



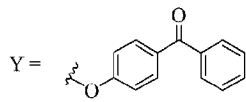
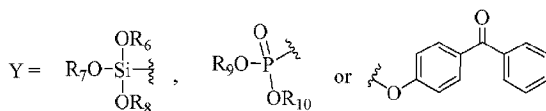
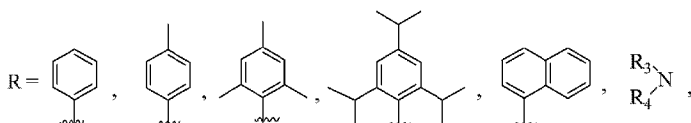
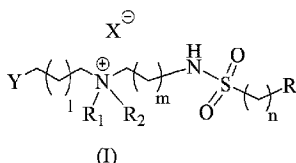
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(54) Titre : PREPARATION D'AGENTS ANTIMICROBIENS CONTENANT DU SULFONAMIDE ET COMPOSITIONS DE
TRAITEMENT DE SUBSTRAT CONTENANT DES AGENTS ANTIMICROBIENS CONTENANT DU SULFONAMIDE
(54) Title: PREPARATION OF SULFONAMIDE-CONTAINING ANTIMICROBIALS AND SUBSTRATE TREATING
COMPOSITIONS OF SULFONAMIDE-CONTAINING ANTIMICROBIALS



(57) Abrégé/Abstract:

A quaternary ammonium sulfonamide compound of formula (I): wherein R = (II), C₁-C₃ linear or branched alkyl, R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl, R₃ and R₄ are the same or different and selected from C₁ to



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(57) **Abrégé(suite)/Abstract(continued):**

C₄ linear or branched alkyl, CF₃, OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide, 1 is 1, 2, 3, 4, 5, 6, 7 or 8, m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17, n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl groups of R may be substituted or unsubstituted, X = halogen, and Y = (III) wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl and the benzophenone is selected from the group consisting of substituted benzophenone and unsubstituted benzophenone, processes for preparing the compound and antimicrobial surface coating compositions of the compound.

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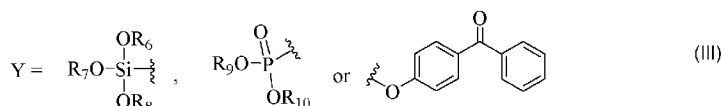
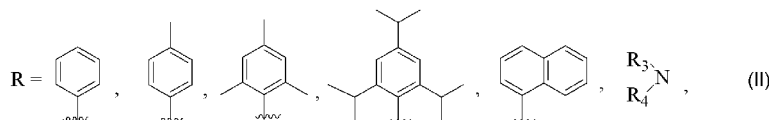
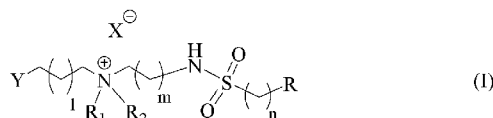
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(54) Title: PREPARATION OF SULFONAMIDE-CONTAINING ANTIMICROBIALS AND SUBSTRATE TREATING COMPOSITIONS OF SULFONAMIDE-CONTAINING ANTIMICROBIALS



(57) Abstract: A quaternary ammonium sulfonamide compound of formula (I): wherein R = (II), C₁-C₃ linear or branched alkyl, R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl, R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide, l is 1, 2, 3, 4, 5, 6, 7 or 8, m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17, n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl groups of R may be substituted or unsubstituted, X = halogen, and Y = (III) wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl and the benzophenone is selected from the group consisting of substituted benzophenone and unsubstituted benzophenone, processes for preparing the compound and antimicrobial surface coating compositions of the compound.

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TITLE

Preparation of sulfonamide-containing antimicrobials and substrate treating compositions of sulfonamide-containing antimicrobials

FIELD OF THE DISCLOSURE

- 5 This disclosure relates to dual-action antimicrobial compounds and compositions for treating substrates, preferably surfaces, to reduce, preferably inhibit microbe growth and biofouling on treated substrates.

BACKGROUND

- 10 One of the main challenges faced by the medical industry is infection control and reducing the spread of microorganisms such as fungi, bacteria and viruses. Several microorganisms have the ability to attach to surfaces, for example porous surfaces and to proliferate forming colonies called biofilms. The use of antibiotics to treat infectious diseases caused by biofilms has become one of the biggest milestones in the history of medicine. However, after widespread use of these antibiotics, and other chemicals used for the purpose of disinfection, several strains of
- 15 microorganisms (e.g. bacteria), have developed resistance to them. For the growing number of microorganisms with clinical importance (one example is pathogens), there is either no effective therapy or only one or two antibiotics that are hard to administer, expensive and/or have increasingly toxic side effects. Furthermore, when growing on surfaces as biofilms, microorganisms are generally more persistent, and it is now acknowledged that the majority of
- 20 infections involve biofilms. Biofilms also pose a notable threat of contamination in food processing facilities and spoilage of other products susceptible to microbial attack.

- Bacterial infections in hospital environments are spread by two different ways: external contamination or in vivo contamination from implants. Patients can develop external infections through contact with surfaces such as door handles, pens, telephones, health care workers uniforms
- 25 ("HCWU"), stethoscopes, or sterile packaging that have been colonized by microorganisms. Hospital-acquired infections ("HAI") from contact with pathogenic microorganisms affect approximately 2 million people and result in more than 100,000 deaths in the U.S.A. each year. Such infections require 10-20 days of additional patient hospitalization, costing the already

strained U.S. health-care systems approximately \$25,000-30,000 per infection totaling billions of dollars per year.

The second route for bacteria to infect patients is through hospital invasive support equipment such as intravascular lines and implanted medical devices such as artificial prosthetics, cardiovascular implants and urinary catheters. Implant associated infections ("IAI") occur in more than one million patients and cost an estimated \$3 billion in the U.S. per year. For example, approximately 10-50% of patients with implanted catheters run the risk of developing urinary tract infections ("UTI") resulting in additional healthcare costs. The rise in the frequency and severity of HAI's and IAI's can be attributed to decreased antibiotic efficacy against drug-resistant strains of pathogens found in surface biofilms.

Biofilm formation involves three phases beginning with the initial reversible adhesion of bacteria on a surface through polysaccharides and adhesion proteins on the bacterial membrane (phase I). Under appropriate conditions, bacteria subsequently firmly attach to a surface (phase II), followed by the secretion of a protective polymeric matrix (biofilm, phase III) in which the bacteria typically show a marked increase in resistance to antibiotics, compared to none-adherent bacteria. As a result, once the infection occurs, it becomes difficult to treat. Thus, strategies that prevent bacterial contamination or destroy adsorbed microorganisms that lead to biofilm formation are actively sought.

One approach in preventing biofilm formation, and thus the potential to cause spoilage or infection is the use of antimicrobial coatings on surfaces that are not susceptible to the development of resistance by the target microorganisms. These coatings have bacteriostatic (inhibiting) or bactericidal (killing) properties and thus afford a preventative strategy compared to disinfection, which is reactive, often after some damage or infection has occurred. In contrast to conventional antibiotics, bacteria do not readily develop resistance to antimicrobial coatings that inhibit microorganisms in a mechanical, as opposed to a chemical fashion. This important distinction, and the related alarming rate at which the number of effective antibiotics decline, is a primary reason for the rapidly growing interest in these antimicrobial coatings in recent years.

Quaternary ammonium compounds ("QACs") have gained recognition as surfactants with antimicrobial activity. QAC's consist of an irreversibly positively charged quaternary nitrogen

atom where often at least one substituent is a long aliphatic chain. The synthesis of these compounds involves the quaternization of a tertiary amine following the Menshutkin reaction (i.e. a reaction of a tertiary amine with an alkyl halide).

Without being bound by any particular theory, the mode of action of QAC's in killing bacteria is multi-stepped. First, the QAC is adsorbed into the bacterial cell wall. Second, the long hydrophobic alkyl chain of the QAC interacts with the phospholipid bilayer making up the bacteria cell membrane and alters its fluidity and structure which adds stress to the cell wall. Finally, this added stress on the cell wall upsets the bilayer, expelling cytoplasmic material and ultimately caused cell death.

Polymeric antimicrobial coatings have the advantage of being chemically stable, non-toxic and non-volatile making them more efficient, selective and environmentally safe compared to traditional antimicrobial coatings which depend on leaching of the chemical from the substrate. It has become common practice over the past 35 years to incorporate antimicrobial coatings in thermoplastic polymer solutions. Furthermore, solvents commonly used to incorporate the antimicrobials in the thermoplastic polymers include tetrahydrofuran ("THF") and dimethyl formamide ("DMF"). These solvents have the ability of attacking polymeric surfaces including those of polyurethane, polyisoprene, butyl rubber, polycarbonate, etc. This often distorts the surface, altering the integrity of the material at the surface, which in turn may ultimately enhance attachment by microbial cells resistant to the antimicrobial ingredient, and other microbes later when the concentration of the antimicrobial ingredient drops below the threshold required for inhibition. Also, once the prior art coatings are applied to the surfaces, drying times on the order of almost 24 hours are required to completely evaporate the solvent from the surface.

Development of antimicrobial coatings is limited by the availability of suitable antimicrobials that may be incorporated into thermoplastic polymers. Silver is one common agent used both in elemental and salt form. However, the technology to incorporate silver into polymeric materials is tedious, expensive and not environmentally friendly. Moreover, the performance of silver is weak taking up to eight hours to reach efficacious levels against microbes and discolouration is common in silver treated materials. Thus there exists a long-felt need for a composition to eradicate microbes and prevent biofilm formation that is low-cost, durable and efficacious without these deleterious side effects. In an effort to increase the stability of antimicrobial films on polymer

surfaces, irreversible covalent attachment of the antimicrobial to the surface desirable. Methods for grafting antimicrobials to polymer surfaces have been developed usually using functionalized surfaces and/or antimicrobial molecules. However, some of these functionalizing techniques are expensive and require extensive synthetic methodologies. Recently, light-activated systems involving photoreactive groups have been reported. Benzophenone is a popular photoreactive group and is commonly used in fragrances and cosmetics.

The first quaternary ammonium phosphonate compounds (phosphonate quats) were disclosed in the early 1950's in U.S. Patent 2,774,786 and Dutch patent NL 79189 for use as synthetic detergents. In the patents syntheses, the final product could only be isolated as a sodium salt of the phosphobetaine after hydrolysis of the phosphonate ester with HCl followed by treatment with NaHCO₃. In a similar synthesis Germanaud et al., (*Bulletin de la Societe Chimique de France*, 1988, **4**, 699-704) published the isolation of the phosphonate quats as betaines by purification on an anion exchange resin. The products disclosed in the patents were not spectrally characterized and were used as is, while Germanaud's purification was costly and the product wasn't isolated as a phosphonic acid.

Phosphonate monolayers for the antimicrobial treatment of surfaces have been shown to be advantageous over self-assembled monolayers (SAMs) of thiols in terms of durability, long-term stability and surface coverage, especially on titanium and stainless steel. Thiol-based SAM's lack substrate specificity (mainly reserved for gold surfaces) and long-term stability needed for biomedical applications, (i.e. implants). Over time, the thiol-based SAM's become oxidized to sulfonates, which lack affinity for gold and become displaced from the surface.

Listeria has been observed to increase biofilm production when conditions become more unstable or non-ideal for active growth (Nilsson, R., Ross, T. and Bowman, J. (2011) Variability in biofilm production by *Listeria monocytogenes* correlated to strain origin and growth conditions. *International Journal of Food Microbiology* 150. Pages 14-24). It appears that *Listeria* use biofilm production as a form of defense, and the strength of their survival seems linked to the maturity of the biofilm as does their resistance to antimicrobials.

Biofilms allows for essential cell to cell interactions as well as providing protection to harmful conditions. *Listeria* biofilms are structurally simple and a mature community can be formed after 24 hours, which is the incubation period of the large droplet tests.

In general, actively growing *Listeria* cells are susceptible to quaternary ammonium compounds (QACs), even at relative short exposure times over broad temperature and pH ranges. In contrast, it appears that mature biofilms are more resistant against QACs, which suggests that a component of the mature biofilm, potentially an extra-cellular polymeric substance (EPS), could provide protection against QACs. This behavior could be unique to *Listeria* strains, but there are likely other microorganisms that possess similar mechanisms for surviving exposure to antimicrobials.

In addition to biofilm maturity, it appears that other factors such as high pH and smooth attachment surfaces may impact on antimicrobial efficacy of QACs against *Listeria* (Yang, H., Kendall, P., Medeiros and L., Sofos, J. (2009) Efficacy of sanitizing agents against *Listeria monocytogenes* biofilms on high-density polyethylene cutting board surfaces. Journal of Food Protection, Vol. 72, No. 5, Pages 990–998). Lastly the possibility of non-lethal doses of disinfectants being exposed to the community over time results in resistance by the microbial community (Feliciano, L., Li, J., Lee, J., Pascall, M. (2012) Efficacies of sodium hypochlorite and quaternary ammonium sanitizers for reduction of norovirus and selected bacteria during ware-washing operations. PLOS ONE, Vol 7, Issue 12. E50273). The *Listeria* strains isolated could be of a stock that has built up these resistances.

