

REPLACED SHEETS SG

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MARINE STRUCTURE

FIELD OF THE INVENTION

The present invention relates to marine structures, in particular immersed marine structures, having an external antifouling coating on the part of the structure immersed in water, as well as antifouling paint compositions that prevent unwanted fouling organisms from attaching and growing on immersed structures that come in contact with water, especially sea-water, for example vessels (including but not limited to boats, yachts, motorboats, motor launches, ocean liners, tugboats, tankers, container ships and other cargo ships, submarines, and naval vessels of all types), pipes, shore and off-shore machinery, constructions and objects of all types such as piers, pilings, bridge substructures, underwater oil well structures, nets and other aquatic culture installations, and buoys etc..

BACKGROUND OF THE INVENTION

On underwater structures and on ship hulls which are exposed to sea- and/or fresh-water, attaching and growing of marine organisms such as green algae, such as *Enteromorpha spp.* and *Ulva spp.*, diatoms, such as *Amphora spp.*, tubeworms, barnacles such as *Balanus spp.*, mussels such as *Mytilus spp.*, bryozoans such as *Bugula spp.*, ascidians, sponges, hydroids etc. cause severe economic losses because of the increased friction (and therefore increased consumption of fuel), or increased resistance to waves or currents (for static structures such as off-shore rigs), and because of increased dry-docking time.

A large number of agents useful for controlling fouling organisms in sea-water or fresh water are being employed today, e.g. copper compounds and organotin compounds. The antifouling agents can be applied in the form of e.g. paints, solutions, dispersions, pastes, or emulsions, which on

application to underwater structures and on ship hulls produce an antifouling effect. In the present context, the term "antifouling effect" is to be understood as a prevention or at least reduction of attachment and growth of marine organisms.

One of the environmental problems is related to pollution of rivers, channels, bays, harbours, lakes and other bodies of water with a low or limited water exchange with heavy metals and toxic compounds by use of such materials in e.g. paintings for application on underwater structures, e.g. a ship's surface. Especially, certain heavy metal compounds are known to accumulate in the animal body such as fish and humans.

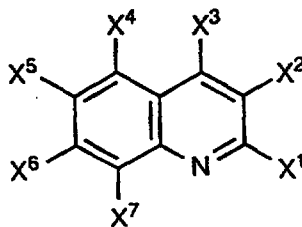
With the use of the antifouling agents disclosed in the present text, it is possible to abolish or minimize the use of heavy metal based components while at the same time obtaining excellent antifouling properties.

SUMMARY OF THE INVENTION

The present inventors have attempted to develop environmentally compatible and effective antifouling compounds. It has been found that quinoline compounds (optionally in combination with other antifouling compounds) have an excellent antifouling effect.

The present invention provides antifouling paint compositions comprising, i.a. as an active ingredient, a quinoline compound of formula I

Formula I



wherein

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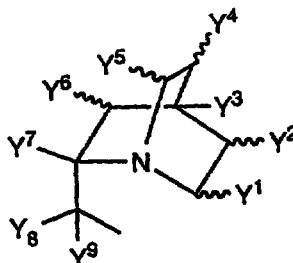


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O=S(=O)c1cnc(C#N)n1COCCOCCOCCOCCOCCOc1ccc2ncncc2c1

X^3 designates the same groups as defined for X^1 above, or X^3 is a group of the formula I'

Formula I'



wherein Y^1 , Y^2 , Y^3 , Y^4 , Y^5 , Y^6 and Y^7 independently designate the same groups as defined for X^1 above or designate C_{6-12} -alkyl, and Y^8 and Y^9 independently designate the same groups as defined for X^1 above or designate C_{6-12} -alkyl or together form oxo, and the wavy lines signify that the substituents in question may be in either of the two possible isomeric configurations;

or an N-oxide or a salt thereof;

with the proviso that if X^1 , X^2 , X^3 , X^4 , X^5 , and X^6 each is hydrogen, and the compound of formula I is not an N-oxide, then X^7 is not hydroxy.

DETAILED DESCRIPTION OF THE INVENTION

The term "immersed" in the present context relates to structures intended for immersion into any kind of water, salt, brackish or fresh water.

In the present context, the term " C_{1-5} -alkyl" is intended to mean alkyl groups with 1-5 carbon atoms which may be straight or branched or cyclic such as methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, pentyl, isopentyl, neopentyl, cyclopentyl, etc.

In the present context, the term " C_{1-12} -alkyl" is intended to mean alkyl groups with 1-12 carbon atoms which may be straight or branched or cyclic such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl, octyl, dodecyl, cyclopentyl, cyclohexyl, decalanyl, etc. Similarly, the term " C_{6-12} -alkyl" is intended to mean alkyl groups with 6-12 carbon atoms which may be straight or branched or cyclic, e.g. appropriate groups among those listed above.

The term "substituted C_{1-12} -alkyl" is intended to mean a C_{1-12} -alkyl group which is substituted with one or more, preferably 1-3, groups selected from carboxy; protected carboxy such as a carboxy ester, e.g. C_{1-12} -alkoxycarbonyl; aminocarbonyl; mono- and di(C_{1-12} -alkyl)aminocarbonyl; amino- C_{1-12} -alkyl-aminocarbonyl; mono- and di(C_{1-12} -alkyl)amino- C_{1-12} -alkyl-aminocarbonyl; amino; mono- and di(C_{1-12} -alkyl)amino; C_{1-12} -alkylcarbonylamino; hydroxy; protected hydroxy such as acyloxy, e.g. C_{1-12} -alkanoyloxy; sulphonyloxy; C_{1-12} -alkylsulphonyloxy; nitro; optionally substituted aryl; optionally substituted heterocyclyl; halogen, e.g. fluorine, chlorine, bromine or iodine. Similarly, the term "optionally substituted C_{1-12} -alkyl" is intended to mean a C_{1-12} -alkyl group which is unsubstituted or is substituted with one or more, preferably 1-3, groups selected from those listed immediately above.

Examples of such substituted C_{1-12} -alkyl groups are carboxy- C_{1-12} -alkyl (e.g. carboxymethyl and carboxyethyl), protected carboxy- C_{1-12} -alkyl such as esterified carboxy- C_{1-12} -alkyl (e.g. C_{1-12} -alkoxycarbonyl- C_{1-12} -alkyl such as methoxycarbonylmethyl, ethoxycarbonylmethyl, and methoxycarbonylethyl), aminocarbonyl- C_{1-12} -alkyl (e.g. aminocarbonylethyl, aminocarbonylethyl and aminocarbonylpropyl), C_{1-12} -alkylaminocarbonyl- C_{1-12} -alkyl (e.g. methylaminocarbonylmethyl and ethylaminocarbonylmethyl), amino- C_{1-12} -alkyl-aminocarbonyl- C_{1-12} -alkyl (e.g. aminomethylaminocarbonylmethyl and aminoethylaminocarbonylmethyl), mono- or di(C_{1-12} -alkyl)amino- C_{1-12} -alkylamino-

carbonyl- C_{1-12} -alkyl (e.g. dimethylaminomethylaminocarbonylmethyl and dimethylaminoethylaminocarbonylmethyl), mono- or di(C_{1-12} -alkyl)amino- C_{1-12} -alkyl (e.g. dimethylaminomethyl and dimethylaminoethyl), hydroxy- C_{1-12} -alkyl (e.g. hydroxymethyl and hydroxyethyl), protected hydroxy- C_{1-12} -alkyl such as acyloxy- C_{1-12} -alkyl (e.g. C_{1-12} -alkanoyloxy- C_{1-12} -alkyl such as acetyloxyethyl, acetyloxypropyl, acetyloxybutyl, acetyloxy-pentyl, propionyloxymethyl, butyryloxymethyl, and hexanoyloxymethyl).

In the present context, the term " C_{2-12} -alkenyl" is intended to mean mono-, di- or polyunsaturated alkyl groups with 2-12 carbon atoms which may be straight or branched or cyclic in which the double bond(s) may be present anywhere in the chain or the ring(s), for example vinyl, 1-propenyl, 2-propenyl, hexenyl, decenyl, 1,3-heptadienyl, cyclohexenyl etc. Some of the substituents exist both in a cis and a trans configuration. The scope of this invention comprises both the cis and trans forms.

In the present context, the term " C_{2-12} -alkynyl" is intended to mean a straight or branched alkyl group with 2-12 carbon atoms and incorporating one or more triple bond(s), e.g. ethynyl, 1-propynyl, 2-propynyl, 2-butynyl, 1,6-heptadiynyl, etc.

In the expressions "optionally substituted C_{2-12} -alkenyl" and "optionally substituted C_{2-12} -alkynyl", the term "optionally substituted" is intended to mean that the moiety may be substituted one or more times, preferably 1-3 times, with one of the groups defined above for "optionally substituted C_{1-12} -alkyl".

