Natural Products as Environmentally Friendly Antifoulants

Iwao Omae

Pharmceutical University

Omae Research Laboratories

In many countries, alternative TBT-free antifoulants in coatings have already been used for small vessels since 1990.

Especially, Irgarol 1051 and Diuron which are relatively stable and cost-effective herbicides, are the most frequently used in many countries.

As a result, the high levels of contamination have been observed in many harbors, particularly in marinas in the world.

Already, many countries have reached on an agreement on the restriction of these two herbicides.

The resolutions in the international convention regarding to the total ban on the use of TBT will become effective on September 17, 2008.

Hence, the best TBT-free antifoulants selected from the other organic booster biocides besides Irgarol 1051 and Diuron, and natural products which are expected to be environmentally friendly antifouling agents, should be explored as soon as possible.

Natural Products

1. Terpenes
    - Monoterpenes, susquiterpenes, diterpenes, sesterterpenes
2. Nitrogen-containing compounds
    - Heterocyclic compounds
        - Gramines, pyrrols, pyrazoles, others
    - Amides
    - Other nitrogen-containing compounds
3. Phenols
    - Monophenols, polyphenols
4. Steroids
5. Others
    - Higher fatty acids, polyacetylenes, polycyclic compounds, isocyanides, quinones, enzymes, etc.

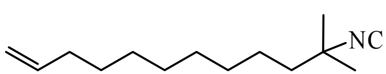
Table 1 Sesquiterpenes from nudibranchs of the family phyllidiidae and their antifouling activity against larvae of the barnacle, *Balanus amphitrite*

Compound	Antifouling activity IC_{50} (μ g mL^{-1})
3-Isocyanotheonellin **1**	0.13
10-Isocyano-4-cadinene **2**	0.14
10-*epi*-Axisonitrile-3 **3**	10
Axisonitrile-3 **4**	3.2
(-)-10-Isothiocyano-4-amorphene **5**	7.2
2-Thiocyanatoneopupukeanane **6**	4.6
4-Thiocyanatoneopupukeanane **7**	2.3
10-Isocyano-4-amorphene **8**	0.7
2-Isoxyanotrachyopsane **9**	0.33
17-Epidioxy-5-cadinene **10**	>50
Cu_2SO_4	0.15

Okino T, Yoshimura E, Firota H, Fusetani N (1996) Tetrahedron 52:9447

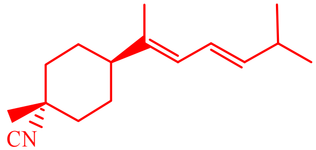
Table 2 Antifouling activity and toxicity of simple linear isocyanides and $CuSO_4$ against cyprid larvae of the barnacle after 120 h

Compound	EC_{50} (μ g mL^{-1})	LD_{50} (μ g mL^{-1})
1,1-dimethyl-10-undecyl isocyanide **11**	0.046	30 <
Cu_2SO_4	0.30	2.95



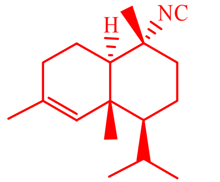
11

Y. Nogata, Y. Kitano, E. Yoshimura, K. Shinshima, I. Sakaguchi, Biofouling 2004, 20, 87.



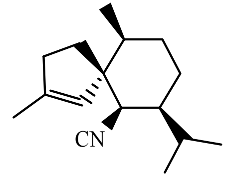
3-isocyanotheonellin

1



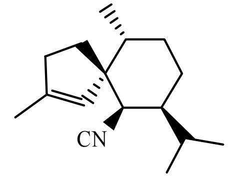
10-isocyano-4-cadinene

2



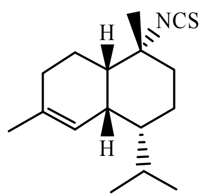
10-*epi*-axisonitrile-3

3



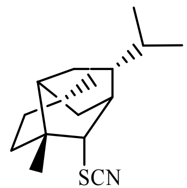
Axisonitrile-3

4



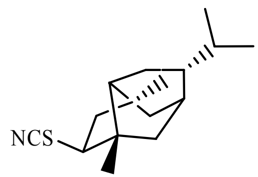
(-)-10-isothiocyano-4-amorphene

5



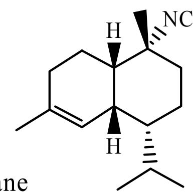
2-thiocyanatoneopupukeanane

6



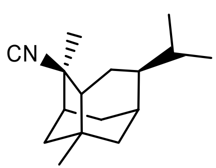
4-thiocyanatoneopupukeanane

7



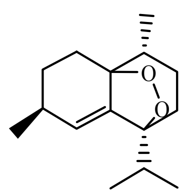
10-isocyano-4-amorphene

8



2-isoxyanotrachyopsane

9



17-epidioxy-5-cadinene

10

Table 3 Diterpenes from marine sponge *Acanthella carvernosa* and their antifouling activity against the larval attachment and metamorphosis of the barnacle *Balanus amphitrite*