In order to prevent the formation of biofilm, strategies have been employed in the past to make surfaces inhospitable to bacteria. For example, small molecule monolayers or polymer thin films either “grafted to” or “grown from” a surface have been widely used to prepare antimicrobial surfaces and clothing. These prior art monolayers or polymer coatings include, for example, non-biofouling coatings which are passive strategies that rely on preventing bacterial adhesion with hydrophobic or zwitterionic thin films, but do not kill the approaching bacteria. A second class of antibacterial thin films kills microbes on contact either by releasing a biocidal agent or immobilizing a biocidal agent. A third class of antibacterial thin films utilize a combination strategy of including a non-biofouling and biocidal component into the coating. Currently, there

are no known environmentally-safe sulfonamide quaternary ammonium coatings used to protect surfaces from bio-fouling.

U.S. Patent No. 3,697,402 teaches photocurable thiol-capped polyalkene polymers which when applied to a surface and exposed to ultra-violet ("UV") light forms a solid product for use, among
5 other things, as a sealant, coating, and adhesive.

U.S. Patent No. 4,948,819 teaches water-soluble, quaternary ammonium methacrylate coatings having a photo-active linking molecule, with uses as an UV-cured lacquer coating. U.S. Patent 5,714,360 teaches a chemical cross-linking agent X-Y-X where X is a photoreactive radical and Y is a nitrogen containing group used to attach chemical compounds to other compounds or to
10 substrates.

J.C. Tiller et al., (Proceedings of the National Academy of Sciences, 2001, 98, 5981) teaches a surface coating composition of polyvinylpyrrolidone ("PVP")-QAC in which the surface is a pre-functionalized glass surface and PVP-QAC is bonded to the functional groups. The surface needs to be pre-functionalized with an acyl-chloride compound in order for the coating to bond to the
15 glass surface.

U.S. Patent Application Publication No. 2006/0147413 teaches a water-soluble, photo-activatable polymer bonded through a reactive group biomaterial used to deploy molecular therapeutics such as proteins, genes, vectors and cells.

U.S. Patent Application Publication No. 2007/0231291 teaches a polymeric QAC-polyethyleneimine used to protect surfaces against bacteria and fungi attack. International Patent Application Publication WO2010/065421 teaches UV-curable coatings containing rheology modifiers or antimicrobial agents wherein the antimicrobial agents are not covalently linked to the coating polymer.

International Patent Application Publication WO2010/096444 teaches a UV-curable polyethyleneimine polymer that can be attached to pre-functionalized surfaces giving the surface antimicrobial activity. The surfaces are functionalized by reacting the surfaces with 7-octenyl trichlorosilane.

V.P. Dhende et al (Application of Material Interfaces, 2001, 3, 2830) teaches a UV-curable polyethyleneimine co-polymer that can be attached to pre-functionalized surfaces giving the surface antimicrobial activity. The surfaces are functionalized by reacting the surfaces with octyltrichlorosilane.

- 5 International Patent Application Publication WO2011/139817 teaches a UV-curable vinyl-substituted polyethyleneimine that can be attached to pre-functionalized surfaces and imparting antimicrobial activity to the surfaces. The surfaces are functionalized by reacting the surface with 7-octenyl trichlorosilane.

- Mustafa Baris Yagci ("Self-Stratifying Antimicrobial Coatings", Ph.D. dissertation, January 16, 10 2012) teaches *inter alia* a QAC-bonded polyurethane surface coating.

- Lawrence C.A. et al., Journal of the American Pharmaceutical Association, 1948, 37, 424-428 teaches quaternary ammonium compounds modified with sulfonamide functionalities and their antibacterial activity. Specifically, the compounds comprise a *para*-substituted benzene ring wherein one end contains the sulfonamide functionality and the other constitutes the quaternary 15 ammonium site. The absence of a linker group in the compounds precludes covalent attachment of the compounds to substrates.

Song D. et al., European Journal of Medicinal Chemistry, 2013, 69, 670-677 teaches quaternary ammonium sulfonamides and their use as anti-cancer agents.

- International Patent Application Publication WO2014/089680 teaches UV cured, benzophenone- 20 capped quaternary ammonium compounds and their use as antimicrobial surface treatments.

International Patent Application Publication WO2014/127451 teaches quaternary ammonium multi-dentate phosphonate compounds and their use as durable, antimicrobial surface treatments.

U.S. Patent No. 5,104,649 teaches biocide-treated polymers and surfaces in which the biocide is linked to the surface through a multi-step process.

- 25 U.S. Patent Application Publication No. 2007/0287750 teaches polycationic sulfonamide compounds used for treating diseases.

U.S. Patent Application Publication No. 2013/0255061 teaches systems and methods for coating a polymeric surface, specifically medical devices, with a biocide compound.

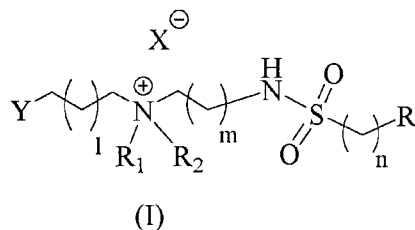
U.S. Patent Application Publication No. 2015/0175812 teaches an antimicrobial polymer used for touch sensitive surfaces in which the polymer contains pendant antimicrobial groups.

- 5 International Patent Application Publication WO2013/019918 teaches covalent attachment of sulfonyl-quaternary ammonium compounds to fabric surfaces having OH groups via a sulfur-oxygen linkage.

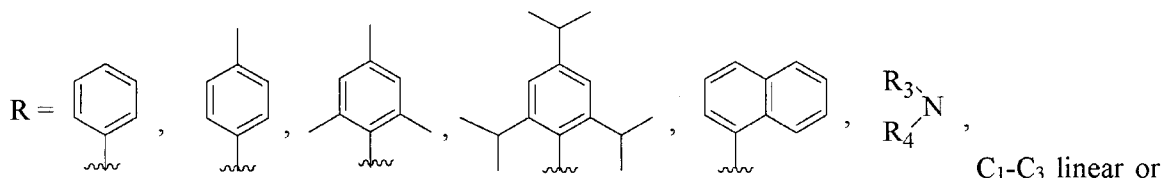
Thus, there has been a long-felt need for a durable and environmentally safe antimicrobial quaternary ammonium sulfonamide for use in surface treatment and a process to manufacture the
10 same.

SUMMARY

In one aspect of the present disclosure there is provided a quaternary ammonium sulfonamide compound of formula (I):



15 wherein



branched alkyl,

R_1 and R_2 are the same or different and selected from C_1 to C_{18} linear or branched alkyl,

R_3 and R_4 are the same or different and selected from C_1 to C_4 linear or branched alkyl, CF_3 , OR_5

20 where R_5 is C_1 to C_8 linear or branched alkyl or polyethylene oxide,

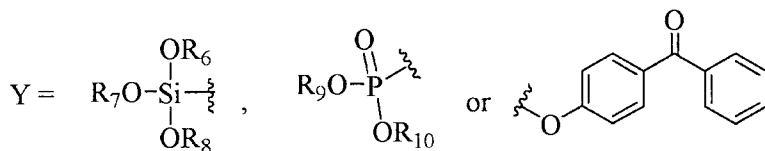
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m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

wherein the aryl rings of R may be substituted or unsubstituted,

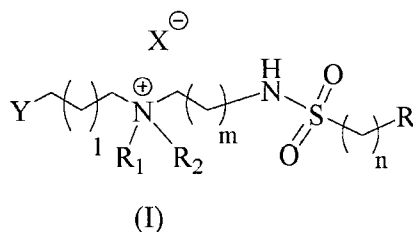
X = halogen, and



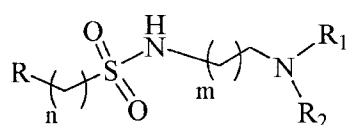
wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl, and the phenyl rings of the benzophenone may be substituted or unsubstituted.

In a preferred embodiment, the halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment, R₁ and R₂ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₃ and R₄ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R₅ is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R₆, R₇ and R₈ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₉ and R₁₀ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups.

In another aspect of the present disclosure there is provided a process for preparing a quaternary ammonium sulfonamide of formula (I):

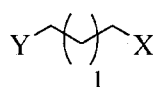


comprising reacting a compound of formula (II)



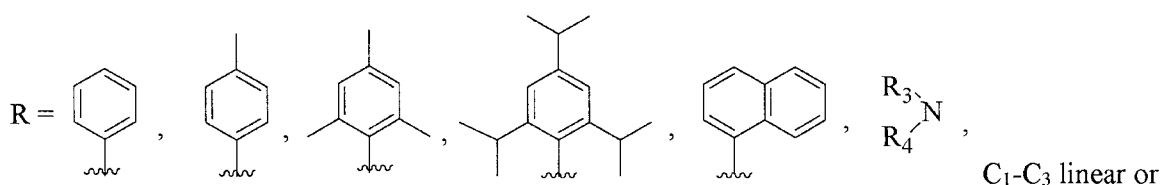
(II)

with an alkyl halide of formula (III)



(III)

wherein



5

C₁-C₃ linear or

branched alkyl,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅

where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

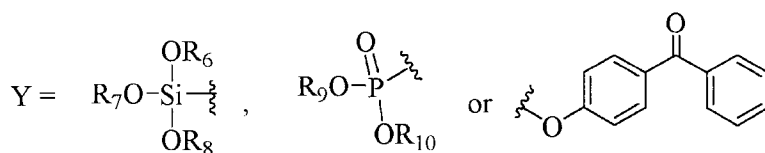
10 l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

wherein the aryl rings of R may be substituted or unsubstituted,

X = halogen, and



15

wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl, and wherein the phenyl rings of the benzophenone may be substituted or unsubstituted.

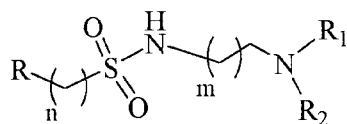
In a preferred embodiment, halogen is selected from the group consisting of Cl, Br and I. In a

20 preferred embodiment, R₁ and R₂ are the same and selected from methyl, ethyl, n-propyl or

isopropyl groups, more preferably methyl groups. In a preferred embodiment, R_3 and R_4 are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R_5 is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R_6 , R_7 and R_8 are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R_9 and R_{10} are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups.

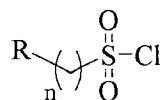
In a preferred embodiment the process may take place in at least one polar, aprotic solvent, preferably selected from the group consisting of dichloromethane (DCM), dimethylformamide (DMF), tetrahydrofuran (THF), acetonitrile (ACN) and combinations thereof, more preferably ACN. The process may be carried out at an elevated temperature up to proximate the refluxing temperature of the at least one polar, aprotic solvent. The reaction duration may be from formation of some product to complete reaction, preferably about 2 hours to about 48 hours, more preferably from about 3 hours to about 12 hours. The final product may be purified, preferably by washing, more preferably by washing with a dialkyl ether, preferably diethyl ether. The final product may be dried, preferably under vacuum of about 10^{-3} mmHg and preferably at room temperature. In a preferred embodiment, where Y is selected from benzophenone the drying step is preferably carried out in the absence of light. In a preferred embodiment, where Y is selected from a silane the drying step is preferably carried out in the absence of moisture.

In another aspect of the present disclosure there is provided a process for preparing a compound of formula (II)



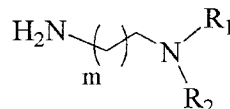
(II)

comprising reacting a compound of formula (IV)



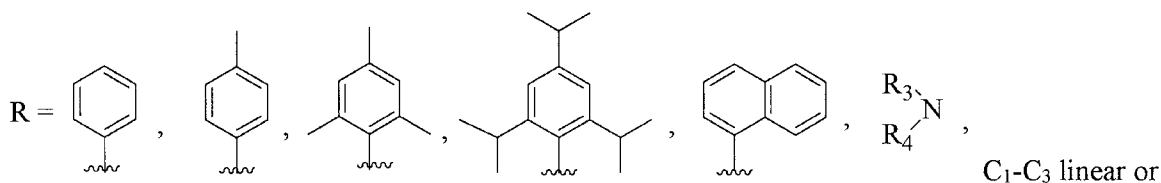
(IV)

with a compound of formula (V)



(V)

optionally in the presence of a base, wherein



branched alkyl,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

10 m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17, and

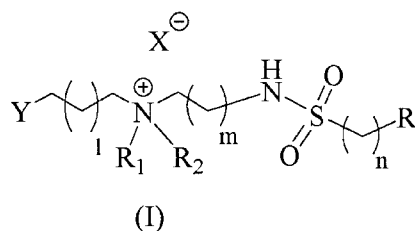
n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R may be substituted or unsubstituted.

Preferably the optional base is selected from an amine, preferably an alkylamine or pyridine, more preferably a trialkylamine, most preferably triethylamine. In a preferred embodiment, R₁ and R₂ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₃ and R₄ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₅ is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0.