The term " C_{1-12} -alkoxy" designates groups comprising an oxy function which groups optionally may be substituted one or more times with the substituents indicated for "optionally substituted alkyl" described above.

In the present context, the term "aryl" is intended to mean phenyl, biphenyl, naphthyl, fluorenyl, tetralinyl, etc..

In the present context, the term "optionally substituted aryl" is intended to mean aryl as defined above which may be substituted with one or more, preferably 1-3, substituents selected from the group consisting of hydrogen; hydroxy; optionally substituted C₁₋₁₂-alkyl; optionally substituted C₂₋₁₂-alkenyl; optionally substituted C₂₋₁₂-alkynyl; optionally substituted C₁₋₁₂-alkoxy; optionally substituted heterocyclyl; optionally substituted aryl; optionally substituted aryloxy; halogen; nitro; nitroso; cyano; amino; mono(C₁₋₁₂-alkyl)amino; di(C₁₋₁₂-alkyl)amino; (optionally substituted C₁₋₁₂-alkyl)carbonylamino; aminocarbonyl; mono(C₁₋₁₂-alkyl)aminocarbonyl; di(C₁₋₁₂-alkyl)aminocarbonyl; optionally substituted C₁₋₁₂-acyl; optionally substituted C₁₋₁₂-acyloxy; (optionally substituted C₁₋₁₂-acyl)-C₁₋₁₂-alkyl; carboxy; C₁₋₁₂-alkoxycarbonyl; thio; (optionally substituted C₁₋₁₂-alkyl)thio; optionally substituted arylthio; (optionally substituted C₁₋₁₂-alkyl)sulphonyl; optionally substituted arylsulphonyl; mono(optionally substituted C₁₋₁₂-alkyl)amino-sulphonyl; di(optionally substituted C₁₋₁₂-alkyl)amino-sulphonyl; sulphono (SO₃H); sulphino (SO₂H); halosulphonyl; isocyano; isothiocyano; thiocyano.

In the present context, the term "optionally substituted heterocyclyl" is intended to mean a 5- or 6-membered monocyclic or a 11- or 12-membered bicyclic, aromatic or partially or fully hydrogenated, heterocyclic group containing one or more, preferably 1-3, heteroatoms selected from oxygen, nitrogen and sulphur, which said ring or ring system optionally being substituted with one or more substituents selected from the group consisting of hydrogen; hydroxy; optionally substituted C₁₋₁₂-alkyl; optionally substituted C₂₋₁₂-alkenyl; optionally substituted C₂₋₁₂-alkynyl; optionally substituted C₁₋₁₂-alkoxy; optionally substituted heterocyclyl; optionally substituted aryl; optionally substituted aryloxy; halogen; nitro; nitroso; cyano; amino;

mono(C₁₋₁₂-alkyl)amino; di(C₁₋₁₂-alkyl)amino; (optionally substituted C₁₋₁₂-alkyl)carbonylamino; aminocarbonyl; mono(C₁₋₁₂-alkyl)aminocarbonyl; di(C₁₋₁₂-alkyl)aminocarbonyl; optionally substituted C₁₋₁₂-acyl; optionally substituted C₁₋₁₂-acyloxy; (optionally substituted C₁₋₁₂-acyl)-C₁₋₁₂-alkyl; carboxy; C₁₋₁₂-alkoxycarbonyl; thiolo; optionally substituted C₁₋₁₂alkylthio; optionally substituted arylthio; (optionally substituted C₁₋₁₂-alkyl)sulphonyl; optionally substituted arylsulphonyl; mono(optionally substituted C₁₋₁₂-alkyl)amino-sulphonyl; di(optionally substituted C₁₋₁₂-alkyl)amino-sulphonyl; sulphono (SO₃H); sulphino (SO₂H); halosulphonyl; isocyano; isothiocyano; thiocyano.

Examples of the heterocyclic groups are pyrrolyl, furanyl, 2,3-dihydrofuranyl, tetrahydrofuranyl, thienyl, 2,3-dihydrothienyl, tetrahydrothienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, pyrrolinyl, pyrrolidinyl, pyridinyl, piperidinyl, pyrimidinyl, purinyl, quinolinyl, 1,2-dihydroquinolinyl, isoquinolinyl, indolyl, piperazinyl, pyrazinyl, dioxolanyl, dioxanyl, 1,3,5-trioxanyl, tetrahydrothiapyranyl, dithiolanyl, pyrazolidinyl, iminazolidinyl, pyridazinyl, sym-triazinyl, sym-tetrazinyl, quinazolinyl, 1,5-naphtyridinyl, pteridinyl, isoindolyl, 2,3,2',3'-pyrrolopyrrolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, benzimidazolyl, indazolyl, benzofuranyl, isobenzofuranyl, benzothiophenyl, thienothiophenyl, isoxazolyl, 1,2,5-oxadiazolyl, isothiazolyl, 1,3,4-thiadiazolyl, benzoxazolyl, benzothiazolyl etc.

In the present context, the term "acyl" comprises C₁₋₁₂-alkanoyl (e.g. formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl and hexanoyl), C₁₋₁₂-alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl and t-butoxycarbonyl) etc.

In the present context, the term "acyloxy" designates an oxy group to which is attached a group as defined above for "acyl". Optional substituents on acyl or acyloxy groups may

be the same as those described for optionally substituted alkyl above.

In the present context, the term "pyranosyl" is intended to mean galactopyranosyl, glucopyranosyl, mannopyranosyl, allopentopyranosyl, altropyransyl, gulopyranosyl, idopyranosyl, talopyranosyl, etc, as well as O-C₁₋₁₈-alkylated, O-C₁₋₁₈-alkanoylated or benzoylated derivatives thereof. The pyranosyl moieties can exist in both the α -anomeric and the β -anomeric forms.

In the present context, the term "furanosyl" is intended to mean fructofuranosyl, arabinofuranosyl, psicofuranosyl, sorbofuranosyl, xylofuranosyl, lyxofuranosyl, etc, as well as O-C₁₋₁₈-alkylated, O-C₁₋₁₈-alkanoylated or benzoylated derivatives thereof. The furanosyl moieties can exist in both the α -anomeric and the β -anomeric forms.

The term "salt" is intended to comprise a salt such as an organic acid addition salt (e.g. acetate, valerate, salicylate, galacturonate, gluconate, tannate, trifluoroacetate, maleate, tartrate, methanesulphonate, benzenesulphonate, formate, thiocyanate and toluenesulphonate), an inorganic acid addition salt (e.g. hydrochloride, hydrobromide, hydroiodide, dihydrochloride, dihydrobromide, dihydroiodide, sulphate, hydrogensulphate, halosulphate such as iodosulphate, nitrate, phosphate, and carbonate), a salt with an amino acid (e.g. arginine, aspartic acid and glutamic acid), a metal salt such as an alkali metal salt (e.g. sodium salt and potassium salt) and an earth alkali metal salt (e.g. calcium salt and magnesium salt), an ammonium salt, an organic alkali salt (e.g. trimethylamine salt, triethylamine salt, pyridine salt, picoline salt, dicyclohexylamine salt and N,N'-dibenzylethylenediamine salt), and hydrates thereof.

The term "N-oxide" is intended to comprise compounds of the present invention where the ring nitrogen of the quinoline ring system is oxidized to the N-oxide.

In preferred embodiments, the quinoline derivative of formula I is substituted in the 2-position with a substituent selected from the group consisting of H, OH, CH₃, CH₂Cl, F, Cl, Br, COOH, and quinolinyl; in the 3-position with a substituent selected from the group consisting of H, NH₂, CHO, COOH, F, Cl, and Br; in the 4-position with a substituent selected from the group consisting of H, OH, CH₃, F, Cl, Br, NH₂, NO₂, CHO, mono- or di(C₁₋₆-alkyl)amino-C₁₋₆-alkylamino, amino-C₁₋₆-alkylamino, a group I' as defined above, and COOH; in the 5-position with a substituent selected from the group consisting of H, OH, F, Cl, Br, and SO₃H; in the 6-position with a substituent selected from the group consisting of H, NH₂, CH₃, F, Cl, Br, and OCH₃; in the 7-position with a substituent selected from the group consisting of H, F, Cl, I and Br; in the 8-position with a substituent selected from the group consisting of H, OH, F, Cl, Br, SO₃H, CH₃, NH₂, mono- or di(C₁₋₆-alkyl)amino-C₁₋₆-alkylamino, amino-C₁₋₆-alkylamine, OCH₂CH₃ and SO₂Cl; and the nitrogen atom of the quinoline ring system is at the normal oxidation stage or oxidized to the N-oxide.

