons

Sesquiterpene-Quinone	Marine Source	Activity	References
bolinaquinone, ***160***	*Dysidea villosa*	Cytotoxic against Hela cell line.	[63, 90, 158, 159]
21-dehydroxybolina quinone, ***161***	*Dysidea villosa*		[90]
Dysideamine,[$] ***178*** [$]	*Dysidea sp.*	Neuroprotective effect against iodoacetic acid induced cell death.	[184]
neodactyloquinone, ***162***	*Dactylospongia elegans*	Cytotoxic against línea celular HeLa.	[33, 160]
dysidine, ***163***	*Dysidea villosa*	PTP1B inhibitor	[90, 158]
frondosin A, ***164*** *	*Dysidea frondosa*	Inhibits the binding of interleukin-8 to its receptor (anti-inflammatory to prevent autoimmune disorders: rheumatoid arthritis and psoriasis) Anti HIV	[161, 162, 163, 165]

[$] Compound **178** was isolated during the preparation of this paper. For this reason it appears with a number out of the order both in the structure listing and in the tables.

Table 7. Contd….

Sesquiterpene-Quinone	Marine Source	Activity	References
frondosin B, ***165*** *	*Dysidea frondosa* *Euryspongia sp.*	Inhibits the binding of interleukin-8 to its receptor (anti-inflammatory to prevent autoimmune disorders: rheumatoid arthritis and psoriasis)	[161, 163-167]
frondosin C, ***166***	*Dysidea frondosa*	Inhibits the binding of interleukin-8 to its receptor (anti-inflammatory to prevent autoimmune disorders: rheumatoid arthritis and psoriasis	[161, 163, 165]
frondosin D, ***167***	*Dysidea frondosa* *Euryspongia sp.*	Inhibits the binding of interleukin-8 to its receptor (anti-inflammatory to prevent autoimmune disorders: rheumatoid arthritis and psoriasis Anti HIV	[161, 163, 165, 167]
frondosin E, ***168***	*Dysidea frondosa*	Inhibits the binding of interleukin-8 to its receptor (anti-inflammatory to prevent autoimmune disorders: rheumatoid arthritis and psoriasis	[163, 165]
peyssonol B, ***169***	*Peyssonnelia sp.* *Hyatella intestinales*		[15, 18]

Table 8. Dimmers and Related Compounds

Sesquiterpene-Quinone	Marine Source	Activity	References
bispuupehenone, ***170***	*Hyrtios eubamma* *Dysidea sp.*		[1, 44, 168]
dipuupehetriol, ***171***	*Hyrtios sp.*		[42]
dipuupehedione, ***172***	*Hyrtios sp.* *Dysidea sp.*	Cytotoxic	[34, 35, 169]
popolohuanone A, ***173***	*Dysidea sp.*		[170]
popolohuanone B, ***174***	*Dysidea sp.*		[170]
popolohuanone C, ***175***	*Dysidea* *Dysidea avara*	Inhibitor of protein tyrosine kinase.	[51, 58, 159, 171]
popolohuanone D, ***176***	*Dysidea avara*	Inhibitor of protein tyrosine kinase	[58, 171]
popolohuanone E, ***177***	*Dysidea sp.*	Inhibitor of topoisomerase II Cytotoxic against A549 cell line Antitumour.	[172-175]

* Structures that have been synthesized as well as isolated from natural sources

- Synthetic aspects

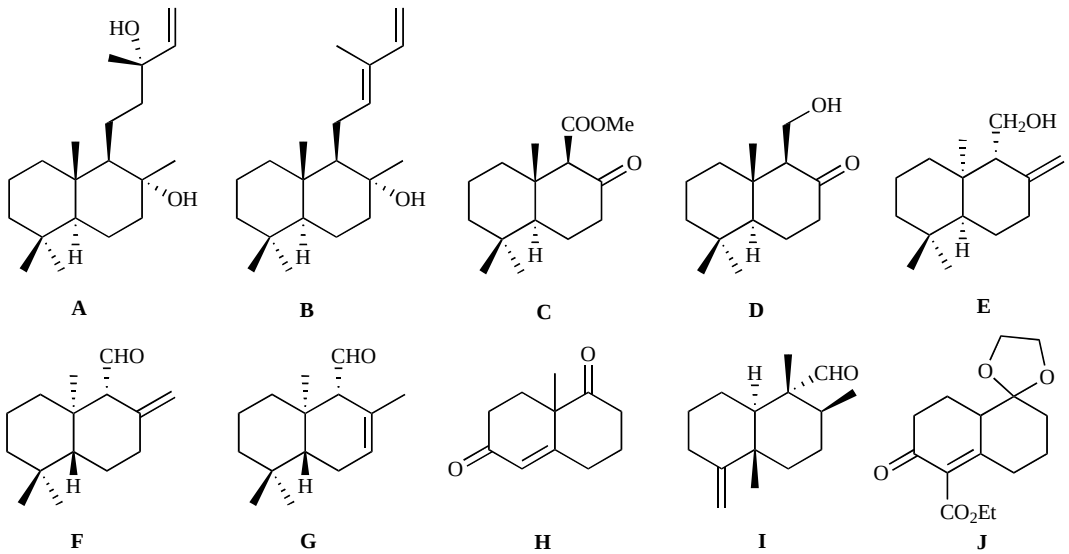


Fig. (10). Contd…

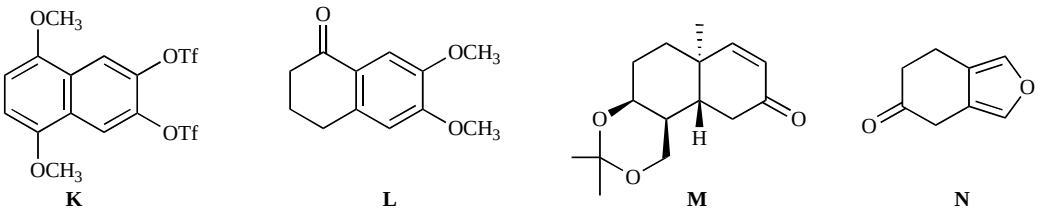


Fig. (10). Starting material for the synthesis of sesquiterpenes quinone hydroquinone.