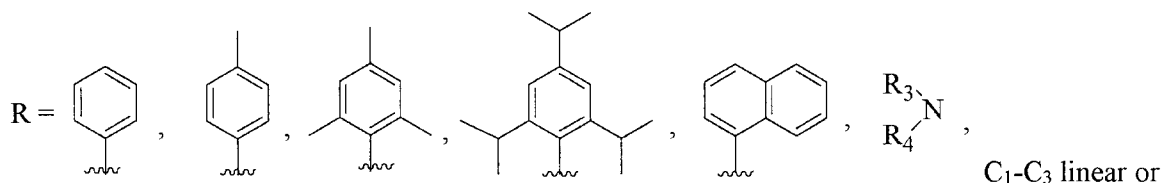
In a preferred embodiment the process may take place in a polar, aprotic solvent, preferably selected from the group consisting of ACN, DMF, THF, DCM, and combinations thereof,

preferably DCM. The addition of reactants may be carried out at the a temperature from about -20°C to about 10°C, more preferably from about -10°C to about 5°C and most preferably at about 0°C. The reaction may proceed from about 0°C to about room temperature and from formation of some product to complete reaction, preferably from about 2 hours to about 8 hours, more preferably from about 3 hours to about 6 hours.

In another aspect of the present disclosure there is provided an antimicrobial substrate treating, preferably substrate coating, more preferably surface coating composition comprising at least one compound of formula (I)



wherein



branched alkyl,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅

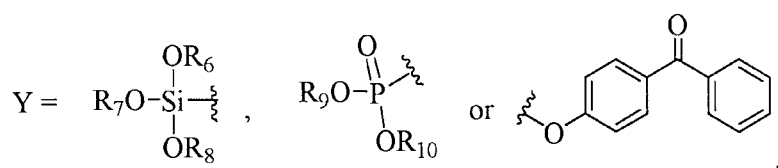
where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R may be substituted or unsubstituted,

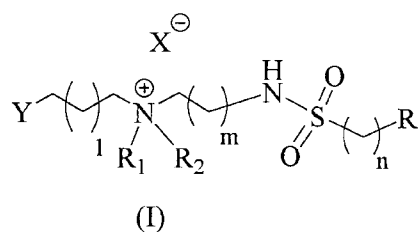
X = halogen, and



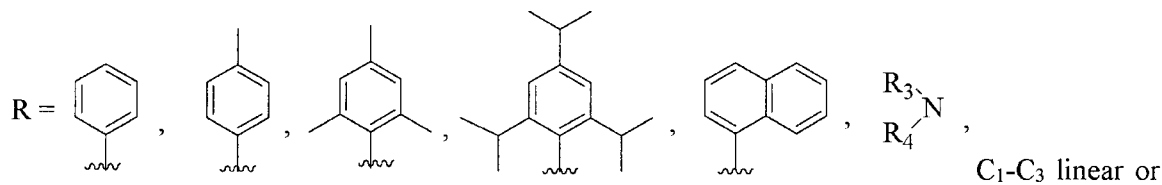
wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl, wherein the phenyl rings of the benzophenone may be substituted or unsubstituted, and an environmentally friendly carrier. In a preferred embodiment halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment, R₁ and R₂ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₃ and R₄ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R₅ is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R₆, R₇ and R₈ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₉ and R₁₀ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups.

In a preferred embodiment, the environmentally friendly carrier is water, preferably a mixture of water, preferably distilled water, and at least one alkanol, preferably said alkanol is selected from the group consisting of methanol, ethanol, isopropanol and combinations thereof, wherein the alkanol is preferably methanol or ethanol and said water is preferably, distilled water. In a preferred embodiment the mixture of alkanol and water has a ratio of alkanol to water from about 5:95 to about 80:20, more preferably from about 10:90 to about 75:35 and most preferably from about 10:90 to about 70:30. In a preferred embodiment when the alkanol is methanol the ratio of alkanol to water is from about 30:70 to about 70:30. In a preferred embodiment when the alkanol is ethanol the ratio of alkanol to water is from about 10:90 and about 40:60. In a preferred embodiment the concentration of antimicrobial quaternary ammonium sulfonamide in the composition is from about at least 0.1%, preferably from about 0.5% to about 2%, more preferably from about 0.75% to about 1.5% and most preferably from about 0.75% to about 1.25%.

In another aspect of the present disclosure there is provided a process for treating, preferably coating, a substrate with an antimicrobial comprising the steps of (i) contacting the substrate with an antimicrobial composition comprising at least one compound of formula (I)

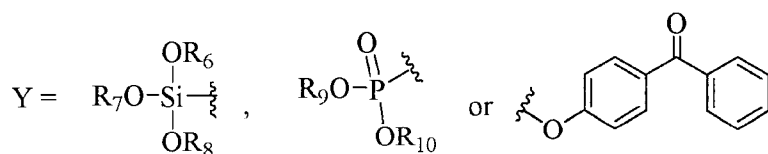


wherein



branched alkyl,

- 5 R_1 and R_2 are the same or different and selected from C_1 to C_{18} linear or branched alkyl,
 R_3 and R_4 are the same or different and selected from C_1 to C_4 linear or branched alkyl, CF_3 , OR_5
 where R_5 is C_1 to C_8 linear or branched alkyl or polyethylene oxide,
 l is 1, 2, 3, 4, 5, 6, 7 or 8,
 m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,
 10 n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R may
 be substituted or unsubstituted,
 X = halogen, and

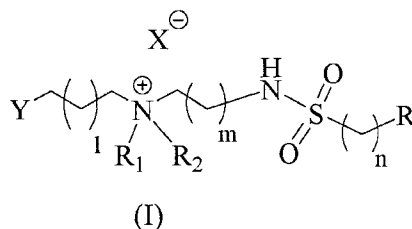


- wherein R_6 , R_7 , R_8 , R_9 and R_{10} are the same or different and selected from C_1 to C_6 linear or
 15 branched alkyl, wherein the phenyl rings of the benzophenone may be substituted or unsubstituted,
 and an environmentally friendly carrier, (ii) drying the treated substrate, in one embodiment
 allowing for passively drying and in another embodiment actively drying, and (iii) optionally
 irradiating the treated substrate.

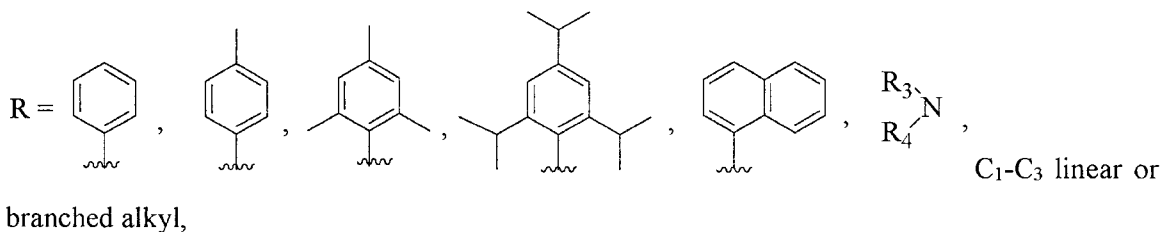
- In a preferred embodiment, the halogen is selected from the group consisting of Cl, Br and I. In a
 20 preferred embodiment, R_1 and R_2 are the same and selected from methyl, ethyl, n-propyl or

isopropyl groups, more preferably methyl groups. In a preferred embodiment, R_3 and R_4 are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R_5 is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R_6 , R_7 and R_8 are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R_9 and R_{10} are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups.

- 10 In another preferred embodiment, the substrate may be a porous or a non-porous substrate, in yet another preferred embodiment, the substrate may be a surface. In a preferred embodiment, passively drying may include allowing the treated substrate, preferably coated substrate, more preferably coated surface to dry at room temperature. More preferably room temperature is from about 15°C to about 30°C and most preferably from about 20°C to about 25°C. In a preferred
- 15 embodiment, actively drying may include allowing the treated substrate, preferably coated substrate, more preferably coated surface to dry at a temperature above room temperature and at a pressure at or below room pressure. More preferably the temperature above room temperature is at least 40°C. More preferably the pressure at or below room pressure is from about 10^{-3} mm Hg to about 760 mm Hg.
- 20 In another aspect of the present disclosure there is provided a process for treating, preferably coating a substrate, preferably a surface, with an antimicrobial comprising the steps of (i) contacting the substrate, preferably the surface with an antimicrobial composition comprising a compound of formula (I)



25 wherein



R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅

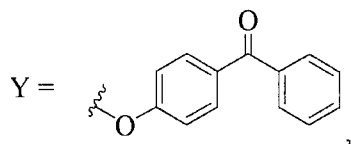
5 where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R may be substituted or unsubstituted,

10 X = halogen, and

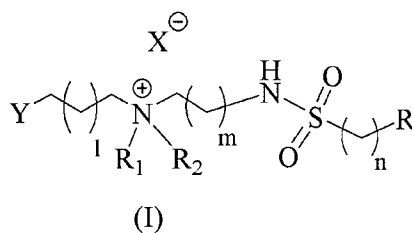


wherein the phenyl rings of the benzophenone may be substituted or unsubstituted, and an environmentally friendly carrier, (ii) drying the treated, preferably coated substrate, preferably coated surface, in one embodiment passively or in another embodiment actively, and (iii)

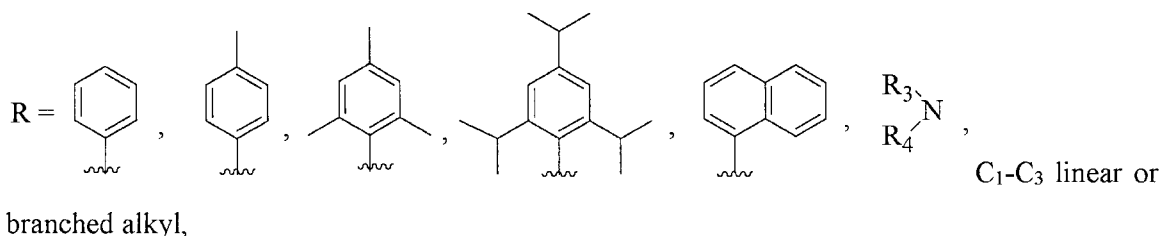
15 irradiating the treated, preferably coated substrate, more preferably coated surface. In a preferred embodiment, halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment the substrate, preferably surface, may be a porous or non-porous substrate, preferably a porous or non-porous surface. Preferably the substrate, more preferably the surface, is a polymer or a non-cellulosic fibre. Preferably the substrate, more preferably the surface, may include, but
20 not be limited to, polymers such as polyethylene, polypropylene, acrylonitrile- butadiene-styrene, polyurethane, polyvinyl chloride or nylon articles such as food trays, molded bedding parts, desk chairs and assorted furniture, disposable syringes, plastic handles for appliances, bathroom fixtures, window blinds and the like. Depending on the article or substrate, preferably surface to be treated, preferably coated, the skilled person would take the steps necessary to ensure the
25 composition substantially treats, preferably coats the substrate, preferably the surface, preferably fully coats the substrate, more preferably fully coats the surface. For example, an article may only

require one application of the composition, or the article may require multiple applications of the composition to ensure the article is substantially treated, preferably substantially coated. In a preferred embodiment the irradiating step comprises irradiating the treated, preferably coated substrate, more preferably coated surface, preferably with UV light.

- 5 In yet another aspect of the present disclosure there is provided a process for treating, preferably coating a substrate, preferably a surface, with an antimicrobial comprising the steps of (i) contacting the substrate, preferably a surface with, an antimicrobial composition comprising a compound of formula (I)



- 10 wherein



R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅

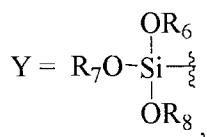
- 15 where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

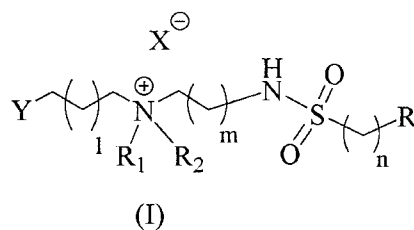
n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R may be substituted or unsubstituted,

- 20 X = halogen, and

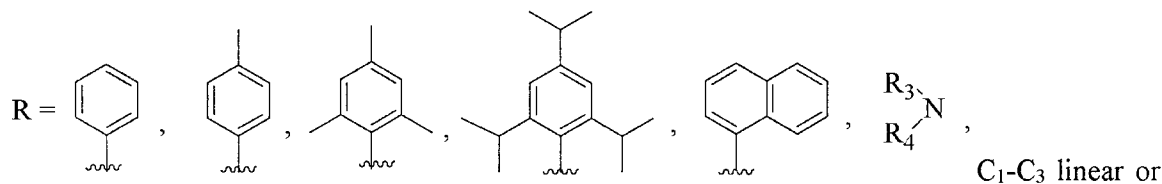


wherein R₆, R₇ and R₈ are the same or different and selected from C₁ to C₆ linear or branched alkyl, and an environmentally friendly carrier, preferably with stirring and heating, (ii) drying the treated substrate, preferably coated substrate, more preferably coated surface and washing the treated substrate, preferably coated substrate, more preferably coated surface. Preferably the washing step may be carried out using water. In a preferred embodiment, halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment, R₁ and R₂ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₃ and R₄ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R₅ is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R₆, R₇ and R₈ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. The substrate may be a porous or a non-porous substrate. Preferably the substrate, more preferably the surface, may include, but not be limited to, glass, cellulosic material, cotton and cotton-blended articles such as textiles, clothing, towels, bandages, outdoor fabrics and the like. In a preferred embodiment the heating is from a radiant heat source to produce a treating temperature from about 30°C to about 80°C, more preferably from about 35°C to about 75°C and most preferably about 40°C. In a preferred embodiment the stirring occurs from about 3 minutes to about 5 minutes, most preferably about 4 minutes. Depending on the article or substrate to be treated, preferably coated, the skilled person would take steps necessary to ensure the composition substantially treats, preferably coats the substrate, preferably surface, and preferably fully coats the substrate, preferably the surface. For example, an article may only require one application of the composition, or the article may require multiple applications of the composition to ensure the article is substantially treated, preferably substantially coated.