In especially preferred embodiments of the invention the quinoline derivative of formula I is substituted in the 2-position with a substituent selected from the group consisting of H, Cl, CH₃, and CH₂Cl; in the 3-position with a CHO; in the 4-position with a substituent selected from the group consisting of H, Cl, Br, CHO, CH₃, NH₂, NO₂, a group I' as defined above, di(C₁₋₆-alkyl)amino-C₁₋₆-alkylamino, and amino-C₁₋₆-alkylamino; in the 5-position with a substituent selected from the group consisting of H, Cl, and OH; in the 6-position with a substituent selected from the group consisting of H, CH₃, OCH₃; in the 7-position with a substituent selected from the group consisting of H, Cl, I and Br; in the 8-position with a substituent selected from

the group consisting of H, OH, CH₃, di(C₁₋₆-alkyl)amino-C₁₋₆-alkylamino, amino-C₁₋₆-alkylamino, NH₂, and SO₂Cl; and the nitrogen atom of the quinoline ring system is at the normal oxidation stage or oxidized to the N-oxide.

It will be obvious to a person skilled in the art that the group defined by the formula I' contains several asymmetric carbon atoms and that the compounds of formula I therefore can exist as several stereoisomers. The present invention comprises each of such stereoisomers as well as mixtures thereof, such as racemic mixtures. It is preferred that the orientation of substituents on the group of formula I' correspond to the orientation in the corresponding 1-azabicyclo[2,2,2]octylmethyl group in cinchona alkaloids such as quinine and quinidine.

Examples of quinoline compounds of formula I are given in Table 1 below.

TABLE 1

<u>No.</u>	<u>Compound</u>
1	quinidine
2	quinine
3	cinchonidine
4	cinchonine
5	cinchotoxin
6	quinaidine
7	chloroquine
8	quinine hydrochloride
9	3-aminoquinoline
10	6-aminoquinoline
11	8-aminoquinoline
12	4-aminoquinaidine
13	2,2'-biquinoline
14	O-(4-chlorobenzoyl)hydroquinidine
15	O-(4-chlorobenzoyl)hydroquinine
16	5-chloro-8-hydroxy-7-iodoquinoline

17	5-chloro-8-hydroxyquinoline
18	2-(chloromethyl)quinoline hydrochloride
19	chloroquine diphosphate
20	2-chloroquinoline
21	4-chloroquinoline
22	5,7-dibromo-8-hydroxyquinoline
23	4,7-dichloroquinoline
24	8-ethoxyquinoline-5-sulphonic acid
25	hydroquinidine
26	hydroquinine
27	8-hydroxy-7-iodoquinoline-5-sulphonic acid
28	8-hydroxyquinaldine
29	kynurenic acid
30	lepidine
31	6-methoxyquinoline
32	6-methylquinoline
33	8-methylquinoline
34	4-nitroquinoline-1-oxide
35	primaquine diphosphate
36	quinaldic acid
37	quinoline
38	quinoline-3-carboxaldehyde
39	quinoline-4-carboxaldehyde
40	quinoline-3-carboxylic acid
41	quinoline-4-carboxylic acid
42	quinoline-N-oxide hydrate
43	8-quinolinesulphonyl chloride
44	1-(8-quinolinesulphonyl)-3-nitro-1H-1,2,4-triazole
45	2-quinolinol
46	4-quinolinol
47	5-quinolinol
48	8-quinolinol N-oxide
49	tetraethylene glycol bis(8-quinolinyl)ether
50	xanthurenic acid

Some of the quinoline compounds expressed by formula I are known compounds which can be extracted from natural sources or prepared synthetically by conventional methods known in the art. Thus, quinoline compounds of formula I can be synthesized by conventional methods known in the art. This includes, e.g., nucleophilic substitution reactions; electrophilic substitution reactions; homolytic substitution reactions; cyclisation reactions; the Skraup reaction; the Chichibabin reaction; the Doebner-von Miller synthesis; Combes' synthesis; the Friedländer synthesis; cyclisation of o-substituted benzenes; the Balz-Schiemann reaction; aldol condensations, Claisen condensations and other carbanion reactions; reduction reactions; esterification reactions; displacement reactions involving aryne intermediates; sulphonation; nitration; catalytic alkylations; Ladenburg rearrangements; decarboxylations; the Reissert reaction; Friedel-Craft substitutions; hydrolysis reactions etc. (See "The Chemistry of Heterocyclic Compounds" edited by E. C. Taylor, Vol. 32, part I, II and III, John Wiley & Sons, New York, 1990).

For example, quinine (compound no. 2 in Table 1) can be obtained by extraction from *Cinchona* spp. as described by N. L. Butta and C. Quassim in *Indian J. Chem.* 6(19) (1968), 566-567, or by synthesis from n-benzoyl-meroquinene methyl ester and 6-methoxylepidine as described by J. Gutzwiller and M. Uskoković, *J. Am. Chem. Soc.* 92(1), (1970), 204-5.

The quinoline compounds, used as an active ingredient, may be used alone or in combination with other antifouling agents. The active ingredient may be used as a crude extract or in a purified form.

The antifouling agents may be used in various formulations including paints, solutions, dispersions, pastes, emulsions etc.. For example, when the antifouling agent is to be used in a paint, an antifouling paint is prepared by mixing one or

several of the active ingredients of the formula I with one or more of the components described below.

A typical antifouling paint composition for use in providing a marine structure according to the invention comprises at least one antifouling agent of the formula I as well as one or more components selected among binders, fillers, pigments, dyes, solvents, and additives.

Typical examples of binders are gum rosin; wood rosin; tall oil rosin; commercial rosin derivatives; copolymers of vinyl acetate and vinyl isobutyl ether; copolymers of vinyl chloride and vinyl isobutyl ether; alkyd resins or modified alkyd resins; hydrocarbon resins such as petroleum fraction condensates; chlorinated rubbers; styrene copolymers such as styrene/butadiene copolymers and styrene/acrylate copolymers; acrylic resins such as isobutyl methacrylate copolymers, methyl methacrylate/n-butyl methacrylate copolymers; polyamide resins such as polyamide based on dimerized tall oil fatty acids; cyclized rubbers; epoxy esters; epoxy urethanes; polyurethanes; epoxy polymers; silicates; silicone resins or silicone elastomers; etc., as well as mixtures thereof. The binder may be erodible (self-polishing) or non-erodible (non-soluble). The amount of binder in a paint composition is typically in the range of 10-80 percent by weight in the wet paint, preferably 10-40 percent by weight in the wet paint.

Typical examples of fillers are calcium carbonate, dolomite, talc, mica, barium sulphate, kaolin, quartz flour, etc.. The amount of filler in the paint composition is typically in the range 0-20 percent by weight in the wet paint.

Typical examples of pigments are grades of titanium dioxide, zinc oxide, red iron oxide, carbon black, graphite, yellow iron oxide, phthalocyanine blue, phthalocyanine green. The amount of pigment in a paint composition may typically be in

the range of 1-60 percent by weight in the wet paint, preferably 5-60 percent.

Typical examples of dyes are 1,4-bis(butylamino)anthraquinone and other anthraquinone derivatives.

Typical examples of solvents in which the components of the antifouling paint are dissolved, dispersed or emulsified are water; alcohols such as methanol, ethanol, propanol, isopropanol, butanol, isobutanol, and benzyl alcohol; alcohol/water mixtures such as ethanol/water mixtures; aliphatic, cycloaliphatic, and aromatic hydrocarbons such as white spirit, cyclohexane, toluene, xylene, and naphtha solvent; ketones such as methyl ethyl ketone, acetone, methyl isobutyl ketone, methyl isoamyl ketone, diacetone alcohol, and cyclohexanone; ether alcohols such as 2-butoxyethanol, propylene glycol monomethyl ether, and butyl diglycol; esters such as methoxypropyl acetate, n-butyl acetate, and 2-ethoxyethyl acetate; chlorinated hydrocarbons such as methylene chloride, tetrachloroethane, and trichloroethylene; and mixtures thereof as well as any other solvents usually employed within the coating industry. The amount of solvent in a paint composition is typically in the range of 0-50 percent by weight in the wet paint, preferably 15-35 percent.