Sesquiterpenes synthesized from:

- sclareol, **A**: ***2***, ***69***, ***25***, ***32***, ***63***, ***64***, ***143***, ***42***, ***38***
- *cis*-abienol, **B**: ***64***, ***25***, ***63***
- β-ketoester **C**: ***44***, ***63***, ***3***
- β-ketoester **C** dervative , **D**: ***44***
- albicanol, **E**: ***140***
- albicanal, **F**: ***44***, ***1***, ***36***, ***20***, ***2***
- albicanal isomer, **G**: ***11***, ***41***
- Wieland-Miescher, enone **H**: ***96***, ***82***, ***129***, ***76***, ***92***, ***93***, ***94***, ***11***, ***130***, ***108***, ***91***, ***114***, ***86***, ***146***, ***156***
- Geraniol derivative, **I**: ***134***
- Compund **J**: ***129***
- Naftalen derivative **K**: ***146***, ***156***
- Tetrahidronaftalen derivative **L**: ***146***, ***156***
- Decalone **M**: ***147***
- Tetrahidro benzofuran **N**: ***147***
- Xestoquinone ***147***: ***148***, ***149***

Halenaquinone, ***146*** has been synthesized both through a strategy based on an intramolecular inverse-electron-demand Diels Alder reaction and intramolecular Heck cyclization [143, 144].

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REFERENCES

[1] Capon, R. J. "*Studies in Natural Products Chemistry, Structure and Chemistry* (Part C)"; Atta-Ur Rahman, Ed.; Elsevier: Amsterdam, **1995**; Vol. *15*, pp. 289-326.
[2] Fraga, B. M. Natural sesquiterpenoids**.** *Nat. Prod. Rep.* **2008**, *25*, 1180.
[3] Blunt, J. W.; Copp, B. R.; Hu, W.-P.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep.* **2009**, *26*, 170.
[4] Fujimoto, H.; Nakamura, E.; Kim, Y. P.; Okuyama, E.; Ishibashi, M.; Sassa, T. Immunomodulatory constituents from an ascomycete, *Eupenicillium crustaceum*, and revised absolute structure of macrophorin D. *J. Nat. Prod.* **2001**, *64*, 1234.
[5] Zhi-Hui, D.; Ze-Jun, D.; Ji-Kai, L. Albaconol, A novel prenylated resorcinol (=Benzene-1,3-diol) from basidiomycetes *Albatrellus confluens. Helv. Chim. Acta* **2001**, *84*, 259.
[6] Kono, K.; Tanaka, T.; Ogita, T.; Hosoya, T.; Kohama, T. F-12509A, a new sphingosine kinase inhibitor, produced by a discomycete. *J. Antibiot.* **2000**, *53*, 459.
[7] Minale, L.; Sodano, R.; Sodano, G. Avarol a novel sesquiterpenoid hydroquinone with a rearranged drimane skeleton from the sponge *Dysidea avara*. *Tetrahedron Lett.* **1974**, *15*, 3401.
[8] Djura, P.; Stierle, D. B.; Sullivan, B.; Faulkner, D. J. Some metabolites of the marine sponges Smenospongia aurea and Smenospongia (.ident.Polyfibrospongia) echina. *J. Org. Chem.* **1980**, *45*, 1435.
[9] Laube, T.; Beil, W.; Seifert, K. Total synthesis of two 12-nordrimanes and the pharmacological active sesquiterpene hydroquinone yahazunol. *Tetrahedron* **2005**, *61*, 1141.
[10] Laube, T.; Schröder, J.; Stehle, R.; Seifert, K. Total synthesis of yahazunol, zonarone and isozonarone. *Tetrahedron* **2002**, *58*, 4299.
[11] Schröder, J.; Magg, C.; Seifert, K. Total synthesis of the marine sesquiterpene hydroquinones zonarol and isozonarol and the sesquiterpene quinones zonarone and isozonarone. *Tetrahedron Lett.* **2000**, *41*, 5469.
[12] Laube, T.; Bernet, A.; Dahse, H.; Jacobsen, I. D.; Seifert, K. Synthesis and pharmacological activities of some sesquiterpene quinones and hydroquinones. *Bioorg. Med. Chem.* **2009**, *17*, 1422.
[13] Kurata, K.; Taniguchi, K.; Suzuki, M. Cyclozonarone, a sesquiterpene-substituted benzoquinone derivative from the brown alga *Dictyopteris undulada*. *Phytochemistry* **1996**, *41*, 749.
[14] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **2003**, *20*, 392.
[15] Talpir, R.; Rudi, A.; Kashman, Y. Three new sesquiterpene hydroquinones from marine origin. *Tetrahedron* **1994**, *50*, 4179.
[16] Yong, K. W. L.; Jankam, A.; Hooper, J. N. A.; Suksamrarn, A.; Garson, M. A. Stereochemical evaluation of sesquiterpene quinones from two sponges of the genus *Dactylospongia* and the implication for enantioselective processes in marine terpene biosíntesis. *Tetrahedron* **2008**, *64*, 6341.
[17] Alvarez-Manzaneda, E.; Chahboun, R.; Cabrera, E.; Alvarez, E.; Haidour, E.; Ramos, J. M.; Alvarez-Manzaneda, R.; Tapia, R.; Es-Samti, H.; Fernández, A.; Barranco, I. A convenient enantiospecific route towards bioactive merosesquiterpenes by cationic-resin-promoted friedel-crafts alkylation with α,β-enones. *Eur. J. Org. Chem.* **2009**, 1139.
[18] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **1996**, *13*, 307.
[19] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **1995**, *12*, 223.
[20] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **2001**, *18*, 1.
[21] Bernet, A.; Schröder, J.; Seifert, K. Total synthesis of the marine sesquiterpene quinones hyatellaquinone and spongiaquinone. *Helv. Chim. Acta* **2003**, *86*, 2009.
[22] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **2001**, *18*, 650.
[23] Maezawa, N.; Furuichi, N.; Tsuchikawa, H.; Katsumura, S. Synthesis of a novel sphingosine kinase inhibitor (−)-F-12509A and determination of its absolute configuration. *Tetrahedron Lett.* **2007**, *48*, 4865.
[24] Wijeratne, E. M. K.; Paranagama, P. A.; Marron, M. T.; Gunatilaka, M. K.; Arnold, A. E.; Gunatilaka, A. A. L. Sesquiterpene quinones and related metabolites from *Phyllosticta spinarum*, a fungal strain endophytic in *Platycladus orientalis* of the sonoran desert. *J. Nat. Prod.* **2008**, *71*, 218.
[25] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **2002**, *19*, 650.
[26] McNamara, C. E.; Larse, L.; Perry, N. B.; Harper, J. L.; Berridge, M. V.; Chia, E. W.; Kelly, M.; Webb, V. L. Anti-inflammatory Sesquiterpene-quinones from the New Zealand Sponge *Dysidea* cf. *cristagalli*. *J. Nat. Prod.* **2005**, *68*, 1431.
[27] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **2006**, *23*, 943.
[28] Blunt, J. W.; Copp, B. R.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep.* **2007**, *24*, 31.
[29] Kazlauskas, R.; Murphy, P. T.; Warren, R. G.; Wells, R. J.; Blount, J. F. New quinones from a dictyoceratid sponge. *Aust. J. Chem.* **1978**, *31*, 2685.
[30] Jankam, A.; Somerville, M. J.; Hooper, J. N. A.; Brecknell, D. J.; Suksamrarn, A.; Garson, M. A. Dactylospongiaquinone, a new meroterpenoid from the Australian marine sponge *Dactylospongia* n. sp. *Tetrahedron* **2007**, *63*, 1577.
[31] Mitome, H.; Nagasawa, T.; Miyaoka, H.; Yamada, Y.; Soest, W. M. Dactyloquinones C, D and E novel sesquiterpenoid quinones, from the Okinawan marine sponge, *Dactylospongia elegans*. *Tetrahedron* **2002**, *58*, 1693.
[32] Piña, I. C.; Sanders, M. L.; Crews, P. Puupehenone Congeners from an Indo-Pacific *Hyrtios* Sponge. *J. Nat. Prod.* **2003**, *66*, 2.
[33] Blunt, J. W.; Copp, B. R.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep.* **2005**, *22*, 15.
[34] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **1998**, *15*, 73.
[35] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **1998**, *15*, 113.
[36] Urban, S.; Capon, R. J. Deoxyspongiaquinones: new sesquiterpene quinones and hydroquinones from a southern australian marine sponge *Euryspongia* sp. *Aust. J. Chem.* **1996**, *49*, 611.
[37] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **1999**, *16*, 155.
[38] Blunt, J. W.; Copp, B. R.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep.* **2006**, *23*, 26.
[39] Quideau, S.; Lebon, M.; Lamidey, A. M. Enantiospecific synthesis of the antituberculosis marine sponge metabolite (+)-puupehenone. The arenol oxidative activation route. *Org. Lett.* **2002**, *4*, 3975.