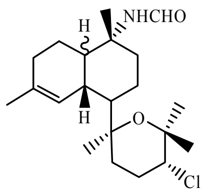
Compound	Antifouling activity IC_{50} ($\mu g\ mL^{-1}$)
Kalihinene X **12**	0.49
Kalihinene Y **13**	0.45
Kalihinene Z **14**	1.1
Kalihinol A **15**	0.087
10-Formamidokalihinene **16**	0.095
10β-Formamido-5-isocyanatokalihinol-A **17**	ca. 0.05
Cu_2SO_4	0.15

Okino T, Yoshimura E, Hirota H, Fusetani N (1996) J Nat Prod 59:1081
Okino, T.; Yoshimura, E.; Hirota, H.; Fusetani, N. Tetrahedron Lett. ***1995****, 36, 8637.*
Hirota H, Tomono Y, Fusetani N (1996) Tetrahedron 52:2359

Table 4 Diterpenes from gorgonian *Junceella juncea* and their antifouling activity against the larval settlement of barnacle *Balanus amphitrite*

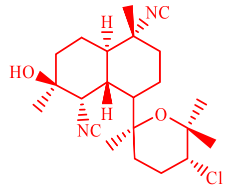
Compound	Antifouling activity EC_{50} ($\mu g\ mL^{-1}$)
Briarane diterpene, juncin R **18**	0.004
Briarane diterpene, juncin X **19**	0.004

S.-H. Qi; S. Zhang; P.-Y. Qian, Z.-H. Xiao, M.-Y. Li, Tetrahedron 2006, 62, 9123.



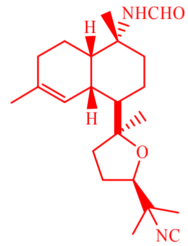
Kalihinene

1β-H, 14-α–Cl **12**
1α-H, 14-α–Cl **13**
1β-H, 14-β–Cl **14**



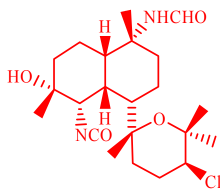
Kalihinol A

15



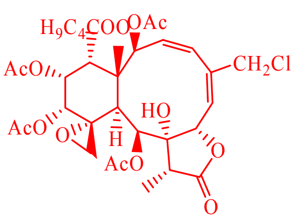
10-Formamidokalihinene

16



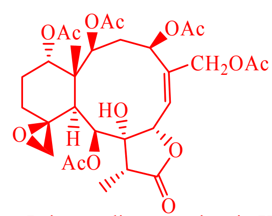
10 -Formamido-5-isocyanatokalihinol-A

17



Briarane diterpene, juncin R

18



Briarane diterpene, juncin X

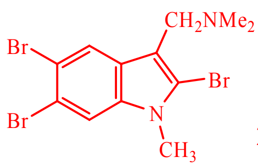
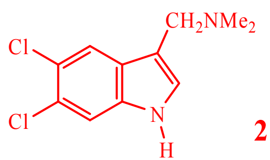
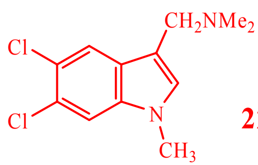
19

Table 5 Minimum inhibitory concentration (MIC) for larval settlement of the blue mussel and 30% lethal concentration (LC_{30}) values of 2,5,6-tribrom-1-methylgramine (TBG) and TBTO (ppm) for reared cyprids

Substance	MIC	LC_{30}
TBG **20**	0.03	0.60
TBTO	0.20	0.06

Kon-ya K, Shimidzu N, Adachi K, Miki W (1994) Fish Sci 60:773

Table 6 Antifouling activity of gramine compounds [28]

Compound	Antifouling activity (ppm)
 **20**	0.063
 **21**	0.008
 **22**	0.063
TBTO	0.127
Cu_2O	1.25

Kawamat M, Kaneko F, Fukunaga J, Fukushima K (2000) Taisei Kensetsu Gijyutu Kenkyushoho 33:89

Gramine is the extract from *Zoobotron pellucidum*.