Typical examples of additives are:

plasticizers such as chlorinated paraffin; low molecular weight polybutene; phthalates such as dibutyl phthalate, benzylbutyl phthalate, dioctyl phthalate, and diisodecylphthalate; phosphate esters such as tricresyl phosphate, and 2-ethylhexyl diphenyl phosphate; sulphone amides such as alkyl-p-toluene sulphone amide; and polymeric acrylic plasticizers. Plasticizers may be present in amounts in the range of 0-10 percent by weight in the wet paint;

surfactants such as derivatives of propylene oxide or ethylene oxide such as alkylphenol-ethylene oxide conden-

sates; ethoxylated monoethanolamides of unsaturated fatty acids such as ethoxylated monoethanolamides of linoleic acid; sodium dodecylsulphate; alkylphenol ethoxylates; and soya lecithin. Surfactants may be present in amounts in the range of 0-2 percent by weight in the wet paint;

defoaming agents such as silicone oils which may be present in amounts in the range of 0-1 percent by weight in the wet paint;

catalysts such as polymerization catalysts and initiators, e.g. azobisisobutyronitrile, ammonium persulphate, dilaurylperoxide, di-t-butylperoxide, cumenehydroperoxide, and p-toluenesulphonic acid; dryers, e.g. metal octoates and metal naphthenates; and activators, e.g. salicylic acid and benzyl alcohol. Catalysts may be present in amounts in the range of 0-3 percent by weight in the wet paint;

stabilizers such as stabilizers against light and heat, e.g. 2-hydroxy-4-methoxybenzophenone, 2-(5-chloro-(2H)-benzotriazol-2-yl)-4-methyl-6-(tert-butyl)phenol, 2,4-ditert-butyl-6-(5-chlorobenzotriazol-2-yl)phenol, which may be present in amounts in the range of 0-2 percent by weight in the wet paint; stabilizers against moisture such as molecular sieves or water scavengers, which may be present in amounts in the range of 1-3 percent by weight in the wet paint; stabilizers against oxidation such as tert-butylhydroquinone; butylated hydroxyanisole; butylated hydroxytoluene; propylgallate; tocopherols; L-ascorbyl palmitate; carotens; vitamin A, which may be present in amounts in the range of 0-2 percent by weight in the wet paint;

polymerization inhibitors, e.g. para-benzoquinone, hydroquinone and methyl-hydroquinone, which may be present in amounts in the range of 0-3 percent by weight in the wet paint;

inhibitors against corrosion such as zinc phosphate; zinc metaborate, which may be present in amounts in the range of 0-20 percent by weight in the wet paint;

coalescing agents such as glycols, which may be present in amounts in the range of 0-5 percent by weight in the wet paint; and

thickeners and anti-settling agents such as colloidal silica, aluminium stearate, hydrogenated castor oil, polyethylene fibres and organo-modified clays, which may be present in amounts in the range of 2-6 percent by weight in the wet paint.

It is often advantageous to incorporate into the coating on the marine structure, preferably in the same layer as the quinoline derivative of formula I, a substance which enhances the antifouling activity of the quinoline compound. In the present specification and claims, the term "enhances the antifouling activity" is intended to indicate, that the substance has an additive effect or even a synergistic effect together with the quinoline compound. Thus, apart from the quinoline compounds of the formula I, an antifouling paint may contain other secondary substances which enhance the antifouling activity of the quinoline compound(s). Typical examples of such enhancing substances to be used in combination with the quinoline compounds of formula I are:

organometals such as trialkyltin salts such as hydroxytriphenylstannane, dibutylbis(1-oxododecyloxy)-stannane, fluorotriphenylstannane, chlorotriphenylstannane, tributylfluorostannane, and tributyltin maleate; hexabutyl-distannoxane; trialkyltin copolymers such as tributyltin resinate, tributyltin acrylate copolymer, and tributyltin methacrylate copolymer; metallo-dithiocarbamates such as bis(dimethyldithiocarbamato)zinc, ethylene-bis(dithiocarbamato)zinc, ethylene-bis(dithiocarbamato)manganese, and complexes

between these; bis(1-hydroxy-2(1H)-pyridinethionato)-O,S copper; copper acrylate; zinc pyridine-2-thiol-1-oxide; phenyl(bispyridyl)-bismuth dichloride;

metal biocides such as copper, copper metal alloys such as copper-nickel alloys; metal oxides such as cuprous oxide, and cupric oxide; metal salts such as cuprous thiocyanate, barium metaborate, and copper sulphide;

heterocyclic nitrogen compounds such as 3a,4,7,7a-tetrahydro-2-((trichloromethyl)thio)-1H-isoindole-1,3(2H)-dione, pyridine-triphenylborane, 1-(2,4,6-trichlorophenyl)-1H-pyrrole-2,5-dione, 2,3,5,6-tetrachloro-4-(methylsulphonyl)-pyridine, and 2-methylthio-4-tert-butylamino-6-cyclopropylamine-s-triazine;

heterocyclic sulphur compounds such as 2-(4-thiazolyl)-benzimidazole, 4,5-dichloro-2-octyl-3(2H)-isothiazolone, 1,2-benzisothiazolin-3-one, 4,5-dichloro-2-octyl-3(2H)-isothiazoline, 1,2-benzisothiazolin-3-one, and 2-(thiocyanatomethylthio)-benzothiazole;

urea derivatives such as N-(1,3-bis(hydroxymethyl)-2,5-dioxo-4-imidazolidinyl)-N,N'-bis(hydroxymethyl)urea and 3-(3,4-dichlorophenyl)-1,1-dimethyl urea;

amides or imides of carboxylic acids, sulphonic acids and of sulphenic acids such as 1,1-dichloro-N-((dimethylamino)sulphonyl)-1-fluoro-N-(4-methylphenyl)-methanesulphenamide, 2,2-dibromo-3-nitrilo-propionamide, N-methylol formamide, N-(dichlorofluoromethylthio)-phthalimide, and N,N-dimethyl-N'-phenyl-N'-(dichlorofluoromethylthio)-sulphamide;

salts or esters of carboxylic acids such as 2-((3-iodo-2-propynyl)oxy)-ethanol phenylcarbamate and N,N-didecyl-N-methyl-poly(oxyethyl)ammoniumpropionate;

amines such as dehydroabiethylamines and cocodimethylamine;

substituted methane such as di(2-hydroxy-ethoxy)methane, 5,5'-dichloro-2,2'-dihydroxydiphenylmethane, and methylene-bisthiocyanate;

substituted benzene such as 2,4,5,6-tetrachloro-1,3-benzenedicarbonitrile, 1,1-dichloro-N-((dimethylamino)-sulphonyl)-1-fluoro-N-phenylmethanesulphenamide, and 1-((diiodomethyl)sulphonyl)-4-methyl-benzene;

tetraalkyl phosphonium halogenides such as tri-n-butyltetradecyl phosphonium chloride;

Guanidine derivatives such as n-dodecylguanidine hydrochloride;

disulphides such as bis-(dimethylthiocarbamoyl)-disulphide and tetramethylthiuramdisulphide;

and mixtures thereof.

In the antifouling paint composition, the total amount of the compound(s) of formula I as well as any secondary or enhancing antifouling agent(s) may be in the range of 2-50 percent by weight in the wet paint, preferably 5-50 percent.

The antifouling paint composition may be prepared by any suitable technique that is commonly used within the field of paint production. Thus, the various components may be mixed together using a high speed disperser, a ball mill, a pearl mill, a three-roll mill, etc..

The antifouling paint composition according to the invention may be applied to the marine structure to be protected by means of any of the usual techniques used within the paint field such as by means of a brush, a roller, a pad, by dip-

ping, by spraying, etc.. The exact technique chosen depends upon the object to be protected and also upon the particular composition (such as its viscosity etc.) and upon the particular situation. Preferred applications techniques are spraying and by means of a brush or a roller.

The antifouling paint composition according to the invention may be applied to the marine structure to be protected in one or several successive layers, typically 1 to 3 layers. The total dry film thickness of the coating will typically be 10-1000 μm , preferably 40-450 μm .

The marine structure to which the paint composition according to the invention may be applied to may be any of a wide variety of solid objects that come into contact with water, in particular sea-water, for example vessels (including but not limited to boats, yachts, motorboats, motor launches, ocean liners, tugboats, tankers, container ships and other cargo ships, submarines (both nuclear and conventional), and naval vessels of all types); pipes; shore and off-shore machinery, constructions and objects of all types such as piers, pilings, bridge substructures, underwater oil well structures, etc.; nets and other mariculture installations; and buoys; and is especially applicable to the hulls of ships and boats and to pipes.

Prior to the application of a paint composition of the invention to a marine structure, the marine structure may first be coated with a primer-system which may comprise several layers and may be any of the conventional primer systems used in connection with application of antifouling paints to marine structures. Thus, the primer system may include a first layer of a tar or bitumen composition followed by a layer of an adhesion-promoting primer. In a preferred embodiment, the primer-system is a sea-water non-erodible paint having a composition as that of the antifouling paint but which erodes at a rate of less than 1 μm per 10,000 nautical miles.

Suitable quinoline derivatives of the present invention are for example those which, in the Rhizoid test performed as described in Example 1 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, preferably an activity of at least 80% at a nominal concentration of the supernatant of 100 ppm, more preferably an activity of at least 80% at a nominal concentration of the supernatant of 50 ppm such as an activity of at least 80% at a nominal concentration of the supernatant of 10 ppm, when the test conditions are calibrated so that the sodium dodecylsulphate reference, in a concentration of 20 ppm gives an activity of 20-60%.