[40] El Sayed, K. A.; Bartyzel, P.; Shen, X. D.; Perry, T. L.; Zjawiony, J. K.; Hamann, M. T. Marine natural products as antituberculosis agents. *Tetrahedron* **2000**, *56*, 949.

[41] Barrero, A. F.; Alvarez-Manzaneda, E. J.; Chahboun, R. Enantiospecific synthesis of (+)-Puupehenone from (-)-Sclareol and protocatechualdehyde. *Tetrahedron Lett.* **1997**, *38*, 2325.

[42] Nasu, E. S.; Yeung, B. K. S.; Hamann, M. T.; Scheuer, P. J. Puupehenone-related metabolites from two Hawaiian sponges, *Hyrtios sp. J. Org. Chem.* **1995,** *60*, 7290.

[43] Urban, S.; Capon, R. J. Absolute stereochemistry of puupehenone and related metabolites. *J. Nat. Prod*. **1996**, *59*, 900.

[44] Ciavatta, M. L.; Lopez Gresa, M. P.; Gavagnin, M.; Romero, V.; Melck, D.; Manzo, E.; Guo, Y-W.; van Soest, R.; Cimino, G. Studies on puupehenone-metabolites of a *Dysidea* sp.: structure and biological activity. *Tetrahedron* **2007**, *63*, 1380.

[45] Barrero, A. F.; Alvarez-Manzaneda, E. J.; Chahboun, R.; Cortés, M.; Armstrong, V. Synthesis and antitumor activity of puupehedione and related compounds. *Tetrahedron* **1999**, *55*, 15181.

[46] Chan, J. A.; Freyer, A. J.; Carte, B. K.; Hemling, M. E.; Hofmann, G. A.; Mattern, M. R.; Mentzer, M. A.; Westley, J. W. Protein kinase c inhibitors: Novel spirosesquiterpene aldehydes from a marine sponge Aka (=Siphonodictyon) coralliphagum. *J. Nat. Prod*. **1994**, *57*, 1543.

[47] Grube, A.; Assman, M.; Lichte, E.; Sasse, F.; Pawlik, J. R.; Köck, M. Bioactive Metabolites from the caribbean sponge *Aka coralliphagum*. *J. Nat. Prod.* **2007**, *70*, 504.

[48] Fenical, W.; Sims, J. J.; Squatrito, D.; Wing, R. M.; Radlick, P. Marine natural products. VII. Zonarol and isozonarol, fungitoxic hydroquinones from the brown seaweed *Dictyopteris zonarioides*. *J. Org. Chem*. **1973**, *38*, 2383.

[49] Barrero, A. F.; Alvarez-Manzaneda, E. J.; Herrador, M. M.; Chahboun, R.; Galera, P. Synthesis and antitumoral activities of marine *ent*-chromazonarol and related compounds. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2325.

[50] Ciminio, G.; De Stefano, S.; Minale, L. Chromazonarol, a chroman-sesquiterpenoid from the sponge *Disidea pallescens*. *Experientia* **1975**, *31*, 1117.

[51] Perez-García, E.; Zubía, E.; Ortega, M. J.; Carballo, J. L. Merosesquiterpenes from Two Sponges of the Genus *Dysidea*. *J. Nat. Prod*. **2005**, *68*, 653.

[52] Faulkner, D. J. Marine natural products: metabolites of marine algae and herbivorous marine molluscs. *Nat. Prod. Rep*. **1984**, *1*, 251.

[53] Ochi, M.; Kotsuki, H.; Muraoka, K.; Tokoroyama, T. The Structure of Yahazunol, a New Sesquiterpene-substituted Hydroquinone from the Brown Seaweed *Dictyopteris undulata* Okamura. *Bull. Chem. Soc. Jpn*. **1979**, *52*, 629.

[54] Sullivan, B.; Djura, P.; McIntyre, E.; Faulkner, J. Antimicrobial constituents of the sponge *Siphonodictyon coralliphagum*. *Tetrahedron* **1981**, *37*, 979.

[55] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **1988**, *5*, 613.

[56] Sullivan, B. W.; Faulkner, D. J.; Matsumoto, G. K.; Cun-Heng, H.; Clardy, J. Metabolites of the burrowing sponge *Siphonodictyon coralliphagum. J. Org. Chem.* **1986**, *51*, 4568.