In yet another aspect of the present disclosure there is provided a process for treating a substrate, preferably a surface, with an antimicrobial comprising the steps of (i) contacting the substrate, preferably a heated substrate, more preferably a heated surface, with an antimicrobial composition comprising a compound of formula (I)

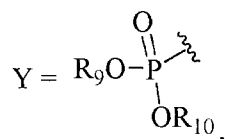


wherein



branched alkyl,

- 5 R_1 and R_2 are the same or different and selected from C_1 to C_{18} linear or branched alkyl,
 R_3 and R_4 are the same or different and selected from C_1 to C_4 linear or branched alkyl, CF_3 , OR_5
 where R_5 is C_1 to C_8 linear or branched alkyl or polyethylene oxide,
 l is 1, 2, 3, 4, 5, 6, 7 or 8,
 m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,
 10 n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R are
 substituted or unsubstituted,
 X = halogen, and



- wherein R_9 and R_{10} are the same or different and selected from C_1 to C_6 linear or branched alkyl,
 15 and an environmentally friendly carrier, (ii) optionally further heating the substrate thereafter and
 (iii) drying the substrate. Preferably the heating is radiative heating. In a preferred embodiment,
 the halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment, R_1
 and R_2 are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably
 methyl groups. In a preferred embodiment, R_3 and R_4 are the same and selected from methyl,
 20 ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l
 is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R_5 is selected from
 methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment,

m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R₉ and R₁₀ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups. The substrate may be a porous or a non-porous substrate.

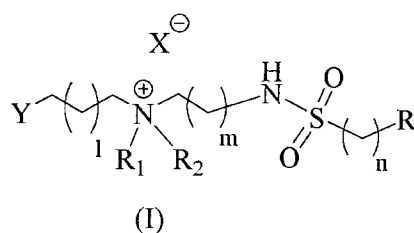
- 5 In a preferred embodiment, the antimicrobial coating composition may be applied onto a given substrate, preferably a surface, preferably by dip coating, painting or with aerosol spraying with an about 1 to an about 20 mM solution of the phosphonate compound for a length of time so as to coat, preferably substantially coat, more preferably completely coat the substrate, preferably the surface. In one embodiment, the coating process may be repeated to apply additional layers of the
- 10 phosphonate antimicrobial. Preferably the antimicrobial coating composition may be coated onto various substrates such as, but not limited to, minerals, metals, metal oxides or metal alloys of aluminum, copper, iron, steel, titanium, zirconium and silicon (silica) and the like. More preferably the substrate is selected from a metal or a metal oxide. Most preferably the substrate is a metal.
- 15 In a preferred embodiment, the environmentally friendly carrier is water, preferably a mixture of water and at least one alkanol, said alkanol is selected from the group consisting of methanol, ethanol, isopropanol and mixtures thereof, wherein the alkanol is preferably selected from methanol and ethanol and said water is distilled water. In a preferred embodiment the mixture of at least one alkanol and water has a ratio of alkanol to water from about 5:95 to about 80:20, more
- 20 preferably from about 10:90 to about 75:35 and most preferably from about 10:90 to about 70:30. In a preferred embodiment when the alkanol is methanol the ratio of alkanol to water is from about 30:70 to about 70:30. In a preferred embodiment when the alkanol is ethanol the ratio of alkanol to water is from about 10:90 and about 40:60.

- 25 In yet another aspect of the present disclosure there is provided a test flow device, preferably made from a plastic, for evaluating antimicrobial quaternary ammonium sulfonamide coated substrates at solid/liquid interfaces. In a preferred embodiment the plastic may be exposed to single or multiple strains of bacteria typically capable of forming biofilms under controlled conditions and evaluated for growth or death of colony forming units.

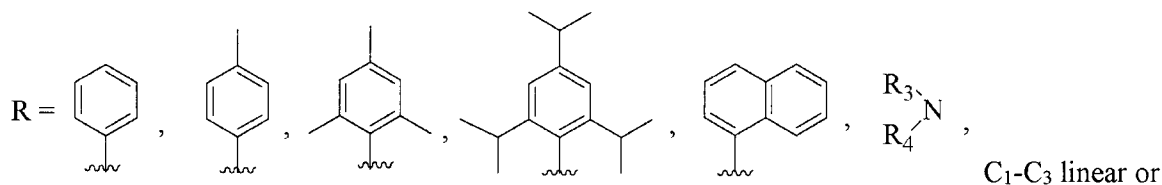
In yet another aspect there is provided an antimicrobial quaternary ammonium sulfonamide for reducing microbial growth at solid/air interfaces. In a preferred embodiment microbial growth may be attributed to a group of microbes consisting of bacterial, fungal and viral.

According to yet another aspect of the present disclosure, there is provided a substrate, preferably a surface, treated, preferably coated, with an antimicrobial as defined herein. In a preferred embodiment the substrate, preferably surface, may be porous or non-porous.

According to yet another aspect of the present disclosure, there is provided a method of reducing growth of at least one microbe on a substrate treated with an antimicrobial composition comprising at least one compound of formula (I)



wherein



R_1 and R_2 are the same or different and selected from C_1 to C_{18} linear or branched alkyl,

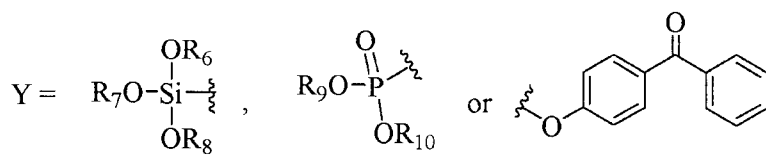
R_3 and R_4 are the same or different and selected from C_1 to C_4 linear or branched alkyl, CF_3 , OR_5 where R_5 is C_1 to C_8 linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl groups of R may be substituted or unsubstituted

$\text{X} = \text{halogen}$, and

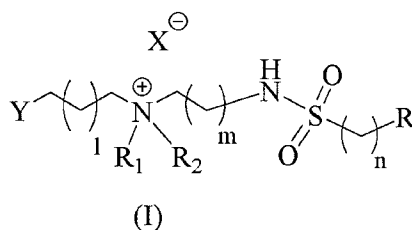


wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl, wherein the phenyl groups of the benzophenone may be substituted or unsubstituted, and an environmentally friendly carrier. In a preferred embodiment halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment, R₁ and R₂ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₃ and R₄ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R₅ is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R₆, R₇ and R₈ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₉ and R₁₀ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups.

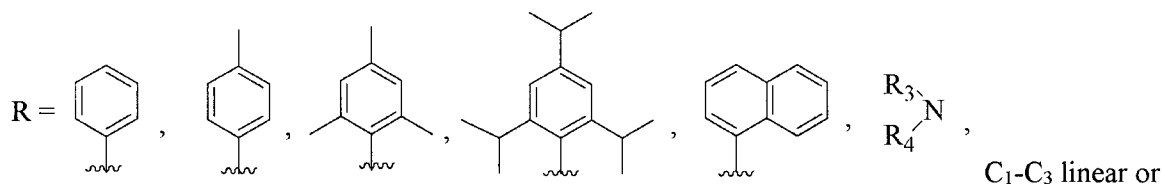
According to yet another aspect of the present disclosure there is provided a method of reducing growth of at least one microbe on a substrate, preferably a surface, treated with an antimicrobial composition comprising at least one compound selected from the group consisting of 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide, 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(4-methylphenylsulfonamido)propyl)propan-1-aminium bromide, 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(phenylsulfonamido)propyl)propan-1-aminium bromide, 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide, N,N-dimethyl-3-(trimethoxysilyl)-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(phenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(naphthalene-1-sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, and combinations thereof. In a preferred embodiment, the at least one microbe

is selected from the group consisting of *Listeria monocytogenes*, *Arthrobacter*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* and combinations thereof.

According to yet another aspect of the present disclosure there is provided a use of an antimicrobial composition comprising a compound of formula (I):



wherein



branched alkyl,

R_1 and R_2 are the same or different and selected from C_1 to C_{18} linear or branched alkyl,

R_3 and R_4 are the same or different and selected from C_1 to C_4 linear or branched alkyl, CF_3 , OR_5 where R_5 is C_1 to C_8 linear or branched alkyl or polyethylene oxide,

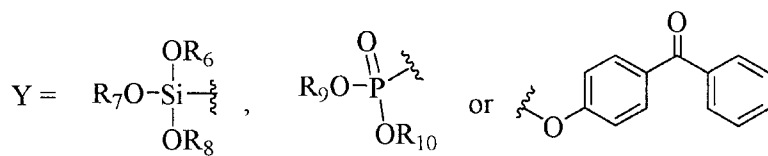
l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl groups of R may

be substituted or unsubstituted,

$\text{X} =$ halogen, and



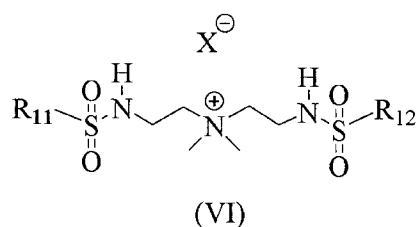
wherein R_6 , R_7 , R_8 , R_9 and R_{10}

are the same or different and selected from C_1 to C_6 linear or branched alkyl, wherein the phenyl groups of the benzophenone may be substituted or unsubstituted, to protect a substrate from bio-

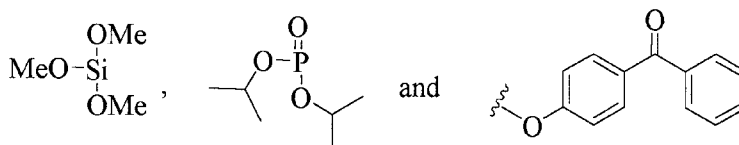
fouling. In a preferred embodiment, the halogen is selected from the group consisting of Cl, Br and I. In a preferred embodiment, R_1 and R_2 are the same and selected from methyl, ethyl, n-

propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₃ and R₄ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, l is selected from 1, 2 or 3, more preferably 1. In a preferred embodiment, R₅ is selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl. In a preferred embodiment, m is selected from 1, 2 or 3, more preferably 2. In a preferred embodiment, n is selected from 0, 1, 2 or 3, more preferably 0. In a preferred embodiment, R₆, R₇ and R₈ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably methyl groups. In a preferred embodiment, R₉ and R₁₀ are the same and selected from methyl, ethyl, n-propyl or isopropyl groups, more preferably isopropyl groups. In a preferred embodiment, the bio-fouling is caused by a biofilm.

According to yet another aspect of the present disclosure there is provided a quaternary ammonium di-sulfonamide compound of the formula (VI):



wherein R₁₁ and R₁₂ are the same or different and are selected from the group consisting of:

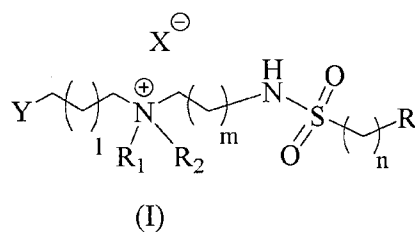


and X is halogen.

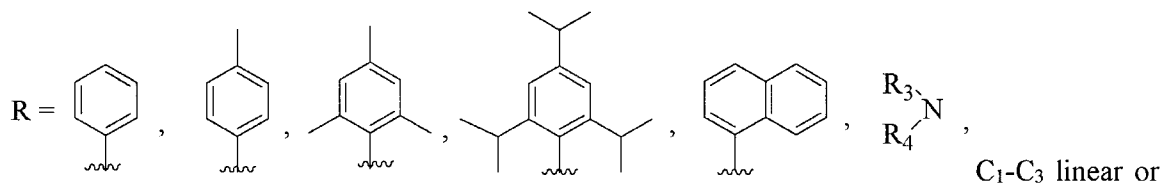
In a preferred embodiment, the halogen is selected from the group consisting of Cl, Br and I. In a

preferred embodiment, R₁₁ and R₁₂ are the same and

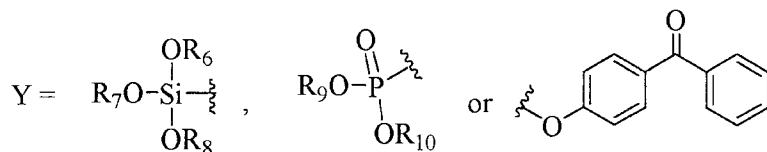
In yet another aspect of the disclosure there is provided a use of a compound of formula (I)



wherein



- 5 R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,
 R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅
 where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,
 l is 1, 2, 3, 4, 5, 6, 7 or 8,
 m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,
 10 n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein the aryl rings of R may
 be substituted or unsubstituted,
 X = halogen, and



- wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or
 15 branched alkyl, wherein the phenyl groups of the benzophenone may be substituted or
 unsubstituted, for reducing bacterial growth on a solid/air interface.