Suitable quinoline derivatives of the present invention are for example those which, in the spore test performed as described in Example 2 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, preferably an activity of at least 80% at a nominal concentration of the supernatant of 100 ppm, more preferably an activity of at least 80% at a nominal concentration of the supernatant of 50 ppm such as an activity of at least 80% at a nominal concentration of the supernatant of 10 ppm, when the test conditions are calibrated so that the TBTO reference, in a concentration of 0.007 ppm gives an activity of 50-100 %.

Suitable quinoline derivatives of the present invention are for example those which, in the Diatom test performed as described in Example 3 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, preferably an activity of at least 80% at a nominal concentration of the supernatant of 100 ppm, more preferably an activity of at least 80% at a nominal concentration of the supernatant of 50 ppm such as an activity of at least 80% at a nominal concentration of the supernatant of 10 ppm, when the test conditions are calibrated so that the sodium dodecylsulphate reference, in a concentration of 30 ppm gives an activity of 20-60%.

Suitable quinoline derivatives of the present invention are for example those which, in the Nitocra test performed as described in Example 4 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, preferably an activity of at least 80% at a nominal concentration of the supernatant of 100 ppm, more preferably an activity of at least 80% at a nominal concentration of the supernatant of 50 ppm such as an activity of at least 80% at a nominal concentration of the supernatant of 10 ppm, when the test conditions are calibrated so that the TBTO reference, in a concentration of 0.007 ppm gives an activity of 5-40 %.

Suitable quinoline derivatives of the present invention are for example those which, in the cyprids test performed as described in Example 5 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, preferably an activity of at least 80% at a nominal concentration of the supernatant of 100 ppm, more preferably an activity of at least 80% at a nominal concentration of the supernatant of 50 ppm such as an activity of at least 80% at a nominal concentration of the supernatant of 100 ppm.

Suitable quinoline derivatives of the present invention are those which when incorporated in a structure alone or in combination with one or more antifouling activity enhancing substances, in a paint prepared as described in Example 6 herein and tested as described in Example 7 herein, with respect to algae or animals, preferably both, result in a rating at least 1 rating units lower than the corresponding rating for the blank sample, when the blank sample has attained a rating in the range of 1 to 4.

Preferred quinoline derivatives of the present invention are those which when incorporated in a structure alone or in combination with one or more antifouling activity enhancing substances, in a paint prepared as described in Example 6 herein and tested as described in Example 7 herein, with

respect to algae or animals, preferably both, result in a rating at least 2 rating units lower than the corresponding rating for the blank sample, when the blank sample has attained a rating in the range of 2 to 4.

More preferred quinoline derivatives of the present invention are those which when incorporated in a structure alone or in combination with one or more antifouling activity enhancing substances, in a paint prepared as described in Example 6 herein and tested as described in Example 7 herein, with respect to algae or animals, preferably both, result in a rating at least 3 rating units lower than the corresponding rating for the blank sample, when the blank sample has attained a rating in the range of 3 to 4.

The invention is illustrated by the following non-limiting examples, in which Examples 1-5 describe *in vitro* tests of compounds of the formula I and Examples 6 and 7 describe how a paint containing such compounds may be prepared and tested, respectively.

EXAMPLE 1

Rhizoid-test

Effect of several quinoline derivatives on *Enteromorpha* spp.

Enteromorpha spp. is a very common fouling organism. When filaments of *Enteromorpha* spp. are cut into segments and exposed to normal sea-water containing no bio-active compounds, rhizoids which are functionally similar to small roots are produced within 3-4 days. A number of quinoline derivatives were tested for their effect on the rhizoid production of *Enteromorpha intestinalis* segments.

Solutions of the quinoline derivative to be tested were prepared as follows: An appropriate amount (by weight) of the quinoline derivative was dissolved in 1 ml acetone and was then resuspended in an appropriate amount (by weight) of filtered natural sea-water (NSW; having a salinity of 15‰) to give the desired nominal concentration (e.g. 50 ppm). The slurry was rotated for 24 hours and then centrifuged. The supernatant was hereafter defined as having the original nominal concentration (e.g. 50 ppm).

The top and the basal part of filaments of *Enteromorpha intestinalis* (collected from the intertidal zone of Øresund, Denmark) was first removed after which the remainder was cut into segments having an approximate length of 1 cm. 30 ml of the prepared supernatant of the quinoline derivative to be tested was added into petri-dishes having a diameter of 9 cm. Dilutions of the prepared supernatant were also added into petri-dishes. Approximately 25 segments of *Enteromorpha intestinalis* were placed in each petri-dish, which was then incubated for 96 hours at a temperature of about 10-15°C and with constant light (3000-4000 lux light level). After 96 hours, for each dilution, the segments were placed onto microscope cover-glasses and sealed with large cover-slips. The number of segments that had produced rhizoids and the number of segments that had not produced rhizoids were counted by using a light microscope, 100x magnification. The activity of each concentration of the compound tested was then calculated as the total number of segments which had not produced rhizoids divided with the total number of segments in the petri-dish.

For comparison purposes, similar tests were carried out using solutions of sodium dodecylsulphate with nominal concentrations of 20 ppm, and also blank tests of the filtered natural sea-water used for the dilutions containing 1% by weight acetone were performed.

In Table 2, the results of the tests are shown. The numbering of the compounds corresponds to the numbering given in Table 1. Since all test-results were not from the same tests-series, the individual test series were conducted using separate blank values, after which the results were corrected using Abbott's formula for the correction of control or blank values:

$$D_A = \frac{(D/N - D_K/N_K)}{1 - D_K/N_K}$$

D_A = Corrected activity/mortality

D = Total number of affected/dead individuals at test concentration

N = Total number of test individuals at test concentration

D_K = Total number of affected/dead individuals in control

N_K = Total number of test individuals in control

The reference value is calculated as a statistical average value with standard deviation based on 15 tests.

TABLE 2

<u>Compound no.</u>	<u>Concentration (ppm)</u>	<u>Activity (%)</u>
1	5	100
	1	31
2	5	100
	1	35
3	10	100
	1	82
	0.1	15
4	10	100
	5	100
	1	2
8	10	100
	1	34
11	100	100
	10	77
19	100	100
	10	54
21	100	100
	10	57
28	100	100
	10	63
34	1	100
	0.1	100
35	10	100
	1	25
Sodium lauryl sulphate	20	46 +/- 25

EXAMPLE 2

Spore-test

Effect of several quinoline derivatives on *Enteromorpha* spp.

If the fertile tip of an *Enteromorpha* filament is given an environmental shock e.g. cold temperature or extreme light, it will release a large number of spores. These spores swim freely for about 10-15 minutes and then settle. Upon attachment, they will produce a small tube (called germ tube) which then develops into an *Enteromorpha* plant.

Spores from *Enteromorpha intestinalis* were collected with a small pipette from spore-releasing filaments from the algae collected as described in Example 1. One drop of the spore suspension was then placed onto a small cover-slip (18 x 18 mm). Then the cover-slips were placed in a dark place and left for 1-2 hours in order to allow settlement. After this period of time, the cover-slips were placed in the test solutions in petri-dishes (the test solutions; i.e. solutions of the quinoline compounds in question, blanks and references, were prepared as described in Example 1) and then incubated at a temperature of about 10-15°C and at constant 3-4000 lux light for 96 hours.

After incubation, the cover-slips were transferred onto cover-glasses. The number of spores which had produced a germ tube and the number of spores which had not produced a germ tube were counted in ten fields of view. The activity was then calculated as the number of spores not producing germ tubes divided by the total number of spores in the ten fields of view.

In Table 3, the results (corrected according to Abbott's formula above) of the spores-test are shown. The compound numbering is the same as in Table 1. The reference value is calculated as a statistical average value with a standard

deviation based on 3 tests using TBTO (tributyl tin oxide) as the reference compound.

TABLE 3

<u>Compound no.</u>	<u>Concentration (ppm)</u>	<u>Activity (%)</u>
3	10	100
	5	66
	1	24
4	10	100
	5	46
	1	13
8	10	100
	5	100
	1	37
TBTO	0.007	78 ± 25

EXAMPLE 3

Diatom test

Effect of several quinoline derivatives on *Amphora* spp.

Diatoms are microalgae which function as fouling organisms and are commonly found on many marine structures such as ship's hulls. One type of diatoms is the *Amphora* spp.. *Amphora coffeaeformis* can be distinguished by its red fluorescence when irradiated with light (mercury lamp with a wavelength of 500-515 nm). This property was used in the test method outlined below.