[57] Mukku, V. J. R. V.; Edrada, R. A.; Schmitz, F. J.; Shanks, M. K.; Chaudhuri, B.; Fabbro, D. New Sesquiterpene Quinols from a Micronesian Sponge, *Aka* sp. *J. Nat. Prod.* **2003**, *66*, 686.

[58] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **1994**, *11*, 533.

[59] Rodríguez, J.; Quiñoá, E.; Riguera, R.; Peters, B. M.; Abrell, L. M.; Crews, P. The structures and stereochemistry of cytotoxic sesquiterpene quinones from *Dactylospongia elegans. Tetrahedron* **1992**, *48*, 6667.

[60] Fraga, B. M. Natural sesquiterpenoids *Nat. Prod. Rep.* **2005**, *22*, 465.

[61] Song, F. H.; Fan, X.; Xu, X. L.; Zhao, J. L.; Han, L. J.; Shi, J. G. A new sesquiterpene-substituted benzoic acid from the brown alga *Dictyopteris divaricata*. *Chin. Chem. Lett.* **2004**, *15*, 316.

[62] Fraga, B. M. Natural sesquiterpenoids. *Nat. Prod. Rep.* **1997**, *14*, 145.

[63] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **2000**, *17*, 7.

[64] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **1997**, *14*, 259.

[65] Coval, S. J.; Conover, M. A.; Mierzwa, R.; King, A.; Puar, M. S.; Phife, D. W.; Pai, J. K.; Burrier, B. E.; Ahn, H. S.; Boykow, G. C.; Patel, M.; Pomponi, S. A. Wiedendiol-A and -B, cholesteryl ester transfer protein inhibitors from the marine sponge *Xestospongia wiedenmayeri*. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 605.

[66] Barrero, A. F.; Alvarez-Manzaneda, E. J.; Chahboun, R. Synthesis of wiedendiol-A and wiedendiol-B from labdane diterpenes. *Tetrahedron* **1998**, *54*, 5635.

[67] Chackalamannil, S.; Wang, Y.; Xia, Y.; Czarniecki, M. An efficient synthesis of Wiedendiol-A from (+)-sclareolide. *Tetrahedron Lett.* **1995**, *36*, 5315.

[68] Arima, Y.; Kinoshita, M.; Akita, H. Natural product synthesis from (8a*R*)- and (8a*S*)-bicyclofarnesols: synthesis of (+)-wiedendiol A, (+)-norsesterterpene diene ester and (−)-subersic acid. *Tetrahedron Asymmetry* **2007**, *18*, 1701.

[69] Barrero, A. F.; Alvarez-Manzaneda, E. J.; Chahboun, R. Enantiospecific Synthesis of Wiedendiol-B from (−)-Sclareol and (+)-*cis*-Abienol. *Tetrahedron Lett.* **1997**, *38*, 8101.

[70] Alvarez-Manzaneda, E. J.; Chahboun, R.; Pérez, I. B.; Cabrera, E.; Alvarez, E., Alvarez-Manzaneda, R. First Enantiospecific Synthesis of the Antitumor Marine Sponge Metabolite (−)-15-Oxopuupehenol from (−)-Sclareol. *Org. Lett.* **2005**, *7*, 1477.

[71] Killday, K. B.; Wright, A. E.; Jackson, R. H.; Sills, M. A. Bis(Sulfato)-cyclosiphonodictyol A, a new disulfated sesquiterpene-hydroquinone from a deep water collection of the marine sponge *Siphonodictyon coralliphagum*. *J. Nat. Prod*. **1995**, *58*, 958.

[72] Spyroudis, S. Hydroxyquinones: synthesis and reactivity. *Molecules* **2000**, *5*, 1291.

[73] Urban, S.; Capon, R. J. Marine sesquiterpene quinones and hydroquinones: acid-catalyzed rearrangements and stereochemical investigations. *Aust. J. Chem.* **1994**, *47*, 1023.

[74] Swersey, J. C.; Barrows, L. R.; Ireland, C. M. Mamanuthaquinone: an antimicrobial and cytotoxic metabolite of *Fasciospongia sp*. *Tetrahedron Lett.* **1991**, *32*, 6687.

[75] Stahl, P.; Kissau, M.; Mazitschek, R.; Huwe, A.; Furet, P.; Giannis, A.; Waldmann, H. Total synthesis and biological evaluation of the nakijiquinones. *J. Am. Chem. Soc*. **2001**, *123*, 11586.

[76] Carté, B.; Rose, C.; B.; Faulkner, D. J. 5-Epi-Ilimaquinone, a metabolite of the sponge Fenestraspongia sp. *J. Org. Chem*. **1985**, *50*, 2785.

[77] Utkina, N. K.; Denisenko, V. A.; Scholokova, O. V.; Makarchenko, A. E. Determination of the Absolute Stereochemistry of Cyclosmenospongine. *J. Nat. Prod*. **2003**, *66*, 1263.

[78] Utkina, N. K.; Denisenko, V. A.; Scholokova, O. V.; Virovaya, M.; Prokof'eva, N. G. Cyclosmenospongine, a new sesquiterpenoid aminoquinone from an Australian marine sponge *Spongia sp*. *Tetrahedron Lett*. **2003**, *44*, 101.

[79] Bourguet-Kondracki, M. L., Martin, M. T.; Guyot, M. Smenoqualone a novel sesquiterpenoid from the marine sponge *Smenospongia sp*. *Tetrahedron Lett.* **1992**, *33*, 8079.

[80] Nakamura, M.; Suzuki, A.; Nakatani, M.; Fuchikami, T.; Inoue, M.; Katoh, T. An efficient synthesis of (+)-aureol via boron trifluoride etherate-promoted rearrangement of (+)-arenarol. *Tetrahedron Lett.* **2002**, *43*, 6929.

[81] Lakshmi, V.; Gunasekera, S. P.; Schmitz, F. J.; Ji, X.; Helm, D. Acid-catalyzed rearrangement of arenerol. *J. Org. Chem.* **1990**, *55*, 4709.

[82] Suzuki, A.; Nakatani, M.; Nakamura, M.; Kawaguchi, K.; Inoue, M.; Katoh, T. Highly improved synthesis of (+)-Aureol *via* (-)-Neoavarone and (-)-Neoavarol, by employing salcomine oxidation and acid-induced rearrangement/cyclization strategy. *Synlett* **2003**, *3*, 329.

[83] Nakatani, M.; Nakamura, M.; Suzuki, A.; Kawaguchi, K.; Fuchikami, T.; Inoue, M.; Katoh, T. Enantioselective total synthesis of (+)-aureol via a $BF_3{\cdot}Et_2O$-promoted rearrangement/cyclization reaction of (+)-arenarol. *ARKIVOC* **2003**, 45.