Table 7 Attachement-hibiting activity against the blue mausel, *Mytilus edulis galloprovicialis,* of shogaols, zingerone, zingerols and TBTF in the conventional submerged assay

Compound	Days			
	29[a]	62	101	125
6-Shogaol (**23**) n=4	○[b]	○	×	×
8-Shogaol (**23**) n=6	○	○	○	○
10-Shogaol (**23**) n=8[d]	○	○[c]	×	×
Zingerone (**24**)	○	×	×	×
6-Zingerol (**25**) n=4	○	×	×	×
8-Zingerol (**25**) n=6	○	○	×	×
TBTF	○	○	○	○

a : from 28 June 2001.

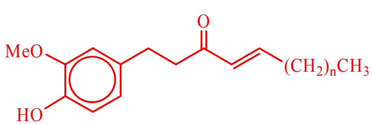
b : ○ activity was apparent; × the degree of fouling was the same as that in the blank zone. Each zone (5 cm in diameter) was coated with 300 mg of a sample.

c : 45 days.

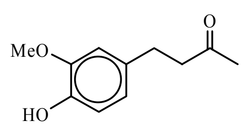
d : 140 mg / 5 cm in diameter.

Etoh H, Kondoh T, Noda R, Singh IP, Sekiwa Y, Morimitsu K, Kubota K (2002) Biosci Biotechnol Biochem 66:1748

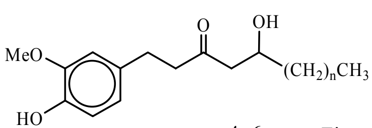
Phenol Derivatives



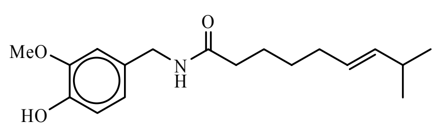
23 n = 4, 6, 8 Shogaols



24 Zingerone



25 n = 4, 6 Zingerols



Capsaicin

Table 8 Repellent activity against the blue mussel, *Mytilus edulis*

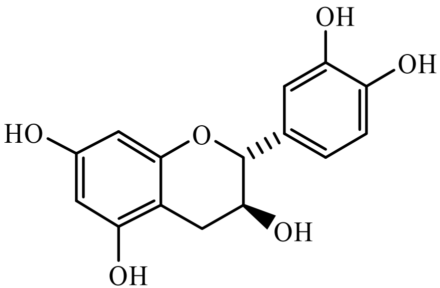
Compound	Repellent activity (Unit[a])
(+) Catechin **26**	6
(-)-Epicatechin **27**	14
Kaempferol coumaroylglucopyranoside **28** (Kaempferol)	227
Polydatin 6"-*O*-(*E*)-*p*-coumarate **29**	185
Raponticin 6"-*O*-(*E*)-*p*-coumarate **30**	179
TBTO	200
TPT acetate	150
$CuSO_4$ [b]	100

a : Unit : $100 \times \frac{\text{minimum dose of } CuSO_4 \text{ for ++ activity } (\mu \text{mol cm}^{-2})}{\text{minimum dose of the sample for ++activity } (\mu \text{mol cm}^{-2})}$

b : Standard sample for repellent activity in the blue mussel assay : 100

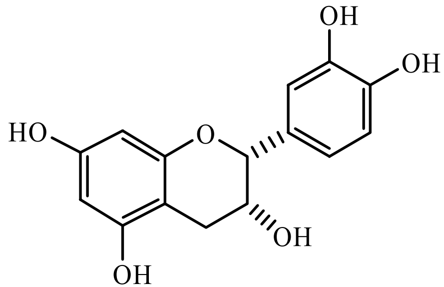
Ina, K. Kagaku to Kogyo ***1991****, 44, 666.*