Slime-containing mixed populations were collected from intertidal structures (e.g. pier pilings and bridge pilings) by scraping the populations off using a scalpel blade. The slime was then transferred to petri-dishes and the populations were covered with filtered natural sea-water (15‰ salinity). The samples were incubated for 24 hours at 24°C

and at a photoperiod of 16 hours light (2500-3000 lux light level) and 8 hours in darkness. The content in the petri-dishes which was not attached to the bottom of the petri-dish was removed and approximately 10 ml of filtered natural sea-water (15‰ salinity) was added to each petri-dish. Using a microscope for identification, *Amphora* cells were removed from the petri-dishes one by one using a rubber tube and a drawn-out glass micropipette. The cells were transferred to new petri-dishes filled with filtered natural sea-water (15‰ salinity), and the samples were incubated as described above. The removal of *Amphora* cells and incubation steps were repeated until only *Amphora coffeaeformis* was isolated. This culture will be referred to as the test population.

A sub-culture was prepared from the test population by removing, with a glass micropipette, cells of *Amphora coffeaeformis* and adding 50-100 cells to new petri-dishes (the number of which corresponded to the number of tests) containing filtered natural sea-water (15‰ salinity). The samples were then incubated for 96 hours at 24°C and at a photoperiod of 16 hours in light (2500-3000 lux light level) and 8 hours in darkness.

Before testing, solutions of the quinoline derivatives to be tested were prepared as described in Example 1. Also a blank reference containing 1% by volume acetone and a sodium dodecylsulphate solution of 30 ppm were prepared.

After the above mentioned incubation period, the content of sea-water was poured out of each petri-dish, and 10 ml of the test solutions was added instead. The petri-dishes were then incubated for further 96 hours under the same experimental conditions.

After 96 hours, the number of dead and the number of alive *Amphora coffeaeformis* cells in each petri-dish were counted. The counting was performed as follows: The liquid content of the petri-dish was poured out and two 18×18 mm² coverslips

were placed onto the base of the dish. An initial inspection under a light microscope ($\times 100$ magnification) was carried out in order to obtain qualitative information of the condition of the cells (the cell-content). After this, the petri-dishes were inspected by means of a $\times 20$ objective lens and under a fluorescent light (a mercury lamp with a wavelength of 500-515 nm). The number of live cells (red) and the number of dead cells (white) were counted. The counting was repeated with ten fields of view. The activity of the test compound was calculated as the number of dead cells divided by the number of cells counted in ten fields of view. In Table 4 the test results (corrected according to Abbott's formula above) of the activity of quinoline derivatives in the diatom-test is shown. The compound numbers corresponds to the numbers given in Table 1. The reference value is calculated as a statistical average value with standard deviation based on 18 tests.

TABLE 4

<u>Compound no.</u>	<u>Concentration (ppm)</u>	<u>Activity (%)</u>
1	10	92
	1	12
2	10	100
	1	10
3	50	90
	10	77
4	10	100
	5	10
8	50	100
	10	100
17	50	100
	10	70
19	10	100
	5	64
28	10	100
	5	100
34	1	100
	0.5	100
35	1	100
	0.5	83
	0.1	60
Sodium lauryl sulphate	30	41 ± 20

EXAMPLE 4

Nitocra test

Effect of several quinoline derivatives on *Nitocra spinipes*

Although *Nitocra spinipes* is not a fouling organism, it is a very useful marine test organism as it is easy to culture. The *Nitocra* test may also give an indication of how the test compound in question may influence fouling crustaceans.

A population of *Nitocra spinipes* (including pregnant females) which was received from Vandkvalitetsinstituttet, Denmark, was used in this experiment. The population was cultured in dishes in the dark at room temperature until pregnant females had released their eggs, these immediately changing to nauplii that developed into adults. The culture was fed with Ewos 20® (A/S Ewos Aqua Korn- og Foderstoffer, Denmark). Before testing, 20 adults were transferred, by a glass pipette, to a crystallization dish containing filtered natural sea-water (15‰ salinity). (The test solutions of the quinoline derivatives, a blank containing 1% dimethylsulphoxide (DMSO) and a reference were prepared as described in Example 1 using DMSO instead of acetone.) For each test solution, four glass tubes are used in this test. To each glass tube, 9 ml of the test solution in question was added. Using a microscope, five *Nitocra spinipes* adults were transferred in ½ ml sea-water with a pipette to each glass tube. ½ ml fresh sea-water was added to the glass tube. The glass tubes were sealed with Parafilm and labelled. The glass tubes were incubated at room temperature for 96 hours in the dark. Immediately afterwards inspection/counting (numbers of dead and alive *Nitocra spinipes*) was performed using a binocular microscope. The activity of the quinoline derivative was calculated as the sum of dead *Nitocra spinipes* in the four test tubes divided by the total number of *Nitocra spinipes* in the four test tubes.

Table 5 gives the test results (Abbott-corrected as above) for a number of quinoline derivatives. The compound numbers correspond to the numbering given in Table 1. The reference value is calculated as a statistical average value with a standard deviation based on 7 tests using TBTO as the reference compound.

TABLE 5

<u>Compound no.</u>	<u>Concentration (ppm)</u>	<u>Activity (%)</u>
3	50	100
	5	100
4	100	100
	10	58
	1	39
6	100	100
	10	40
8	100	100
	10	100
	1	16
16	100	100
	10	100
28	10	100
	1	59
34	1	100
	0.5	100
	0.1	56
TBTO	0.007	22 ± 21

EXAMPLE 5

Barnacle settlement inhibition assay.

Barnacles, in general, are well known fouling organisms in the marine environment. Cyprid stage larvae of the barnacle *Balanus amphitrite amphitrite* Darwin (a warm water species) were used in this assay to screen biologically active compound's effect upon the settling process. The method was based on a procedure described by Rittschof, D. et al., BIOFOULING, 6, (1992), 115-122.

A broodstock of adult *Balanus amphitrite amphitrite* was kept in an aquaria in the laboratory in 2.5-3.0% filtered (1.0 + 0.2 μ m) sea-water (hereafter called filtered sea-water) at

ambient temperature (22-30°C). The broodstock was kept on a diet of newly hatched *Artemia salina* larvae and the micro-algae *Dunaliella tertiolecta*. Feeding was done daily except during the weekends.

Release of nauplii larvae:

Substrates (glass jars or panels) with adult barnacles were transferred into a bucket with filtered sea-water and *Dunaliella tertiolecta* was added to the water. Within a few hours the nauplii larvae were released. They were collected with a Pasteur-pipette after being attracted to a uni-directional light source, and transferred into 50 ml of filtered sea-water.

Culturing of nauplii larvae to the cyprid stage:

A glass container with approx. 8 l of filtered sea-water was added 8.000 to 10.000 nauplii larvae. Beforehand the water was added 1ml of a stock solution of 21.900 ppm Penicillin and 1 ml of a stock solution of 36.500 ppm Streptomycin per l filtered sea-water. The container with the larvae was placed in an incubator at 28°C with a light cycle of 15 h light and 9 h dark. Bacteria filtered air was bubbled through the culture. 1½ l of the microalgae *Rhodomonas sp.* culture was added. On the third day ½l of *Rhodomonas sp.* was added to the culture. On the fifth day the culture was checked for the appearance of cyprid larvae. When more than 50% of the nauplii larvae had gone into the cyprid stage the culture was filtered over a 250 µm and a 125 µm filter. The cyprids were collected on the 125 µm filter. The cyprids were then transferred into a crystallizing dish containing approx. 120 ml of filtered sea-water and the dish was covered with the lid. The cyprids were placed in a 6°C incubator. This procedure was performed on day 0. At day 5 the cyprids were used for testing.

Settlement inhibition test:

Stock-solutions of the test compounds were prepared according to Example 1, with the alteration of excluding acetone. For screening concentrations of ppm-ranges, 100 ppm and 10 ppm (nominal concentrations) were used. 5 ml of the test solution was pipetted into a 5 cm petri dish (Falcon 1006). Filtered sea-water was used as a blank. Each concentration was tested in duplicate. Approx. 20-30 cyprids were added to each dish under a dissecting microscope. The dishes were covered and incubated for 24 h in a 28°C incubator with 15 h light and 9 h dark cycle. After 24 h each dish was viewed under the microscope in order to judge the vitality of the non-settled cyprids. The test was then stopped by adding 4 drops of 4% aqueous formaldehyde to each dish. The content of the dish was filtered through a 0.45 μ m membrane filter. The filter was placed under a dissecting microscope and a count of non-settled cyprids was made. The number of settled, and settled and metamorphosed cyprid larvae in the petri-dish was counted. The total number of larvae in the dish was found by adding the number of settled, the settled and metamorphosed, and the non-settled larvae on the filter. The settlement% and the inhibition% could then be calculated.