Further and other aspects will be appreciated by the skilled reader.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows an image of polymer samples before (light coloured) and after (dark coloured) treatment with benzophenone-anchored sulfonamide quat antimicrobial compound.

Figure 2 shows an image of cotton fabric samples before (light coloured) and after (dark coloured) treatment with silane-anchored sulfonamide quat antimicrobial compound.

Figure 3 shows a graph of the dry-surface change in log (colony forming units) over time upon exposure of untreated control and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide treated polystyrene and N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride treated cotton to *Arthrobacter* spp.

Figure 4 shows a graph of the dry-surface change in log (colony forming units) over time upon exposure of untreated control and N,N-dimethyl-3-(phenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(trimethoxysilyl)-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium chloride and N,N-dimethyl-3-(naphthalene-1-sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride treated cotton to *Arthrobacter* spp.

Figure 5 shows a graph of the dry-surface change in log (colony forming units) over time upon exposure of untreated control and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(phenylsulfonamido)propyl)propan-1-aminium bromide treated polyethylene to *Arthrobacter* spp.

Figure 6 shows a graph of the dry-surface change in log (colony forming units) over time upon exposure of untreated control and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide treated polyethylene to *E. coli* and *S. aureus*.

Figure 7 shows an image of polyethylene samples before (control) and after (treated) treatment with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide containing trace (0.05% w/v) fluorophore.

Figure 8 shows a graph of the dry-surface change in log (colony forming units) over time upon exposure of untreated control and antimicrobial compound 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide containing 0.05% w/v fluorophore compound treated polyethylene to *Arthrobacter* spp.

5 **Figure 9** shows a graph of the solid-liquid interface change in log (colony forming units) over 48 hours exposure of untreated control and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide treated polyethylene test tubes to *Arthrobacter* spp., and planktonic cell survival.

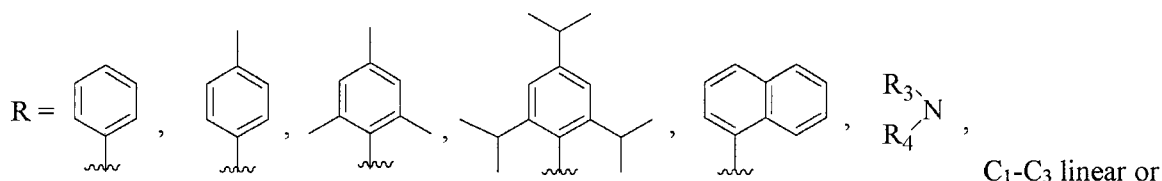
10 **Figure 10** shows a graph of the solid-liquid interface change in log (colony forming units) over 48 hours exposure of untreated control and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide treated polyethylene test tubes to *Arthrobacter* spp., and biofilm cell survival.

DETAILED DESCRIPTION

15 A series of alkyl and aryl, UV and heat curable quaternary ammonium sulfonamide antimicrobials may be prepared by both conventional and microwave synthesis. Common to all the UV curable compounds is the sulfonamide linkage, the quaternary ammonium site and the benzophenone linker moiety. Additionally, compounds containing a silane linker, preferably for attaching to porous substrates and the like, or a phosphonate linker, preferably for attaching to metal substrates
20 and the like, may be prepared using similar techniques.

These materials may be designed with dual functionality: 1) a functional anchoring group that grafts selectively to porous or non-porous substrates and 2) a quaternary ammonium charge and sulfonamide linkage for attracting bacteria, preferably harmful bacteria and kill them, for example, by mechanical means operating at the solid/air interface.

25 The term quaternary ammonium sulfonamide refers to quaternary ammonium compounds that have been substituted with a sulfonamide group $R-S(=O)_2-$ wherein



branched alkyl, wherein the aryl rings of R may be substituted or unsubstituted, wherein R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide, and the sulfonamide moiety is linked to the quaternary ammonium nitrogen centre by a carbon atom chain, preferably a saturated chain, more preferably a three carbon chain, most preferably a saturated three carbon chain.

The term polar, aprotic solvent means a solvent that has a dipole moment but does not have an acidic hydrogen. Non-limiting examples include acetonitrile, dimethylformamide, dimethylsulfoxide and dichloromethane.

- 10 The quaternary ammonium sulfonamide compounds presently disclosed utilize a covalently bound linkage to metal (phosphonate linkage), plastics (UV curable benzophenone linkage) or textiles and glass (silane linkage) and sulfonamide functionality along with a quaternary ammonium salt that renders these materials antimicrobial. Antimicrobial coating compositions of these compounds may be formulated as an alcohol-based, water/alcohol or water based formulations.
- 15 The use of such solvent systems make these compositions non-toxic, low cost, with minimum impact to the environment and may be applied by electrospray or traditional painting techniques.

These formulations require no photoinitiator in order to graft the quaternary ammonium sulfonamide compounds to substrates. These antimicrobial coating compositions may be sprayed, aerosolized or painted on to non-porous and porous surfaces, allowed to dry and are then actively

20 grafted or cured (covalently attached) to these substrates via low heat, air or UV irradiation to form self-assembled monolayers. These cured antimicrobial coatings form durable bonds to these hard-to-stick-to-surfaces and as a result may inhibit biofilm formation at solid/air interface. The solid/air interface is where many biofilms, and the harmful bacteria that can reside in them, exist. These formulations are non-leaching and water-based and may provide effective preventative protection

25 against harmful bacteria. These compounds work at a solid/air interface where desiccant tolerant pathogenic bacteria can persist where individual or colonizing bacteria flourish.

The antimicrobial quaternary ammonium sulfonamide compounds of the present disclosure may be applied to protect a variety of porous and non-porous substrates, preferably surfaces. In one embodiment, benzophenone-attachment compounds may be attached, for example, to polymers including polyethylene and polypropylene; silane-attachment compounds may be attached, for example, to cellulosic fibres and textiles including cotton and cotton blends; and phosphonate-attachment compounds may be attached, for example, to metal and metal oxide substrates, composites and glasses. The substrate attached terminated sulfonamide containing quaternary ammonium salts form a protective self-assembled monolayer that is 1-2 molecules thick at the substrate. These protective coatings may find applications where antimicrobial substrates are required, in particular, biomedical applications.

In one preferred embodiment, coating of a polymer substrate was achieved by first dissolving the quaternary salt in 10:90 solution of ethanol:water, followed by electrostatic spraying (2×), and a short 30 sec UV cure cycle.

Microbiological assessment of antimicrobial quaternary ammonium sulfonamide coated substrates of the present disclosure reveal them to be highly potent.

With reference to Figure 1, the presence of benzophenone-anchored quaternary ammonium sulfonamide on polystyrene, polyethylene, polyvinyl chloride and polyether ether ketone coupons was confirmed by bromophenol blue indicator. Darker coloured samples indicate the presence of benzophenone-anchored quaternary ammonium sulfonamide versus lighter coloured untreated samples.

With reference to Figure 2, the presence of silane-anchored quaternary ammonium sulfonamide on cotton fabric samples was confirmed by bromophenol blue indicator. The light coloured sample shows no treatment; the darker coloured sample shows treatment.

With reference to Figure 3, polystyrene untreated and treated with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide, and cotton untreated and treated with N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride were inoculated with *Arthrobacter* spp. All bacteria on both treated samples were eradicated within three hours compared to the control. See Example 34 for data.

With reference to Figure 4, cotton untreated and treated with N,N-dimethyl-3-(phenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(trimethoxysilyl)-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium chloride or N,N-dimethyl-3-(naphthalene-1-sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride were inoculated with *Arthrobacter* spp. All bacteria on all four samples were eradicated within three hours compared to the control. See Example 34 for data.

With reference to Figure 5, polyethylene coupons untreated and treated with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide or 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(phenylsulfonamido)propyl)propan-1-aminium bromide were inoculated with *Arthrobacter* spp. All bacteria on both samples were eradicated within three hours compared to the control. See Example 34 for data.

With reference to Figure 6, polyethylene coupons untreated and treated with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide were inoculated with *E. coli* or *S. aureus*. All bacteria were eradicated within three hours compared to the control. See Example 34 for data.

With reference to Figure 7, the presence of 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide containing a trace (0.05% w/v) of fluorophore on polyethylene coupons was confirmed by UV imaging. The dark sample shows no treatment; the light sample shows treatment.

With reference to Figure 8, polyethylene coupons untreated and treated with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide containing 0.05% w/v fluorophore were inoculated with *Arthrobacter* spp. All bacteria were eradicated within three hours compared to the control. See Example 34 for data.

With reference to Figure 9, the interior of polyethylene test tubes was coated with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide and inoculated with *Arthrobacter* spp. and planktonic cells were sampled after 48 hours incubation and agitation. Biofilm presence was assessed after washing out the growth media and inoculant. Re-challenge to determine whether the antimicrobial effect persisted after

repeated exposure was performed. In both cases, there was complete eradication of planktonic cells. See Example 35 for data.

With reference to Figure 10, the same test as in Figure 9 was performed to assess biofilm cell survival. After 48 hours biofilm cells were eradicated. See Example 35 for data.

5

The following non-limiting examples are provided.

Acronyms:

ACN- acetonitrile

DCM- dichloromethane

10 Et₂O – diethyl ether

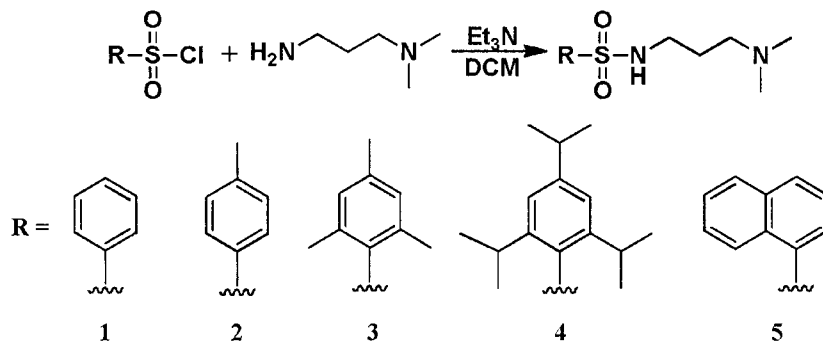
Et₃N – triethylamine

QAC, QUAT – quaternary ammonium compound

TSB – tryptic soy broth

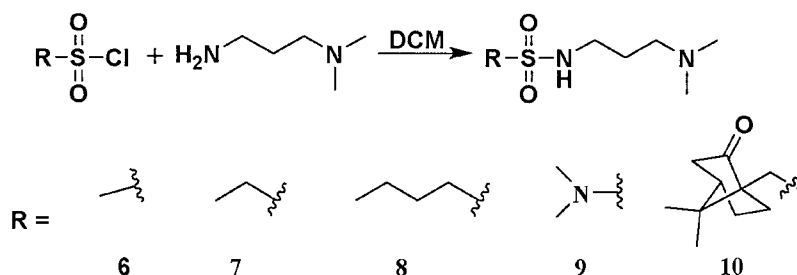
15 General Method 1 Aromatic Sulfonamides Precursor

To a flame dried, round bottom flask on ice bath equipped with a stir bar containing 40 – 50 mL of anhydrous DCM, 1.0 equivalent of respective sulfonyl chloride was added followed by 1.5 equivalents of Et₃N, and dropwise addition of 1.5 equivalents of 3-(dimethylamino)propylamine. The reaction mixture was taken off ice bath and allowed to stir for the indicated time at room temperature. The reaction was then transferred to a separatory funnel and extracted with a 30 – 70 mL of distilled water. Volatiles and/or solvent were removed from the organic phase using a rotary evaporator followed by drying under 10⁻³ mm Hg vacuum.



Scheme 1: General reaction for aromatic sulfonamide precursor**General Method 2 Aliphatic Sulfonamides**

To a flame dried, round bottom flask on ice bath equipped with a stir bar containing 40 – 50 mL of anhydrous DCM, 1.0 equivalent of 3-(dimethylamino)propylamine was added followed by drop wise addition of the respective sulfonyl chlorides (1.0 equivalents). The reaction mixture was taken off ice bath and allowed to stir for 3-5 hours at room temperature. Upon completion the reaction solvent was evaporated using rotary evaporator, the resultant residue was then dissolved in an appropriate amount of potassium carbonate solution (0.05 M) and extracted using 40 – 60 mL of DCM. Volatiles and/or solvent were removed from the organic phase using a rotary evaporator followed by drying under 10^{-3} mm Hg vacuum.