[84] Sakurai, J.; Oguchi, T.; Watanabe, K.; Abe, H.; Kanno, S.; Ishikawa, M.; Katoh, T. Highly efficient total synthesis of the marine natural products (+)-Avarone, (+)-Avarol, (-)-Neoavarone, (-)-Neoavarol and (+)-Aureol. *Chem. Eur. J.* **2008**, *14*, 829.

[85] Kochanowska, A. J.; Rao, K. V.; Childress, S.; El-Alfy, A.; Matsumoto, R. R.; Kelly, M.; Stewart, G. S.; Suftka, K. J.; Hamann, M. T. Secondary metabolites from three florida sponges with antidepressant activity. *J. Nat. Prod*. **2008**, *71*, 186.

[86] Hu, J. F.; Schetz, J. A.; Kelly, M.; Peng, J. N.; Ang, K. K. H.; Flotow, H.; Leong, C. Y.; Ng, S. B.; Buss, A. D.; Wilkins, S. P.; Hamann, M. T. New antiinfective and human 5-HT2 receptor binding natural and semisynthetic compounds from the jamaican sponge *Smenospongia aurea*. *J. Nat. Prod*. **2002**, *65*, 476.

[87] Longley, R. E.; McConell, O. J.; Essich, E.; Harmody, D. Evaluation of marine sponge metabolites for cytotoxicity and signal transduction activity. *J. Nat. Prod*. **1993**, *56*, 915.

[88] Tymiak, A. A.; Rinehart, K. L.; Bakus, G. J. Constituents of morphologically similar sponges : Aplysina and smenospongia species. *Tetrahedron* **1985**, *41*, 1039.

[89] Wright, A. E.; Rueth, S. A.; Cross, S. S. An antiviral sesquiterpene hydroquinone from the marine sponge *Strongylophora hartmani*. *J. Nat. Prod*. **1991**, *54*, 1108.

[90] Li, Y.; Zhang, Y.; Shen, X.; Guo, Y. A novel sesquiterpene quinone from Hainan sponge *Dysidea villosa*. *Bioorg. Med. Chem. Lett*. **2009**, *19*, 390.

[91] De Giulio, A.; De Rosa, S.; Di Venzo, G.; Strazzullo, G. Further bioactive derivative of avarol from *Dysidea avara*. *Tetrahedron* **1990**, *46*, 7971.

[92] Ling, T.; Poupon, E.; Rueden, E. J.; Kim, S. H.; Theodorakis, E. A. Unified synthesis of quinone sesquiterpenes based on a radical decarboxylation and quinone addition reaction. *J. Am. Chem. Soc*. **2002**, *124*, 12261.

[93] Ling, T.; Xiang, A. X.; Theodorakis, E. A. Enantioselective total synthesis of avarol and avarone. *Angew. Chem. Int. Ed*. **1999**, *38*, 3089.

[94] Radeke, H. S.; Digits, C. A.; Bruner, S. D.; Snapper, M. L. New tools for studying vesicular-mediated protein trafficking: synthesis and evaluation of ilimaquinone analogs in a non-radioisotope-based antisecretory assay. *J. Org. Chem.* **1997**, *62*, 2823.

[95] An, J.; Wiemer, D. F. Stereoselective synthesis of (+)-Avarol, (+)-Avarone, and some nonracemic analogues. *J. Org. Chem.* **1996,** *61*, 8775.

[96] Crispino, A.; De Giulio, A.; De Rosa, S.; Strazullo, G. A new bioactive derivative of avarol from the marine sponge *Dysidea avara*. *J. Nat. Prod*. **1989**, *52*, 646.

[97] De Rosa, S.; DeGiulio, A.; Iodice, C. Biological effects of prenylated hydroquinones: structure-activity relationship studies in antimicrobial, brine shrimp, and fish lethality assays. *J. Nat. Prod*. **1994**, *57*, 1711.

[98] Sarma, A. S.; Chattopadhyay, P. Synthetic studies of trans-clerodane diterpenoids and congeners: stereocontrolled total synthesis of (+)-avarol. *J. Org. Chem*. **1982**, *47*, 1727.

[99] Locke, E. P.; Hecht, S. M. Enantiospecific total synthesis of (+)- and (–)-avarone and -avarol. *Chem. Commun*. **1996**, 2717.

[100] Hirsch, S.; Rudi, A.; Kashman, Y. New avarone and avarol derivatives from the marine sponge *Dysidea cinerea*. *J. Nat. Prod*. **1991**, *54*, 92.

[101] Stewart, M.; Fell, P. M.; Blunt, J. W.; Munro, M. H. G. Avarol and related compounds from the new zealand marine sponge *Dysidea* sp. *Aust. J. Chem.* **1997**, *50*, 341.

[102] Salmoun, M.; Devijver, C.; daloze, D.; Braekman, J. C.; Gomez, R.; Kluijver, M.; Soest, R. W. M. new sesquiterpene/quinones from two sponges of the genus *Hyrtios*. *J. Nat. Prod*. **2000**, *63*, 452.

[103] Capon, R. J. The Acid-catalyzed rearrangement and absolute stereochemistry of isospongiaquinone. *J. Nat. Prod*. **1990**, *53*, 753.

[104] Stahl, P.; Waldmann, H. Asymmetric synthesis of the nakijiquinones-selective inhibitors of the Her-2/Neu protooncogene. *Angew. Chem. Int. Ed*. **1999**, *38*, 3710.

[105] Urban, S.; Capon, R. J. 5-epi-Isospongiaquinone, a new sesquiterpene/quinone antibiotic from an australian marine sponge, *Spongia hispida*. *J. Nat. Prod*. **1992**, *55*, 1638.

[106] Bruner, S. D.; Radeke, H. S.; Tallarico, J. A.; Snapper, M. L. Total synthesis of (-)-Ilimaquinone. *J. Org. Chem.* **1995**, *60*, 1114.

[107] Venkateswarlu, Y.; Faulkner, D. J. Smenochromenes, unusual macrocyclic sesquiterpene hydroquinone derivatives from a Seychelles sponge of the genus Smenospongia. *J. Org. Chem*. **1991**, *56*, 6271.

[108] Sladic, D.; Gasic, M. J. reactivity and biological activity of the marine sesquiterpene hydroquinone avarol and related compounds from sponges of the order dictyoceratida. *Molecules* **2006**, *11*, 1.