Settlement% =

$$\frac{\# \text{ settled cyprids} + \# \text{ settled and metamorphosed cyprids}}{\text{Total } \# \text{ cyprids}}$$

= No. of

$$\text{Inhibition\%} = 100\% - \text{Settlement\%}$$

The settling% in the control should be >50% to accept the test.

Correction of control-value:

Correction of control-value was made by using a modified Abbott-correction:

Abbott-corrected inhibition% =

$$\frac{\text{Inhibition\% in test-compound} - \text{Inhibition\% in control}}{100 - \text{Inhibition\% in control}}$$

In Table 6 the test results (corrected according to the modified Abbott formula) of the activity of quinoline derivatives in the cyprid-test is shown. The compound numbers correspond to the numbers given in Table 1.

TABLE 6

<u>Compound no.</u>	<u>Concentration (ppm)</u>	<u>Activity (%)</u>
3	10	100
	1	90
	0.1	18
8	10	100
	1	34
19	10	100
	1	82
26	10	100
	1	57
28	10	100
	1	99
	0.1	13
32	10	94
	1	48
33	100	100
	10	90
34	10	100
	1	100
	0.1	38
35	10	100
	1	100
	0.1	27

EXAMPLE 6**Paint test**

To obtain an impression of the biocidal effect of the compounds of this invention under operational conditions, paints containing the compounds were prepared in the following standard manner:

Standard paint components:

11.9 g gum rosin
3.8 g vinyl resin
22.7 g xylene
2.0 g Bentone (thixotropic bentonite)
3.1 g tricresyl phosphate
49.8 g biologically active agent(s)

In a typical test programme of various paints, the biologically active agent(s) was/were chosen as follows:

Paint no. 1:	49.8 g quinoline compound of formula I
Paint no. 2:	49.8 g cuprous oxide
Paint no. 3:	47.1 g quinoline compound of formula I + 2.7 g cuprous oxide
Paint no. 4:	2.7 g quinoline compound of formula I + 47.1 g cuprous oxide
Paint no. 5:	49.8 g 2-methylthio-4-tert-butylamino-6-cyclopropylamine-s-triazin (Irgarol 1051 ex Ciba-Geigy, Switzerland)
Paint no. 6:	2.7 g 2-methylthio-4-tert-butylamino-6-cyclopropylamine-s-triazin (Irgarol 1051 ex Ciba-Geigy, Switzerland) + 47.1 g cuprous oxide

Generally, the paints were prepared as follows:

11.9 g of gum rosin and 3.8 g vinyl resin were dissolved in 18.9 g of xylene in a 0.5 l metal can until a clear solution was obtained. 2.0 g Bentone, 3.1 g tricresyl phosphate and 49.8 g of the biologically active agent(s) (according to the paint no. in question) were added under stirring, and additional xylene was also added, if necessary. Glass beads were added until a total volume of 0.3 l (paint + glass beads). The can was closed and put on a mechanical shaker until a fineness of grinding according to ASTM D1210 of maximum 30 μm was obtained. The glass beads were filtered off and xylene was added until a slurry which could easily be stirred with a spatula was obtained.

EXAMPLE 7

Testing of antifouling performance of paints

For testing, the paints produced according to Example 6 were applied to xylene-degreased acrylic test panels (10 x 20 cm^2) in a dry film thickness (DFT) of approximately 100 microns. The panels were dried for 24 hours at room temperature.

The test panels were immersed in sea-water from a raft at a test site, e.g in the harbour of Villanueva y Geltrú in northeastern Spain which is situated at a latitude of approximately 41.2 degrees north. In this locality, the sea-water temperature varies between 11-28°C throughout the year, and the salinity varies between 30-35‰.

The antifouling performance was evaluated at intervals of 2-4 weeks. At each inspection, the panels were rated on a scale from 0 to 5 (0 = no fouling; 1 = 0-2% fouling; 2 = 2-5% fouling; 3 = 5-25% fouling; 4 = 25-50 fouling; 5 = 50-100% fouling, the fouling percentages being according to surface

area) with respect to each of two categories of fouling, namely algae and animals.

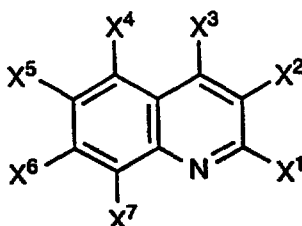
In each test series a blank sample in the form of an non-coated acrylic panel was exposed as well.



CLAIMS

1. A marine structure carrying a coating comprising a layer which contains a quinoline compound having antifouling activity, the quinoline compound having the general formula I

Formula I



wherein

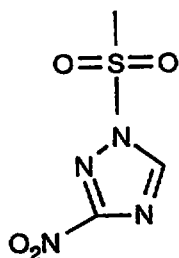
X¹, X², X⁴, X⁵, X⁶ and X⁷ independently designate hydrogen; hydroxy; C₁₋₅-alkyl; substituted C₁₋₁₂-alkyl; optionally substituted C₂₋₁₂-alkenyl; optionally substituted C₂₋₁₂-alkynyl; optionally substituted C₁₋₁₂-alkoxy; optionally substituted heterocyclyl; optionally substituted aryl; optionally substituted aryloxy; halogen; nitro; nitroso; cyano; amino; mono(optionally substituted C₁₋₁₂-alkyl)amino; di(optionally substituted C₁₋₁₂-alkyl)amino; (optionally substituted C₁₋₁₂-alkyl)carbonylamino; aminocarbonyl; mono(optionally substituted C₁₋₁₂-alkyl)aminocarbonyl; di(optionally substituted C₁₋₁₂-alkyl)aminocarbonyl; optionally substituted C₁₋₁₂-acyl; optionally substituted C₁₋₁₂-acyloxy; (optionally substituted C₁₋₁₂-acyl)-(optionally substituted C₁₋₁₂-alkyl); carboxy; (optionally substituted C₁₋₁₂-alkoxy)carbonyl; thiol; (optionally substituted C₁₋₁₂-alkyl)thio; (optionally substituted aryl)thio; (optionally substituted C₁₋₁₂-alkyl)sulphonyl; (optionally substituted aryl)sulphonyl; mono(optionally substituted C₁₋₁₂-alkyl)aminosulphonyl; di(optionally substituted C₁₋₁₂-alkyl)aminosulphonyl; sulphono (SO₃H); sulphino (SO₂H); halosulphonyl; isocyano; isothiocyano; thiocyano; (5-amino-1-methylpentyl)amino; (6-(diethylamino)-1-methylhexyl)amino; (3-nitro-1,2,4-triazol-1-yl)sulphonyl



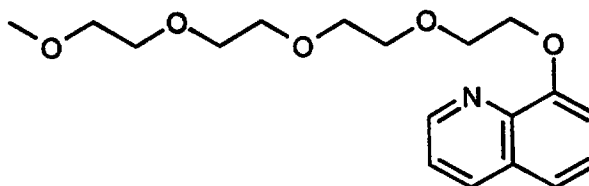


(Formula 1a); 8-quinoliny-1-yl-tetraethylene glycolyl
(Formula 1b); pyranosyl; furanosyl;

Formula 1a

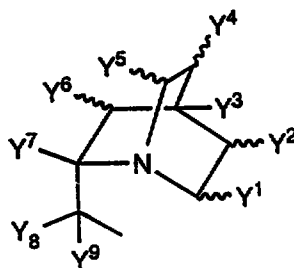


Formula 1b



X³ designates the same groups as defined for X¹ above,
or X³ is a group of the formula I'

Formula I'



wherein Y¹, Y², Y³, Y⁴, Y⁵, Y⁶ and Y⁷ independently
designate the same groups as defined for X¹ above or
designate C₆₋₁₂-alkyl, and Y⁸ and Y⁹ independently
designate the same groups as defined for X¹ above or
designate C₆₋₁₂-alkyl or together form oxo, and the
wavy lines signify that the substituents in question
may be in either of the two possible isomeric
configurations;

or an N-oxide or a salt thereof;
with the proviso that if X¹, X², X³, X⁴, X⁵, and X⁶ each is
hydrogen, and the compound of formula I is not an N-oxide,
then X⁷ is not hydroxy.