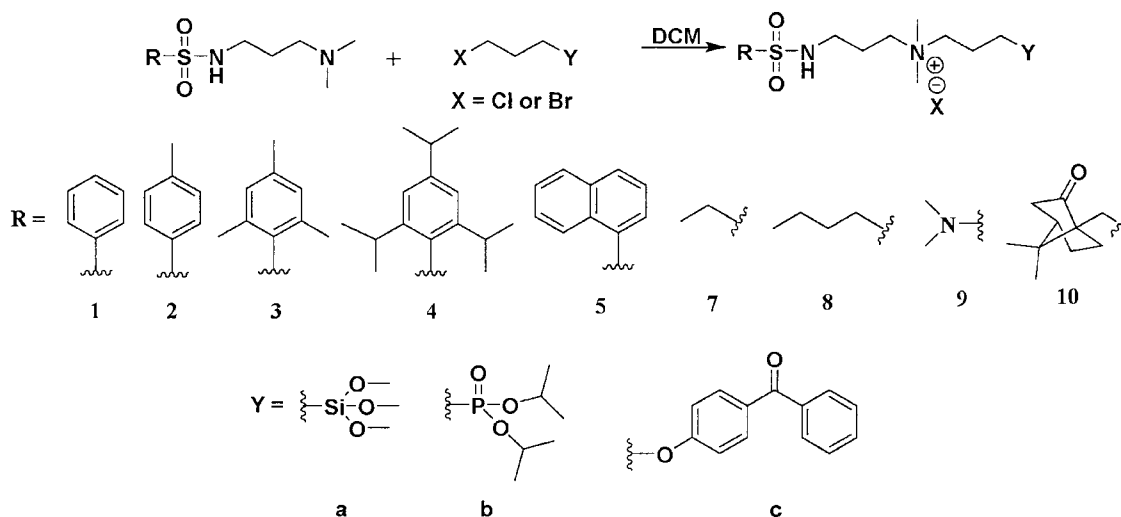
**Scheme 2: General reaction for aliphatic sulfonamide Precursor**

15

General Method 3 Sealed Tube Menshutkin Quaternization Reactions

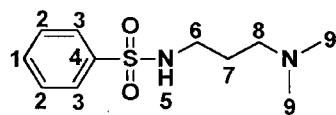
In a 20 mL scintillation / microwave vial 1.0 equivalent of the sulfonamide was added followed by addition of 1.0 - 1.5 equivalents of respective linker group (Silane, phosphonate, or benzophenone) along with a magnetic stir bar and sealed with a screw cap. The reaction mixture was heated using an oil bath at 110 °C for 3-48 hours. The crude material was purified by addition of Et₂O (10-30 mL) directly into the reaction mixture followed by decanting (Et₂O wash x 3) and dried under 10^{-3} mm Hg vacuum.

20



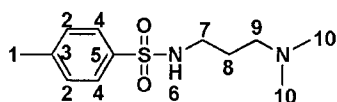
Scheme 3: General reaction for Menshutkin Quaternization reaction

Synthesis of Aromatic Sulfonamides



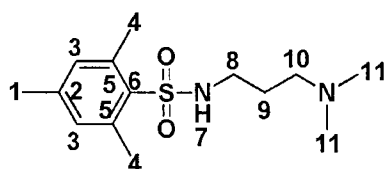
Example 1 - N-(3-(dimethylamino)propyl)benzenesulfonamide (1):

This compound was synthesized according to General Method 1 using benzenesulfonyl chloride (1.4 mL, 11.32 mmol), triethylamine (2.4 mL, 16.99 mmol, 1.5 eqv.), and 3-(dimethylamino)propylamine (2.1 mL, 16.99 mmol, 1.5 eqv.) in DCM (30 mL) for 4 hours yielding a clear solution. The solution was then extracted using distilled water (40 mL), the extracted organic layer was dried using rotary evaporator yielding a greenish yellow oil; which was further dried under 10^{-3} mm Hg vacuum yielding in light yellow waxy solid product. Yield 98 % (2.69 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.68 (dd, 2H, $J_{3-2} = 8.3$ Hz, H3), 7.40-7.30 (m, 3H, H1 and H2), 2.86 (t, 2H, $J_{6-7} = 5.8$ Hz, H6), 2.11 (t, 2H, $J_{8-7} = 5.9$ Hz, H8), 1.98 (s, 6H, H9), 1.45-1.36 (m, 2H, H7) ppm; ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 140.20 (C4), 132.33 (C1), 128.99 (C2), 126.96 (C3), 59.13 (C8), 45.28 (C9), 44.05 (C6), 25.12 (C7) ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ + \text{H}^+]$ calculated for $\text{C}_{11}\text{H}_{19}\text{N}_2\text{O}_2\text{S}_1$, 243.3458, found, 243.1162.



Example 2 - N-(3-(dimethylamino)propyl)-4-methylbenzenesulfonamide (2):

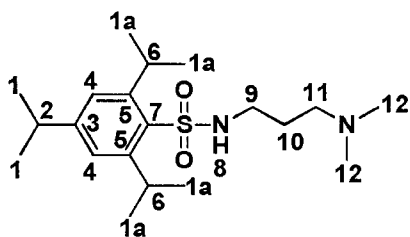
This compound was synthesized according to General Method 1 using *p*-toluenesulfonyl chloride (10.505 g, 55.10 mmol), triethylamine (11.5 mL, 82.65 mmol, 1.5 eqv.), and 3-(dimethylamino)propylamine (10.4 mL, 82.65 mmol, 1.5 eqv.) in DCM (100 mL) for 4 hours yielding a milky white solution. The solution was then extracted using distilled water (100 mL), the extracted organic layer was dried using rotary evaporator yielding a pale yellow oil; which was further dried under 10^{-3} mm Hg vacuum yielding in pale white waxy solid product. Yield 98 % (13.85 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.73 (d, 2H, $J_{4-2} = 8.3$ Hz, H4), 7.29 (d, 2H, $J_{2-4} = 7.9$ Hz, H2), 3.03 (t, 2H, $J_{7-8} = 5.8$ Hz, H7), 2.42 (s, 3H, H1), 2.29 (t, 2H, $J_{9-8} = 5.8$ Hz, H9), 2.16 (s, 6H, H10), 1.62 – 1.53 (m, 2H, H8) ppm; ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 142.83 (C5), 137.11 (C3), 129.44 (C2), 126.88 (C4), 58.76 (C9), 45.15 (C10), 43.65 (C7), 25.23 (C8), 21.32 (C1) ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ + \text{H}^+]$ calculated for $\text{C}_{12}\text{H}_{21}\text{N}_2\text{O}_2\text{S}_1$, 257.3723, found, 257.1322.



Example 3 - N-(3-(dimethylamino)propyl)-2,4,6-trimethylbenzenesulfonamide (3):

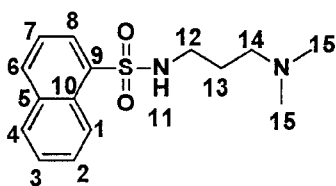
This compound was synthesized according to General Method 1 using 2,4,6-trimethylbenzene-1-sulfonyl chloride (2 g, 9.14 mmol), triethylamine (1.9 mL, 13.72 mmol, 1.5 eqv.), and 3-(dimethylamino)propylamine (1.7 mL, 13.72 mmol, 1.5 eqv.) in DCM (50 mL) for 3 hours yielding a clear solution. The solution was then extracted using distilled water (75 mL), the extracted organic layer was dried using rotary evaporator yielding a clear oil; which was further dried under 10^{-3} mm Hg vacuum yielding in pale white waxy solid product. Yield 98.5 % (2.56 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.04 (br. s, 1H, H7), 6.93 (s, 2H, H3), 2.94 (t, 2H, $J_{8-9} = 5.7$ Hz, H8), 2.61 (s, 6H, H4), 2.32 (t, 2H, $J_{10-9} = 5.6$ Hz, H10), 2.27 (s, 3H, H1), 2.18 (s, 6H, H11), 1.69-1.56 (m, 2H, H9) ppm; ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 141.74 (C6), 139.07 (C2), 133.80 (C5), 131.87 (C3), 59.66 (C10), 45.48 (C11), 43.72 (C8), 24.99 (C9), 22.88 (C4), 20.95 (C1) ppm.

HRMS-ESI-TOF (m/z): [$M^+ + H^+$] calculated for $C_{14}H_{25}N_2O_2S_1$, 285.4255, found, 285.1643.



Example 4 - N-(3-(dimethylamino)propyl)-2,4,6-triisopropylbenzenesulfonamide (4):

- 5 This compound was synthesized according to General Method 1 using 2,4,6-triisopropylbenzene-1-sulfonyl chloride (2 g, 6.60 mmol), triethylamine (1.4 mL, 9.91 mmol, 1.5 eqv.), and 3-(dimethylamino)propylamine (1.2 mL, 9.91 mmol, 1.5 eqv.) in DCM (50 mL) for 3 hours yielding a clear solution. The solution was then extracted using distilled water (75 mL), the extracted organic layer was dried using rotary evaporater yielding a faint green oil; which was further dried under 10^{-3} mm Hg vacuum yielding in pale white waxy solid product. Yield 97 % (2.36 g). ^1H NMR ($CDCl_3$, 400 MHz, δ): 7.15 (s, 2H, H4), 4.23-4.11 (m, 2H, H6), 3.08 (t, 2H, $J_{9-10} = 5.9$ Hz, H9), 2.89 (m, 1H, H2), 2.60-2.40 (br. m, 2H, H11), 2.30 (br. s, 6H, H12), 1.83-1.66 (br. m, 2H, H10), 1.29-1.22 (br. m, 18H, H1 and H1a) ppm; ^{13}C { ^1H } NMR ($CDCl_3$, 100 MHz, δ): 152.48 (C7), 150.45 (C5), 132.57 (C3), 123.79 (C4), 59.03 (C11), 45.28 (C12), 42.93 (C9), 34.25 (C2), 29.74 (C6), 25.61 (C10), 25.10 (C1a), 23.73 (C1) ppm. HRMS-ESI-TOF (m/z): [$M^+ + H^+$] calculated for $C_{20}H_{37}N_2O_2S_1$, 369.5850, found, 369.2570.

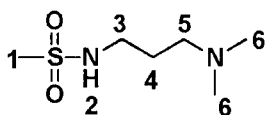


Example 5 - N-(3-(dimethylamino)propyl)naphthalene-1-sulfonamide (5):

- 20 This compound was synthesized according to General Method 1 using naphthalene-1-sulfonyl chloride (4 g, 18.04 mmol), triethylamine (3.8 mL, 27.06 mmol, 1.5 eqv.), and 3-(dimethylamino)propylamine (3.4 mL, 27.06 mmol, 1.5 eqv.) in DCM (50 mL) for 3 hours yielding a clear solution. The solution was then extracted using distilled water (50 mL), the extracted organic layer was dried using rotary evaporater yielding a greenish yellow oil; which

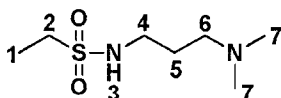
was further dried under 10^{-3} mm Hg vacuum yielding in pale white waxy solid product. Yield 99.7 % (5.27 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 8.67 (d, 1H, $J_{1,2} = 8.5$ Hz, H1), 8.25 (d, 1H, $J_{8,7} = 6.2$ Hz, H8), 8.05 (d, 1H, $J_{6,7} = 8.2$ Hz, H6), 7.95 (d, 1H, $J_{4,3} = 7.8$ Hz, H4), 7.65 (m, 1H, H2), 7.59 (m, 1H, H3), 7.52 (t, 1H, H7), 2.95 (t, 2H, $J_{12,13} = 5.6$ Hz H12), 2.21 (t, 2H, $J_{14,13} = 5.6$ Hz, H 14), 2.12 (s, 6H, H15), 1.55 (m, 2H, H13) ppm; ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 134.85 (C9), 134.45 (C5), 133.96 (C4), 129.79 (C6), 129.16 (C2), 128.42 (C10), 128.21 (C3), 126.82 (C8), 124.76 (C7), 124.28 (C1), 59.80 (C14), 45.56 (C15), 44.77 (C12), 24.68 (C13) ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ + \text{H}^+]$ calculated for $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}_2\text{S}_1$, 293.4044, found, 293.1319.

10 Synthesis of Aliphatic Sulfonamides



Example 6 - N-(3-(dimethylamino)propyl)methanesulfonamide (6):

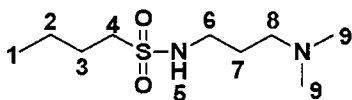
This compound was synthesized according to General Method 2 using methanesulfonyl chloride (1.4 mL, 17.46 mmol) and 3-(dimethylamino)propylamine (2.2 mL, 17.46 mmol, 1.5 eq.) in DCM (50 mL) for 4 hours and extracted using K_2CO_3 (0.05 M, 40 mL) yielding in clear oil after drying under 10^{-3} mm Hg vacuum. Yield: 65 % (2.05 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 3.23 (t, 2H, H3), 2.91 (s, 3H, H1), 2.43 (t, 2H, H5), 2.22 (s, 6H, H6), 1.77-1.65 (m, 2H, H4) ppm; ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 59.26 (C5), 45.37 (C6), 44.08 (C3), 39.70 (C1), 25.72 (C4) ppm.



Example 7 - N-(3-(dimethylamino)propyl)ethanesulfonamide (7):

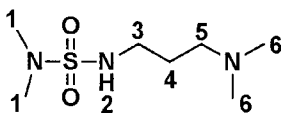
This compound was synthesized according to General Method 2 using ethanesulfonyl chloride (0.7 mL, 7.78 mmol) and 3-(dimethylamino)propylamine (1.5 mL, 11.67 mmol, 1.5 eq.) in DCM (50 mL) for 4 hours and extracted using K_2CO_3 (0.05 M, 50 mL) yielding in clear oil after drying under 10^{-3} mm Hg vacuum. Yield: 61 % (0.92 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 3.19 (t, 2H, $J_{4,5} = 5.8$ Hz, H4), 3.0 (q, 2H, $J_{2,1} = 7.4$ Hz, H2), 2.42 (t, 2H, $J_{6,5} = 5.8$ Hz, H6), 2.22 (s, 6H, H7), 1.75-1.64 (m, 2H, H5), 1.34 (t, 3H, $J_{1,2} = 7.4$ Hz, H1) ppm; ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 59.33 (C6), 46.05 (C2), 45.41 (C7), 44.11 (C4), 25.91 (C5), 8.35 (C1) ppm. HRMS-ESI-TOF

(m/z): [$M^+ + H^+$] calculated for $C_7H_{19}N_2O_2S_1$, 195.1162, found, 195.1167.