[109] Schmitz, F. J.; Lakshmi, V.; Powel, D. R.; Helm, D. Arenarol and arenarone: sesquiterpenoids with rearranged drimane skeletons from the marine sponge *Dysidea arenaria*. *J. Org. Chem.* **1984**, *49*, 241.

[110] Yoo, H.-D.; Leung, D.; Sanghara, J.; Daley, D.; van Soest, R.; Andersen, R. J. Isoarenarol, A new protein kinase inhibitor from the marine sponge *Dysidea arenaria*. *Pharm. Biol*. **2003**, *41*, 223.

[111] Kwak, J. H.; Schmitz, F. J.; Kelly, M. Sesquiterpene quinols/quinones from the micronesian sponge *Petrosaspongia metachromia*. *J. Nat. Prod*. **2000**, *63*, 1153.

[112] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **2002**, *19*, 1.

[113] Iguchi, K.; Sahashi, A.; Kohno, J.; Yamada, Y. New sesquiterpenoid hydroquinone and quinones from the okinawan marine sponge (*Dysidea sp*.) *Chem. Pharm. Bull.* **1990**, *38*, 1121.

[114] Luibrand, R. T.; Erdman, T. R.; Vollmer, J. J.; Scheuer, P. J. Ilimaquinone, a sesquiterpenoid quinone from a marine sponge. *Tetrahedron* **1979**, *35*, 609.

[115] Aoki, S.; Kong, D.; Matsui, K.; Rachmat, R.; Kobayashi, M. Sesquiterpene aminoquinones, from a marine sponge, induce erythroid differentiation in human chronic myelogenous leukemia, K562 cells. *Chem. Pharm. Bull*. **2004**, *52*, 935.

[116] Oda, T.; Wang, W.; Ukai, K.; Nakazawa, T.; Mochizuki, M. A sesquiterpene quinone, 5-Epi-smenospongine, promotes TNF-α production in LPS-stimulated RAW 264.7 cells. *Mar. Drugs* **2007**, *5*, 151.

[117] Shen, Y.; Hsieh, P. New sesquiterpene hydroquinones from a taiwanese marine sponge *Polyfibrospongia australis*. *J. Nat. Prod*. **1997**, *60*, 93.

[118] Kondracki, M.; Guyot, M. Biologically active quinone and hydroquinone sesquiterpenoids from the sponge smenospongia sp. *Tetrahedron* **1989**, *45*, 1995.

[119] Faulkner, D. J. Marine natural products. *Nat. Prod. Rep.* **1990**, *7*, 269.

[120] Capon, R. J.; MacLeod, J. K. Revision of the absolute stereochemistry of ilimaquinone. *J. Org. Chem.* **1987**, *52*, 5059.

[121] Poigny, S.; Guyot, M.; Samadi, M. Efficient total synthesis of (−)-ilimaquinone. *J. Org. Chem.* **1998**, *63*, 5890.

[122] Ling, T.; Poupon, E.; Rueden, E. J.; Theodorakis, E. A. Synthesis of (−)-ilimaquinone via a radical decarboxylation and quinone addition reaction. *Org. Lett.* **2002**, *4*, 819.

[123] Shen, Y.; Hsieh, P. New sesquiterpene hydroquinones from a taiwanese marine sponge *Polyfibrospongia australis*. *J. Nat. Prod*. **1997**, *60*, 93.

[124] Cao, S.; Gao, Z.; Thomas, S. J.; Hetch, S. M.; Lazo, J. S.; Kingston, D. G. I. marine sesquiterpenoids that inhibit the lyase activity of DNA polymerase β. *J. Nat. Prod.* **2004**, *67*, 1716.

[125] Kondracki, M.; Guyot, M. Smenospongine: A cytotoxic and antimicrobial aminoquinone isolated from *Smenospongia* sp. *Tetrahedron Lett*. **1987**, *28*, 5815.

[126] Aoki, S.; Kong, D.; Matsui, K.; Kobayashi, M. Smenospongine, a spongean sesquiterpene aminoquinone, induces erythroid differentiation in K562 cells. *Anti-Cancer Drugs* **2004**, *15*, 363.

[127] Kondracki, M.; Guyot, M. Smenospongine: A cytotoxic and antimicrobial aminoquinone isolated from *Smenospongia* sp. *Tetrahedron Lett*. **1987**, *28*, 5815.

[128] Mitome, H.; Nagasawa, T.; Miyaoka, H.; Yamada, Y.; van Soest, R. W. M. Dactyloquinones A and B, new sesquiterpenoid quinones from the okinawan marine sponge *Dactylospongia elegans*. *J. Nat. Prod*. **2001**, *64*, 1506.

[129] Blunt, J. W.; Copp, B. R.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep*. **2003**, *20*, 1.

[130] Blunt, J. W.; Copp, B. R.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep*. **2004**, *21*, 1.

[131] Anderson, J. C.; Pearson, D. J. A strategy for the synthesis of popolohuanone E: formal total synthesis of (±)-arenarol. *J. Chem. Soc, Perkin Trans. 1* **1998**, 2023.

[132] Watson, A. T.; Park, K.; Wiemer, D. F. Application of the nickel-mediated neopentyl coupling in the total synthesis of the marine natural product arenarol. *J. Org. Chem.* **1995,** *60*, 5102.

[133] Haruo, Y.; Hasegawa, T.; Tanaka, H.; Takahashi, T. Total synthesis of (±)-smenospondiol by Titanium(III)-Mediated tandem radical cyclization. *Synlett* **2001**, *12*, 1935.

[134] Nakamura, H.; Deng, S.; Kobayashi, J.; Ohizumi, Y.; Hirata, Y. Dictyoceratin-A and -B, novel antimicrobial terpenoids from the okinawan marine sponge *Hippospongia* sp. *Tetrahedron* **1986**, *42*, 4197.

[135] Schröder, J.; Matthes, B.; Seifert, K. Total synthesis of the marine sesquiterpene quinone (−)-cyclozonarone. *Tetrahedron Lett.* **2001**, *42*, 8151.

[136] Cortés, M.; Valderrama, J. A.; Cuellar, M.; Armstrong, V.; Preite, M. Synthesis of (+)-cyclozonarone and the absolute configuration of naturally occurring (−)-cyclozonarone. *J. Nat. Prod*. **2001**, *64*, 348.

[137] Goclick, E.; Knig, G. M.; Wright, A. D.; Kaminsky, R. Pelorol from the tropical marine sponge *Dactylospongia elegans*. *J. Nat. Prod.* **2000**, *63*, 1150.