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2. A marine structure according to claim 1, wherein X^1 , X^2 , X^4 , X^5 , X^6 and X^7 independently designates hydrogen; hydroxy; C_{1-5} -alkyl; substituted C_{1-12} -alkyl; optionally substituted C_{2-12} -alkenyl; optionally substituted C_{1-12} alkoxy; optionally substituted heterocyclyl; optionally substituted aryl; optionally substituted aryloxy; fluoro; chloro; bromo; iodo; nitro; mono(optionally substituted C_{1-12} -alkyl)aminocarbonyl; di(optionally substituted C_{1-12} -alkyl)aminocarbonyl; optionally substituted C_{1-12} -acyl; optionally substituted C_{1-12} -acyloxy; (optionally substituted C_{1-12} -acyl)-(optionally substituted C_{1-12} -alkyl); carboxy; (optionally substituted C_{1-12} -alkoxy)carbonyl; mono(optionally substituted C_{1-12} -alkyl)aminosulphonyl; di(optionally substituted C_{1-12} -alkyl)aminosulphonyl; pyranosyl; (6-(diethylamino)-1-methylhexyl)amino; (3-nitro-1,2,4-triazol-1-yl)sulphonyl (Formula 1a); 8-quinolinylnyl-tetraethylene glycolyl (Formula 1b);

X^3 designates the same groups as defined for X^1 above, or X^3 is a group of the formula I' as defined in claim 1;

or an N-oxide or a salt thereof.

3. A marine structure according to claim 1, wherein X^1 , X^2 , X^3 , X^4 , X^5 , X^6 and X^7 independently designate hydrogen; hydroxy; C_{1-5} -alkyl; substituted C_{1-6} -alkyl; optionally substituted C_{2-6} -alkenyl; optionally substituted C_{2-6} -alkynyl; optionally substituted C_{1-6} -alkoxy; optionally substituted heterocyclyl; optionally substituted aryl; optionally substituted aryloxy; halogen; nitro; nitroso; cyano; amino; mono(optionally substituted C_{1-6} -alkyl)amino; di(optionally substituted C_{1-6} -alkyl)amino; (optionally substituted C_{1-6} -alkyl)carbonylamino; aminocarbonyl; mono(optionally substituted C_{1-6} -alkyl)aminocarbonyl; di(optionally substituted C_{1-6} -alkyl)aminocarbonyl; optionally substituted C_{1-6} -acyl; optionally substituted C_{1-6} -





acyloxy; (optionally substituted C_{1-6} -acyl)-(optionally substituted C_{1-6} -alkyl); carboxy; (optionally substituted C_{1-6} -alkoxy)carbonyl; thio; (optionally substituted C_{1-6} -alkyl)thio; (optionally substituted aryl)thio; (optionally substituted C_{1-6} -alkyl)sulphonyl; (optionally substituted aryl)sulphonyl; mono(optionally substituted C_{1-6} -alkyl)aminosulphonyl; di(optionally substituted C_{1-6} -alkyl)aminosulphonyl; sulphono (SO_3H); sulphino (SO_2H); halosulphonyl; isocyano; isothiocyano; thiocyano; (5-amino-1-methylpentyl)amino; (6-(diethylamino)-1-methylhexyl)amino; (3-nitro-1,2,4-triazol-1-yl)sulphonyl (Formula 1a); 8-quinolinyln-tetraethylene glycolyl (Formula 1b); pyranosyl; furanosyl;

X^3 designates the same groups as defined for X^1 above, or X^3 is a group of the formula I' as defined in claim 1;

or an N-oxide or a salt thereof.

4. A structure according to any of claims 1-3 in which the coating comprises a layer comprising a substance which enhances the antifouling activity of the quinoline compound.

5. A structure according to claim 4, wherein the enhancing substance is contained in the same layer as the quinoline compound.

6. A structure according to claim 4 or 5 wherein the enhancing substance is an antifouling active substance which is an organic compound, an organometal, a metal, a metal oxide or a metal salt.

7. A structure according to claim 6 wherein the enhancing substance is an organic antifouling active compound selected from the group of heterocyclic nitrogen compounds; heterocyclic sulphur compounds; urea derivatives; other amides or imides of carboxylic acids, sulphonic acids, or sulphenic acids; salts or esters of carboxylic acids; amines;

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substituted methanes; substituted benzenes; tetraalkyl phosphonium halogenides; guanidine derivatives; and disulphides.

8. A structure according to claim 6 wherein the enhancing substance is an organometal antifouling active compound selected from the group of trialkyltin salts; trialkyltin copolymers; metallo-dithiocarbamates.

9. A structure according to claim 6 wherein the enhancing substance is an antifouling active compound selected from the group consisting of metals; metal oxides; metal salts.

10. A structure according to any of the preceding claims wherein the quinoline derivative is one which, in the Rhizoid test performed as described in Example 1 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, when the test conditions are calibrated so that the sodium dodecylsulphate reference, in a concentration of 20 ppm gives an activity of 20-60%.

11. A structure according to any of the preceding claims wherein the quinoline derivative is one which, in the spore test performed as described in Example 2 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, when the test conditions are calibrated so that the TBTO reference, in a concentration of 0.007 ppm gives an activity of 50-100 %.

12. A structure according to any of the preceding claims wherein the quinoline derivative is one which, in the Diatom test performed as described in Example 3 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, when the test conditions are calibrated so that the sodium dodecylsulphate reference, in a concentration of 30 ppm gives an activity of 20-60%.

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13. A structure according to any of the preceding claims wherein the quinoline derivative is one which, in the *Nitocra* test performed as described in Example 4 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm, when the test conditions are calibrated so that the TBTO reference, in a concentration of 0.007 ppm gives an activity of 5-40 %.

14. A structure according to any of the preceding claims wherein the quinoline derivative is one which, in the cyprids test performed as described in Example 5 herein, gives an activity of at least 50% at a nominal concentration of the supernatant of 50 ppm.

15. A structure according to any of the preceding claims, wherein the quinoline derivative is one which when incorporated, alone or in combination with one or more antifouling activity enhancing substances as defined in any of claims 4-9, in a paint prepared as described in Example 6 herein and tested as described in Example 7 herein, with respect to algae results in a rating at least 1 rating unit lower than the corresponding rating for the blank sample, when the blank sample has attained a rating in the range of 1 to 4.

16. A structure according to any of claims 1-14, wherein the quinoline derivative is one which when incorporated, alone or in combination with one or more antifouling activity enhancing substances as defined in any of claims 4-9, in a paint prepared as described in Example 6 herein and tested as described in Example 7 herein, with respect to animals results in a rating at least 1 rating unit lower than the corresponding rating for the blank sample, when the blank sample has attained a rating in the range of 1 to 4.

17. A structure according to any of claims 1-14, wherein the quinoline derivative is one which when incorporated, alone or in combination with one or more antifouling activity enhancing substances as defined in any of claims 4-9, in a paint





prepared as described in Example 6 herein and tested as described in Example 7 herein, with respect to both algae and animals results in ratings at least 1 rating unit lower than the corresponding ratings for the blank sample, when the blank sample has attained a rating in the range of 1 to 4.

18. A marine antifouling paint composition comprising:
one or more binder component(s);
one or more pigment(s);
one or more quinoline derivative(s) as defined in any of the claims 1-3; and
one or more solvent(s).

19. A marine antifouling paint of the composition:
5-25 g gum rosin
2.5-10.0 g vinyl resin
1.25-5.0 g tricresyl phosphate or other plasticizer
10-60 g of a biologically active agent composition comprising a quinoline compound as defined in any of claims 1-3 or 10-18 and optionally an antifouling activity enhancing substance as defined in any of claims 4-9
2-8 g iron oxide
1-4 g Bentone
0.2-1.0 g wetting agent
8-30 g xylene
2.5-10 g methyl isobutyl ketone
0-7 g magnesium silicate or other filler

wherein the biologically active agent composition preferably consists of 75-97 percent by weight cuprous oxide and 3-25 percent by weight quinoline compound,

or any multiplicable weights of these components.

20. A marine antifouling paint of the composition:
5-25 g gum rosin
2.5-10 g polyamide resin
1.25-5.0 g tricresyl phosphate or other plasticizer





10-60 g of a biologically active agent composition comprising a quinoline compound as defined in any of claims 1-3 or 10-18 and optionally an antifouling activity enhancing substance as defined in any of claims 4-9
2-8 g titanium dioxide
1-4 g Bentone
0.2-1.0 g wetting agent
8-30 g xylene
2.5-10 g butanol
0-7 g magnesium silicate or other filler

wherein the biologically active agent composition preferably consists of 75-97 percent by weight cuprous oxide and 3-25 percent by weight quinoline derivative,

or any multiplicable weights of these components.

21. A marine antifouling paint of the composition:

5-25 g gum rosin
1.5-10 g acrylic resin
1.25-5.0 g tricresyl phosphate or other plasticizer
10-60 g of a biologically active agent composition comprising a quinoline compound as defined in any of claims 1-3 or 10-18 and optionally an antifouling activity enhancing substance as defined in any of claims 4-9
2-8 g black iron oxide
1-4 g Bentone
0.2-1.0 g wetting agent
10-40 g xylene
0-7 g magnesium silicate or other filler

wherein the biologically active agent composition preferably consists of 75-97 percent by weight cuprous oxide and 3-25 percent by weight quinoline derivative,

or any multiplicable weights of these components.

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