Example 8 - N-(3-(dimethylamino)propyl)butane-1-sulfonamide (8):

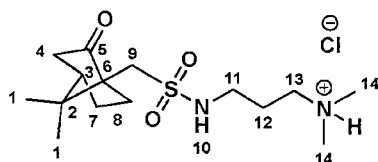
- 5 This compound was synthesized according to General Method 2 using butanesulfonyl chloride (1.7 mL, 12.77 mmol) and 3-(dimethylamino)propylamine (2.4 mL, 19.15 mmol, 1.5 eq.) in DCM (50 mL) for 4 hours and extracted using K_2CO_3 (0.05 M, 50 mL) yielding in clear oil after drying under 10^{-3} mm Hg vacuum. Yield: 81 % (2.31 g). ^1H NMR ($CDCl_3$, 400 MHz, δ): 3.15 (t, 2H, $J_{6-7} = 5.9$ Hz, H6), 2.94 (t, 2H, $J_{4-3} = 7.9$ Hz, H4), 2.38 (t, 2H, $J_{8-7} = 5.9$ Hz, H8), 2.18 (s, 6H, H9),
 10 7.78-1.61 (m, 4H, H), 1.48-1.34 (m, 2H, H2), 0.91 (t, 3H, $J_{1-2} = 7.3$ Hz, H1) ppm; ^{13}C { ^1H } NMR ($CDCl_3$, 100 MHz, δ): 59.08 (C8), 51.56 (C4), 45.38 (C9), 43.83 (C6), 26.05 (C3), 25.70 (C7), 21.54 (C2), 13.63 (C1) ppm. HRMS-ESI-TOF (m/z): [$M^+ + H^+$] calculated for $C_9H_{23}N_2O_2S_1$, 223.1475, found, 223.1480.



Example 9 - N-(2-(dimethylamino)propyl)-N,N-Dimethyl-sulfamide (9):

- This compound was synthesized according to General Method 2 using *N,N*-dimethylsulfamoyl chloride (1.5 mL, 13.93 mmol) and 3-(dimethylamino)propylamine (2.6 mL, 20.89 mmol, 1.5 eq.) in DCM (50 mL) for 4 hours and extracted using K_2CO_3 (0.05 M, 50 mL) yielding in clear oil after
 20 drying under 10^{-3} mm Hg vacuum. Yield: 79.8 % (2.33 g). ^1H NMR ($CDCl_3$, 400 MHz, δ): 3.11 (t, 2H, $J_{3-4} = 6.0$ Hz, H3), 2.75 (s, 6H, H1), 2.38 (t, 2H, $J_{5-4} = 6.0$ Hz, H5), 2.19 (s, 6H, H6), 1.69-1.61 (m, 2H, H4) ppm. ^{13}C { ^1H } NMR ($CDCl_3$, 100 MHz, δ): 59.24 (C5), 45.39 (C6), 44.31 (C3), 38.00 (C1), 25.62 (C4) ppm. HRMS-ESI-TOF (m/z): [$M^+ + H^+$] calculated for $C_7H_{20}N_3O_2S_1$, 210.1271, found, 210.1276.

Example 9A 3-(((1S,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methylsulfonamido)-N,N-dimethylpropan-1-aminium chloride :

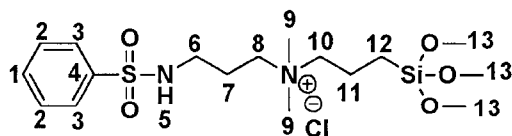


This compound was synthesized according to Method 1 using (1S)-(+)-camphorsulfonyl chloride (20.938 g, 83.75 mmol), and 3-(dimethylamino)propylamine (10.5 mL, 83.75 mmol, 1.0 eqv.) in DCM (50 mL) for 3 hours at room temperature yielding a light yellow cloudy precipitate. The mixture was dried on a rotary evaporated yielding a yellow oil which solidified under a pressurized vacuum system to a pale off white hard solid of the HCl camphor amine salt. Yield 100 % (26.151 g, 83.5 mmol). ¹H NMR (CDCl₃, 400 MHz, δ): 5.44 (s, 1H), 4.33 (s, 4H), 3.69 (s, 4H), 3.44 (s, 4H), 2.77 (s, 4H), 2.71 (s, 4H), 2.52 – 2.48 (m, 8H), 2.43 – 2.06 (m, 37H), 2.10 (d, *J* = 2.3 Hz, 9H), 2.10 (d, *J* = 2.3 Hz, 7H), 2.04 (s, 5H), 1.86 (s, 3H), 1.74 – 1.64 (m, 8H), 1.59 (s, 3H), 1.34 (s, 3H), 1.04 (s, 3H, H1), 0.87 (s, 3H, H1) ppm; Agrees well with literature values. (Eur. J. Pharm. Sci. 65 (2014) 29-37).

General Procedure 4 for the Menshutkin Quaternization

1.0 equivalent of sulfonamide containing tertiary amine and 1.0 – 1.5 equivalents of respective end functionality (silane, phosphorus or benzophenone) halide were mixed in ACN using Method 3 and heated for 3-48 hours. The reaction vial was allowed to cool to RT and the crude product was purified as indicated in Method 3.

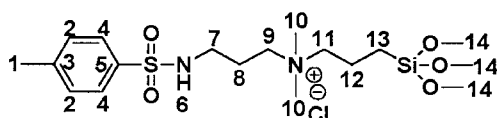
Synthesis of Organosilane based QAC



Example 10 - N,N-dimethyl-3-(phenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride (1a):

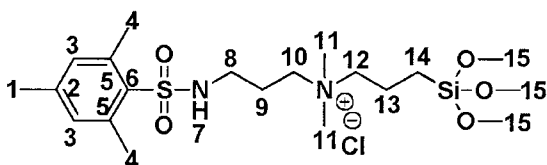
This compound was synthesized using *N*-(3-(dimethylamino)propyl)benzenesulfonamide (1.0 g, 4.13 mmol) and (3-Chloropropyl)trimethoxysilane (1.1 mL, 6.19 mmol, 1.5 eq.) in ACN (3 mL) for 4 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL x 3) and obtained as clear golden brown gummy oil after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 97.5 % (1.77 g). ¹H NMR (CDCl₃, 400 MHz, δ): 8.39 (br. S, 1H, H5), 7.96 (d, 2H, H3), 7.54 – 7.341 (m, 3H, H1 & H2), 3.69 – 3.62 (m, 2H, H8), 3.51 (s, 9H,

H13), 3.37 – 3.30 (t, 2H, H10), 3.21 (s, 6H, H9), 3.03 – 2.96 (m, 2H, H6), 2.12 – 2.015 (m, 2H, H7), 1.80 – 1.68 (m, 2H, H11), 0.59 (t, 2H, $J_{12-11} = 7.8$ Hz, H12) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 139.86 (C4), 132.41 (C1), 129.14 (C2), 127.20 (C3), 65.94 (C10), 62.45 (C8), 51.10 (C9), 50.72 (C13), 39.93 (C6), 22.61 (C7), 16.45 (C11), 5.57 (C12) ppm. ^{29}Si $\{^1\text{H}\}$ NMR (79.4 MHz, CDCl_3 , δ): - 44.41 ppm.



Example 11 - N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride (2a):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)-4-methylbenzenesulfonamide (1.0 g, 3.90 mmol) and (3-Chloropropyl)trimethoxysilane (1.1 mL, 5.85 mmol, 1.5 eq.) in ACN (3 mL) for 3.5 hours resulting in viscous golden yellow brown solution. The product was purified using Et_2O (10 mL X 3) and obtained as clear golden brown gummy oil after drying under 10^{-3} mm Hg vacuum at room temperature. Yield: 97 % (1.67 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 8.18 (br. s, 1H, H6), 7.85 (d, 2H, $J_{4-2} = 7.9$ Hz, H4), 7.29 (d, 2H, $J_{2-4} = 7.7$ Hz, H2), 3.75 – 3.62 (m, 2H, H9), 3.55 (s, 9H, H14), 3.41 – 3.32 (m, 2H, H11), 3.25 (s, 6H, H10), 3.08 – 2.94 (m, 2H, H7), 2.40 (s, 3H, H1), 2.15 – 2.05 (m, 2H, H8), 1.84 – 1.58 (m, 2H, H12), 0.63 (t, 2H, $J_{4-2} = 7.7$ Hz, H13) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 143.08 (C5), 136.85 (C3), 129.70 (C2), 127.85 (C4), 65.82 (C11), 62.45 (C9), 51.10 (C14), 50.70 (C10), 39.91 (C7), 22.66 (C1), 21.46 (C8), 16.44 (C12), 5.57 (C13) ppm. ^{29}Si $\{^1\text{H}\}$ NMR (79.4 MHz, CDCl_3 , δ): - 44.37 ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Cl}^-]$ calculated for $\text{C}_{18}\text{H}_{35}\text{N}_2\text{O}_5\text{Si}_1$, 419.6309, found, 419.2026.

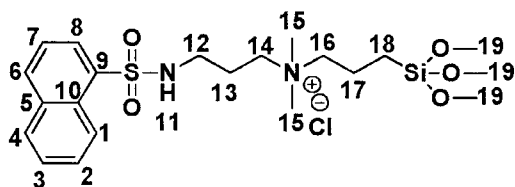


Example 12 - N,N-dimethyl-3-(trimethoxysilyl)-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium chloride (3a):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)-2,4,6-

trimethylbenzenesulfonamide (2.0 g, 7.03 mmol) and (3-Chloropropyl)trimethoxysilane (1.9 mL, 10.55 mmol, 1.5 eq.) in ACN (3 mL) for 4.5 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as clear golden brown gummy oil after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 92.6 % (3.27 g).

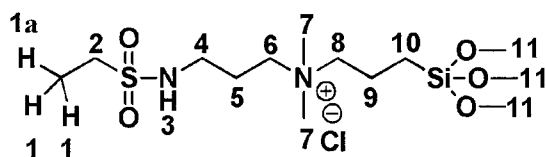
¹H NMR (CDCl₃, 400 MHz, δ): 7.74 (t, 1H, *J*₇₋₈ = 6.0 Hz, H7), 6.90 (s, 2H, H3), 3.70 (t, 2H, *J*₈₋₉ = 7.9 Hz, H8), 3.53 (s, 9H, H15), 3.40 – 3.33 (m, 2H, H12), 3.25 (s, 6H, H11), 3.02 – 2.94 (m, 2H, H10), 2.62 (br. s, 6H, H4), 2.25 (s, 3H, H1), 2.14 – 2.04 (m, 2H, H9), 1.83 – 1.72 (m, 2H, H13), 0.62 (t, 2H, *J*₁₄₋₁₃ = 7.9 Hz, H14) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 142.01 (C6), 139.22 (C5), 133.83 (C2), 132.01 (C3), 66.06 (C12), 62.51 (C10), 51.22 (C11), 50.81 (C15), 39.33 (C8), 23.28 (C4), 22.88 (C1), 20.95 (C9), 16.57 (C13), 5.70 (C14) ppm. ²⁹Si {¹H} NMR (79.4 MHz, CDCl₃, δ): - 44.43 ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Cl⁻] calculated for C₂₀H₃₉N₂O₅Si₁, 447.6840, found, 447.2357.



Example 13 - N,N-dimethyl-3-(naphthalene-1-sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride (5a):

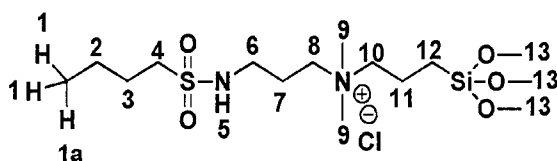
This compound was synthesized using *N*-(3-(dimethylamino)propyl)naphthalene-1-sulfonamide (0.5 g, 2.21mmol) and (3-Chloropropyl)trimethoxysilane (0.6 mL, 3.31 mmol, 1.5 eq.) in ACN (3 mL) for 5 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as clear golden brown gummy oil after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 78.8 % (0.85 g). ¹H NMR (CDCl₃, 400 MHz, δ): 8.83 (d, 1H, *J*₈₋₇ = 8.6 Hz, H8), 8.47 (t, 1H, *J*₁₁₋₁₂ = 5.7 Hz, H11), 8.20 (d, 1H, *J*₆₋₇ = 7.3 Hz, Hs6), 7.99 (d, 1H, *J*₁₋₂ = 8.1 Hz, H1), 7.87 (d, 1H, *J*₄₋₃ = 8.1 Hz, H4), 7.74 – 7.65 (m, 1H, H7), 7.55 – 7.46 (m, 2H, H3 & H2), 3.51 – 3.46 (m, 11H, H14 & H19), 3.22 – 3.16 (m, 2H, H16), 3.09 – 3.01 (m, 8H, H12 & H15), 1.98 – 1.86 (m, 2H, H13), 1.68 – 1.54 (m, 2H, H17), 0.51 (t, 2H, *J*₁₈₋₁₇ = 7.8 Hz, H18) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 135.12 (C9), 134.16 (C5), 133.91 (C1), 129.07 (C6), 128.8 (C4), 128.56 (C7), 128.12 (C10), 127.02 (C3), 125.30 (C8), 124.31 (C2), 65.84 (C16), 62.32 (C14), 50.92 (C15), 50.69 (C19), 39.79 (C12), 22.81 (C13), 16.33 (C17), 5.48 (C18) ppm. ²⁹Si

{¹H} NMR (79.4 MHz, CDCl₃, δ): - 44.49 ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Cl⁻] calculated for C₂₁H₃₅N₂O₅Si₁, 455.2030, found, 455.2018.