[138] Nakamura, M.; Kakuda, T.; Oba, Y.; Ojika, M.; Nakamura, H. Synthesis of biotinylated xestoquinone that retains inhibitory activity against Ca^{2+} ATPase of skeletal muscle myosin. *Bioorg. Med. Chem.* **2003**, *11*, 3077.

[139] Cao,S.; Foster, C.; Brisson, M.; Lazo, J. S.; Kingston, D. G. I. Synthesis of biotinylated xestoquinone that retains inhibitory activity against Ca^{2+} ATPase of skeletal muscle myosin. *Bioorg. Med. Chem.* **2005**, *13*, 999.

[140] Toyooka, N.; Nagaoka, M.; Sasaki, E.; Hongbo, Q.; Kakuda, H.; Nemoto, H. Model studies toward the total synthesis of halenaquinol and halenaquinone. *Tetrahedron* **2002**, *58*, 6097.

[141] Roll, D. M.; Scheuer, P. J.; Matsumoto, G. K.; Clardy, J. Halenaquinone, a pentacyclic polyketide from a marine sponge. *J. Am. Chem. Soc.* **1983**, *105*, 6177.

[142] Schmitz, F. J.; Bloor, S. J. Xesto- and halenaquinone derivatives from a sponge, Adocia sp., from Truk lagoon. *J. Org. Chem.* **1988**, *53*, 3922.

[143] Kienzler, M. A.; Suseno, S.; Trauner, D. Vinyl Quinones as Diels−Alder Dienes: concise synthesis of (−)-Halenaquinone. *J. Am. Chem. Soc.* **2008**, *130*, 8604.

[144] Sutherland, H. S.; Souza, F. E. S.; Rodrigo, R. G. A. A short synthesis of (±)-halenaquinone. *J. Org. Chem.*, **2001**, *66*, 3639.

[145] Kojima, A.; Takemoto, T.; Sodeoka, M.; Shibasaki, M. Catalytic asymmetric synthesis of halenaquinone and halenaquinol. *Synthesis* **1998**, 581.

[146] Kojima, A.; Takemoto, T.; Sodeoka, M.; Shibasaki, M. Catalytic Asymmetric Synthesis of Halenaquinone and Halenaquinol. *J. Org. Chem.* **1996**, *61*, 4876.

[147] Harada, N.; Sugioka, T.; Ando, Y.; Hiyoshi, N.; Uda, H.; Kuriki, T. Total synthesis of (+)-halenaquinol and (+)-halenaquinone. Experimental proof of their absolute stereostructures theoretically determined. *J. Am. Chem. Soc.* **1988**, *110*, 8483.

[148] Kobayashi, M.; Shimizu, N.; Kitagawa, I.; Kyogoku, Y.; Harada, N.; Uda, H. Absolute stereostructures of halenaquinol and halenaquinol sulfate, pentacyclic hydroquinones from the okinawan marine sponge *xestospongia sapra*, as determined by theoretical calculation of CD spectra. *Tetrahedron Lett.* **1985**, *26*, 3833.

[149] Harada, N.; Uda, H.; Kobayashi, M; Shimizu, N.; Kitagawa, I. Absolute stereochemistry of the halenaquinol family, marine natural products with a novel pentacyclic skeleton, as determined by the theoretical calculation of circular dichroism spectra. *J. Am. Chem. Soc.* **1989**, *111*, 5668.

[150] Nakamura, H.; Kobayashi, J.; Kobayashi, M.; Ohizumi, Y.; Hirata, Y. Xestoquinone. A novel cardiotonic marine natural product isolated from the okinawan sea sponge *Xestospongia sapra*. *Chem. Lett.* **1985**, *14*, 713.

[151] Laurent, D.; Jullian, V.; Parenty, A.; Knibiehler, M.; Dorin, D.; Schmitt, S.; Lozach, O.; Lebouvier, N.; Frostin, M.; Alby, F.; Maurel, S.; Doerig, C.; Meijer, L.; Sauvain, M. Antimalarial potential of xestoquinone, a protein kinase inhibitor isolated from a Vanuatu marine sponge *Xestospongia* sp. *Bioorg. Med. Chem.* **2006**, *14*, 4477.

[152] Sutherland, H. S.; Higgs, K. C.; Taylor, N. J.; Rodrigo, R. Isobenzofurans and *ortho*-benzoquinone monoketals in syntheses of xestoquinone and its 9- and 10-methoxy derivatives. *Tetrahedron* **2001**, *57*, 309.

[153] Maddaford,S. P.; Andresen, N. G.; Cristofoli, W. A.; Keay, B. A. Total synthesis of (+)-Xestoquinone using an asymmetric palladium-catalyzed polyene cyclization. *J. Am. Chem. Soc.* **1996**, *118*, 10766.

[154] Harada, N.; Sugioka, T.; Soutome, T.; Hiyoshi, N.; Uda, H.; Kuriki, T. Synthesis and absolute stereochemistry of (+)-adociaquinones A and B. *Tetrahedron Asymmetry* **1995**, *6*, 375.

[155] Kanematsu, K.; Soejima, S.; Wang, G. Formal total synthesis of xestoquinone *via* furan ring transfer reaction strategy. *Tetrahedron Lett.* **1991**, *32*, 4761.

[156] Harada, N.; Sugioka, T.; Uda, H.; Kuriki, T. Total synthesis and absolute stereochemistry of (+)-xestoquinone and xestoquinol. *J. Org. Chem.* **1990**, *55*, 3158.

[157] Kobayashi, J.; Hirase, T.; Shigemori, H.; Ishibashi, M.; Bae, M. A.; Tsuji, T.; Sasaki, T. New pentacyclic compounds from the okinawan marine sponge *Xestospongia sapra*. *J. Nat. Prod*. **1992**, *55*, 994.

[158] Gianinni, C.; Debitus, C.; Lucas, R.; Ubeda, A.; Payá, M.; Hooper, J. N. A.; D'Auria, M. V. New sesquiterpene derivatives from the sponge *Dysidea* species with a selective inhibitor profile against human phospholipase A_2 and other leukocyte functions. *J. Nat. Prod*. **2001**, *64*, 612.

[159] de Guzman, F. S.; Copp, B. R.; Mayne, C. L.; Concepcion, G. P.; Mangalindan, G. C.; Barrows, L. R.; Ireland, C. M. Bolinaquinone: A novel cytotoxic sesquiterpene hydroxyquinone from a philippine *Dysidea* sponge. *J. Org. Chem.* **1998**, *63*, 8042.

[160] Mitome, H.; Nagasawa, T.; Miyaoka, H.; Yamada, Y.; van Soest, R. W. M. A new sesquiterpenoid quinone and other related compounds from the okinawan marine sponge *Dactylospongia elegans*. *J. Nat. Prod.* **2003**, *66*, 46.