Polyphenols



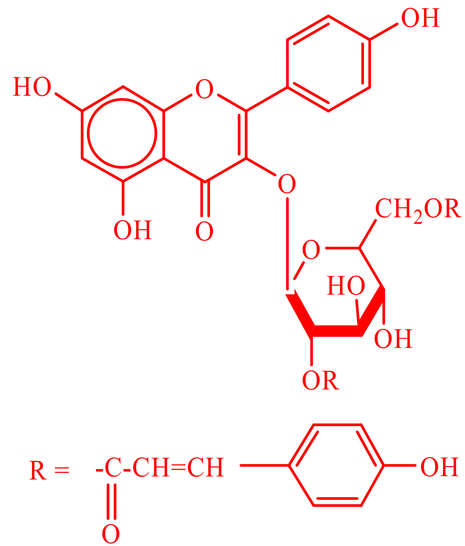
(+) Catechin

26



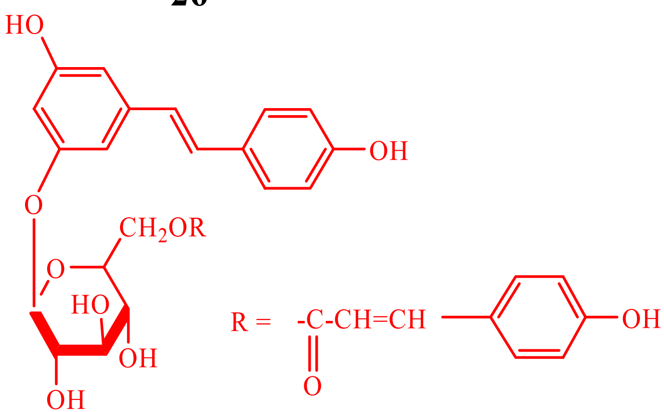
(-)-Epicatechin

27



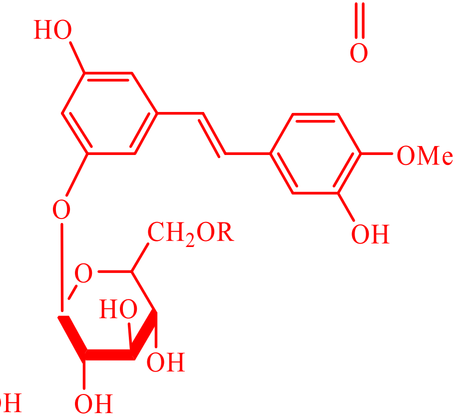
Kaempferol

28



Polydatin 6"-O-(E)-p-coumarate

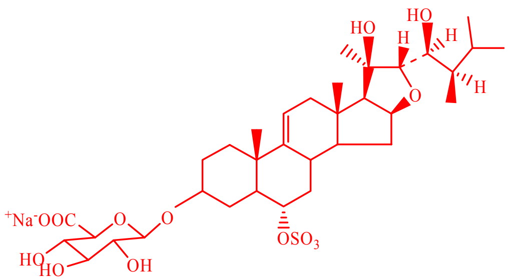
29



Raponticin 6"-O-(E)-p-coumarate

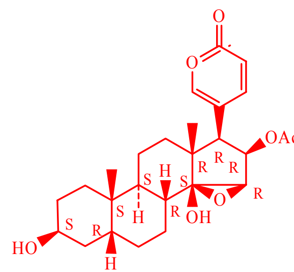
30

Table 9 Antibarnacle activity of bufodienolids and tributyltin chloride				
Antifoulants	Naupliar toxicity		Cyprid antisettlement	
	LD_{50} ng L^{-1}	Relative potency	EC_{50} ng L^{-1}	Relative potency
Bufalin[*1] **31**	27	100.0	10	100.000
Cinobufagin[*2] **32**	37	73.0	162	6.000
TBT Cl (*n*-Bu_3SnCl)	3400	0.8	66000	0.001
*1 = Bufalin = 3,4-Dihydroxybufa-20,22 dienolide				
*2 = Cinobufagin = 16-(Acetyloxy)-14,15-epoxy-3 hydroxybufa-20,22-enolide				



Bufalin

31



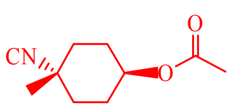
Cinobufagin

32

*D. Rittschof, Biofouling **2000**, 15, 119*

Table 10 Antibarnacle activity of isocyanocyclohexcyl acetate and $CuSO_4$ against the larvae of the barnacle *Balanus amphitrite*

Compound	EC_{50} (μg mL^{-1})
isocyanocyclohexcyl acetate	0.0096
Cu_2SO_4	0.36



isocyanocyclohexcyl acetate

Y. Kitano, Y. Nogata, K. Shinshima, E. Yoshimura, K. Chiba, M. Tada, I. Sakaguchi, Biofouling 2004, 20, 93

Conclusions

1,1-Dimethyl-10-undecyl isocyanide, gramines, shogaols, kaempferols, polydatin, raponticin, bufalin, and isocyanocyclohexyl acetate, showed the similarly high antifouling properties as those of the organotin antifoulants.

Finally, for example, 1,1-dimethyl-10-undecyl isocyanide, gramines and isocyanocyclohexyl acetate show high antifouling activities and these chemical structures are not so complicated.
We expect that some of these natural products or the similar compounds will be utilized in near future as the environmentally friendly antifoulants.