[161] Chambers, C.; Trauner, H.; Trauner, D. Concise total synthesis of (-)-frondosin B using a novel palladium-catalyzed cyclization. *Angew. Chem. Int. Ed.* **2002**, *41*, 1569.

[162] Chambers, C.; Trauner, H.; Trauner, D. Palladium-catalyzed couplings to nucleophilic heteroarenes: the total synthesis of (−)-frondosin B. *Tetrahedron* **2004**, *60*, 9675.

[163] Patil, A. D.; Freyer, A. J.; Killmer, L.; Offen, P.; Carte, B.; Jurewicz, A. J.; Johnson, R. K. Frondosins, five new sesquiterpene hydroquinone derivatives with novel skeletons from the sponge *Dysidea frondosa*: Inhibitors of interleukin-8 receptors. *Tetrahedron* **1997**, *53*, 5047.

[164] Li, X.; Keon, A. E.; Sullivan, J. A.; Ovaska, T. V. Studies toward frondosin A and its analogues. Formal Total Synthesis of (±)-Frondosin A. *Org.Lett.* **2008**, *10*, 3287.

[165] Mehta, G.; Likhite, N. S. A total synthesis of (±)-frondosins A and B. *Tetrahedron Lett.* **2008**, *49*, 7113.

[166] Trost, B. M.; Hu, Y.; Horne, D. B. Total synthesis of (+)-Frondosin A. application of the Ru-Catalyzed [5+2] cycloaddition. *J. Am. Chem. Soc.* **2007**, *129*, 11781.

[167] Hallock, Y. F.; Cardellina, J. H.; Boyd, M. R. (-)-Frondosins A and D, HIV-inhibitory sesquiterpene hydroquinone derivatives from *Euryspongia sp*. *Nat. Prod. Lett.* **1998**, *11*, 153.

[168] Amade, P.; Chevelot, L.; Perzanowski, H. P.; Scheuer, P.J. A Dimer of Puupehenone. *Helv. Chim. Acta* **1983**, *66*, 1672.

[169] Bourguet-Kondracki, M.-L.; Debitus, C.; Guyot, M. Dipuupehedione, a cytotoxic new red dimer from a new caledonian marine sponge *Hyrtios sp*. *Tetrahedron Lett.* **1996**, *37*, 3861.

[170] Rodriguez, A. D.; Yoshida, W. Y.; Scheur, J. Popolohuanone A and B. two new sesquiterpenoid aminoquinones from a pacific sponge *Dysidea sp*. *Tetrahedron* **1990**, *46*, 8025.

[171] Alvi, K. A.; Díaz, M. C.; Crews, P. Evaluation of new sesquiterpene quinones from two Dysidea sponge species as inhibitors of protein tyrosine kinase. *J. Org. Chem.* **1992**, *57*, 6604.

[172] Carney, J. R.; Scheuer, P. J. Popolohuanone E, a topoisomerase-II inhibitor with selective lung tumor cytotoxicity from the Pohnpei sponge *Dysidea sp*. *Tetrahedron Lett.* **1993**, *34*, 3727.

[173] Kawano, H.; Itoh, M.; Katoh, T.; Terahima, S. Studies toward the synthesis of popolohuanone E: Synthesis of natural (+)-arenarol related to the proposed biogenetic precursor of popolohuanone E. *Tetrahedron Lett.* **1997**, *38*, 7769.

[174] Anderson, J. C.; Denton, R. M.; Wilson, C. A biomimetic strategy for the synthesis of the tricyclic dibenzofuran-1,4-dione core of popolohuanone E. *Org. Lett.* **2005**, *7*, 123.

[175] Katoh, T.; Nakatani, M.; Shikita, S.; Sampe, R.; Ishiwata, A.; Ohmori, O.; Nakamura, M.; Terashima, S. Studies toward the total synthesis of popolohuanone E: Enantioselective synthesis of 8-*O*-Methylpopolohuanone E. *Org. Lett.* **2001**, *3*, 2701.

[176] Munday, R. H.; Denton, R. M.; Anderson, J. C. Asymmetric synthesis of 6′-hydroxyarenarol: The proposed biosynthetic precursor to popolohuanone E. *J. Org. Chem.* **2008**, *73*, 8033.

[177] Bernet, A.; Seifert, K. A new approach to sesquiterpene arenes of the 9,11-drimenyl type (=[(*1E,2RS,4aRS,8aRS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2H)-ylidene] methyl type). *Helv. Chim. Acta* **2006**, *89*, 784.

[178] Kobayashi, J.; Madono, T.; Shigemori, I. Nakijiquinones C and D, new sesquiterpenoid quinones with a hydroxy amino acid residue from a marine sponge inhibiting c-erbB-2 kinase. *Tetrahedron* **1995**, *51*, 10867.

[179] Shigemori, H.; Madono, T.; Sasaki, T.; Mikami, Y.; Kobayashi, J. Nakijiquinones A and B, new antifungal sesquiterpenoid quinones with an amino acid residue from an Okinawan marine sponge. *Tetrahedron* **1994**, *50*, 8347.

[180] Yang, L.; Williams, D. E.; Mui, A.; Ong, C.; Krystal, G.; van Soest, R.; Andersen, R. J. Synthesis of pelorol and analogues: Activators of the inositol 5-Phosphatase SHIP. *Org. Lett*. **2005**, *7*, 1073.

[181] Blunt, J. W.; Copp, B. R.; Munro, M. H.; Northcote, P. T.; Prinsep, M. R. Marine natural products. *Nat. Prod. Rep*. **2008**, *25*.

[182] Dave, M.-N.; Kusumi, T.; Ishitsuka, M.; Iwashita, T.; Kakisawa, M. A piscicidal chromanol and a chromenol from the brown alga Dictyopteris undulata. *Heterocycles* **1984**, *22*, 2301.

[183] Wright, A. E.; Cross, S. S.; Burres, N. S.; Koehn, F. Antivial and antitumor terpene hydroquinones from marine sponge and methods of use. *Harbor Branch Oceanographics Institution, Inc., USA*, PCT WO 9112250 A1 August 22, 1991.

[184] Suna, H.; Arai, M.; Tsubotani, Y.; Hayashi, A.; Setiawan, A. Dysideamine, a new sesquiterpene aminoquinone, protects hippocampal neuronal cells against iodoacetic acid-induced cell death. *Bioorg. Med. Chem.* **2009**, *17*, 3968.

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