Example 14 - 3-(ethylsulfonamido)-N,N-dimethyl-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride (7a):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)ethanesulfonamide (1.0 g, 5.15 mmol) and (3-Chloropropyl)trimethoxysilane (1.4 mL, 7.72 mmol, 1.5 eq.) in ACN (3 mL) for 5 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as clear golden brown gummy oil after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 86.0 % (1.73 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.63 (s, 1H, H3), 3.75 – 3.47 (m, 11H, H6 & H1), 3.39 – 3.31 (m, 2H, H8), 3.25 – 3.15 (m, 8H, H7 & H4), 3.07 – 2.98 (m, 2H, H2), 2.19 – 2.02 (m, 2H, H5), 1.88 – 1.69 (m, 2H, H9), 1.31 (td, 3H, *J*₁₋₂ = 7.3 Hz, *J*_{1-1a} = 3.4 Hz, H1 & H1a), 0.62 (t, 2H, *J*₁₀₋₉ = 7.8 Hz, H10) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 65.89 (C8), 62.40 (C6), 51.18 (C7), 50.81 (C11), 46.37 (C2), 40.09 (C4), 23.58 (C5), 16.54 (C9), 8.28 (C1), 5.73 (C10) ppm. ²⁹Si {¹H} NMR (79.4 MHz, CDCl₃, δ): - 44.51 ppm.

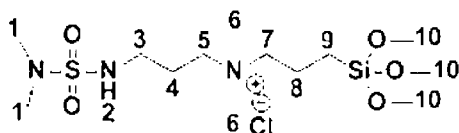


Example 15 - 3-(butylsulfonamido)-N,N-dimethyl-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride (8a)

This compound was synthesized using *N*-(3-(dimethylamino)propyl)butanesulfonamide (1.0 g, 4.50 mmol) and (3-Chloropropyl)trimethoxysilane (1.2 mL, 6.75 mmol, 1.5 eq.) in ACN (3 mL) for 5 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 5) and obtained as clear golden brown gummy oil after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 60.0 % (1.13 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.62 (br. s, 1H, H5), 3.67 – 3.60 (m, 2H, H8), 3.51 (s, 9H, H13), 3.36 – 3.29 (m, 2H, H4), 2.15 – 2.04 (m, 2H,

H7), 1.83 – 1.66 (m, 4H, H11 & H3), 1.41 – 1.33 (m, 2H, H2), 0.87 (td, $J_{1-2} = 7.3$ Hz, $J_{1-1a} = 3.1$ Hz, H1 & H1a), 0.60 (t, 2H, $J_{12-11} = 7.3$ Hz, H12) ppm. ^{13}C { ^1H } NMR (CDCl_3 , 100 MHz, δ): 65.82 (C10), 51.81 (C4), 51.12 (C9), 50.74 (C13), 40.04 (C6), 25.38 (C3), 23.50 (C7), 21.58 (C2), 16.50 (C11), 13.62 (C1), 5.68 (C12) ppm. ^{29}Si { ^1H } NMR (79.4 MHz, CDCl_3 , δ): - 44.50 ppm.

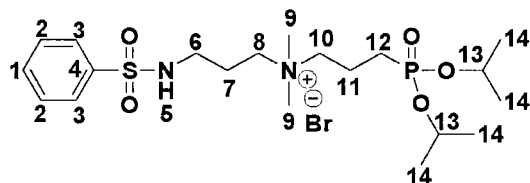
5 HRMS-ESI-TOF (m/z): [$\text{M}^+ - \text{Cl}^-$] calculated for $\text{C}_{15}\text{H}_{37}\text{N}_2\text{O}_5\text{Si}_1$, 385.2187, found, 385.2185.



Example 16 - 3-((N,N-dimethylsulfamoyl)amino)-N,N-dimethyl-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride (9a)

10

Synthesis of Organophosphorus based QAC



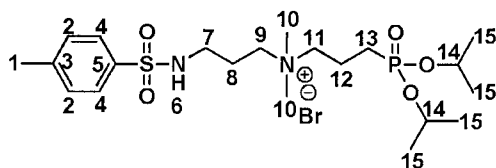
Example 17 - 3-(diisopropoxyphosphoryl)-N,N-dimethyl-N-(3-(phenylsulfonamido)propyl)propan-1-aminium bromide (1b):

15 This compound was synthesized using *N*-(3-(dimethylamino)propyl)benzenesulfonamide (1.0 g, 4.13 mmol) and diisopropyl (3-bromopropyl)phosphonate (1.10 mL, 4.13 mmol, 1 eq.) in ACN (3 mL) for 4 hours resulting in viscous golden yellow brown solution. The product was purified using Et_2O (10 mL X 3) and obtained as pale yellow fluffy/gummy powder after drying under 10^{-3} mm Hg vacuum at room temperature. Yield: 86.0 % (1.87 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.94 (d, 2H, $J_{3-2} = 6.5$ Hz, H3), 7.65 (t, 1H, $J_{5-6} = 5.9$ Hz, H5), 7.54 – 7.46 (m, 3H, H1 & H2), 4.70 – 4.57 (m, 2H, H13), 3.73 – 3.65 (m, 2H, H8), 3.64 – 3.56 (m, 2H, H10), 3.27 (s, 6H, H9), 3.02 (dd, 2H, $J_{6-5} = 11.3$ Hz, $J_{6-7} = 5.6$ Hz, H6), 2.16 – 1.94 (m, 4H, (H7, H11, & ACN)), 1.79 (dt, 2H, $J_{12-P} = 17.7$ Hz, H8, $J_{12-11} = 7.2$ Hz, H12), 1.28 (dd, 12H, $J_{14-P} = 6.2$ Hz, H8, $J_{14-13} = 1.7$ Hz, H14) ppm.

20 ^{13}C { ^1H } NMR (CDCl_3 , 100 MHz, δ): 139.57 (C4), 132.59 (C2), 129.23 (C1), 127.19 (C3), 70.82 (d, $^2J_{13-P} = 6.7$ Hz, C13), 6.74 (d, $^3J_{10-P} = 15.1$ Hz, C10), 62.41 (C8), 51.28 (C9), 39.89 (C6), 24.12 (d, $J_{14-P} = 4.5$ Hz, C14), 23.99 (d, $J_{14-P} = 4.0$ Hz, C14), 23.82 & 22.38 (d, $J_{12-P} = 144.3$ Hz, C12),

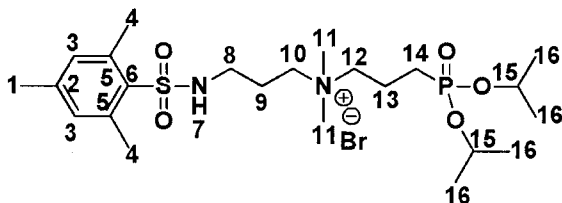
25

22.68 (C7), 16.67 (C11) ppm. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121.45 MHz, δ): 27.36 ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Br}^-]$ calculated for $\text{C}_{20}\text{H}_{38}\text{N}_2\text{O}_5\text{P}_1\text{S}_1$, 449.2234, found, 449.2232.



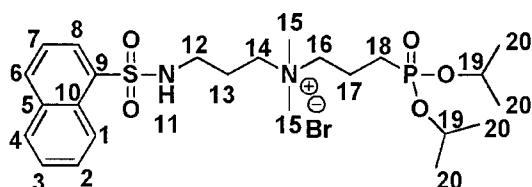
Example 18 - 3-(diisopropoxyphosphoryl)-N,N-dimethyl-N-(3-(4-methylphenylsulfonamido)propyl)propan-1-aminium bromide (2b):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)-4-methylbenzenesulfonamide (0.50 g, 1.95 mmol) and diisopropyl (3-bromopropyl)phosphonate (0.50 mL, 1.95 mmol, 1 eq.) in ACN (3 mL) for 3 hours resulting in pale yellow solution with some precipitate formation. The product was purified using Et_2O (10 mL X 3) and obtained as white puffy powder after drying under 10^{-3} mm Hg vacuum at room temperature. Yield: 89.5 % (0.95 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.78 (d, 2H, $J_{4-2} = 8.2$ Hz, H4), 7.55 (t, 1H, $J_{6-7} = 5.8$ Hz, H6), 7.28 – 7.23 (m, 2H, H2 and CDCl_3), 4.72 – 4.49 (m, 2H, H14), 3.72 – 3.63 (m, 2H, H9), 3.62 – 3.54 (m, 2H, H11), 3.25 (s, 6H, H10), 3.00 – 2.90 (m, 2H, H7), 2.36 (s, 3H, H1), 2.16 – 1.90 (m, 4H, H8 & H12), 1.75 (dt, 2H, $J_{13-P} = 17.8$ Hz, $J_{13-12} = 7.1$ Hz, H13), 1.25 (dd, 12H, $J_{15-P} = 56.15$ Hz, $J_{15-14} = 2.1$ Hz, H15) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 143.25 (C5), 136.46 (C3), 129.74 (C2), 127.22 (C4), 70.71 (d, $^2J_{14-P} = 6.7$ Hz, C14), 63.67 (d, $^3J_{11-P} = 15.8$ Hz, C11), 62.42 (C9), 51.17 (C10), 39.86 (C7), 24.10 (d, $J_{15-P} = 4.5$ Hz, C15), 23.97 (d, $J_{15-P} = 4.0$ Hz, C15), 23.79 & 22.36 (d, $J_{13-P} = 144.1$ Hz, C13), 22.52 (C8), 21.47 (C1), 16.69 (d, $^2J_{12-P} = 4.1$ Hz, C12) ppm. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121.45 MHz, δ): 27.15 ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Br}^-]$ calculated for $\text{C}_{21}\text{H}_{40}\text{N}_2\text{O}_5\text{P}_1\text{S}_1$, 463.5909, found, 463.2394.



Example 19 - 3-(diisopropoxyphosphoryl)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide (3b):

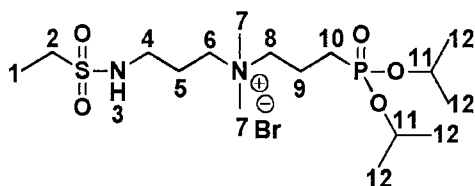
This compound was synthesized using *N*-(3-(dimethylamino)propyl)-2,4,6-trimethylbenzenesulfonamide (0.50 g, 1.76 mmol) and diisopropyl (3-bromopropyl)phosphonate (0.40 mL, 1.76 mmol, 1 eq.) in ACN (3 mL) for 4 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as pale yellow fluffy/gummy powder after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 71.0 % (0.71 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.14 (t, 1H, *J*₇₋₈ = 6.0 Hz, H7), 6.92 (s, 2H, H3), 4.71 – 4.57 (m, 2H, H15), 3.84 – 3.75 (m, 2H, H10), 3.74 – 3.60 (m, 2H, H12), 3.32 (s, 6H, H11), 3.01 (dd, 2H, *J*₈₋₇ = 11.2 Hz, *J*₈₋₉ = 5.6 Hz, H8), 2.63 (s, 6H, H4), 2.27 (s, 3H, H1), 2.22 – 2.00 (m, 4H, H9 & H13), 1.81 (dt, 2H, *J*_{14-P} = 17.8 Hz, *J*₁₄₋₁₃ = 7.0 Hz, H14), 1.30 (d, 12H, *J*₁₆₋₁₅ = 6.2 Hz, H16) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 142.11 (C6), 139.07 (C2), 133.33 (C5), 132.00 (C3), 70.80 (d, ²*J*_{15-P} = 6.7 Hz, C15), 63.68 (d, ²*J*_{12-P} = 15.0 Hz, C112), 62.35 (C10), 51.32 (C11), 39.20 (11C8), 24.13 (d, *J*_{16-P} = 4.5 Hz, C16), 24.00 (d, *J*_{16-P} = 4.0 Hz, C16), 23.81 & 22.38 (d, *J*_{14-P} = 144.3 Hz, C14), 23.22 (C4), 22.68 (C9), 20.89 (C1), 16.76 (C13) ppm. ³¹P {¹H} NMR (CDCl₃, 121.45 MHz, δ): 27.16 ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Br⁻] calculated for C₂₃H₄₄N₂O₅P₁Si₁, 491.2703, found, 491.2693.



Example 20 - 3-(diisopropoxyphosphoryl)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide (5b):

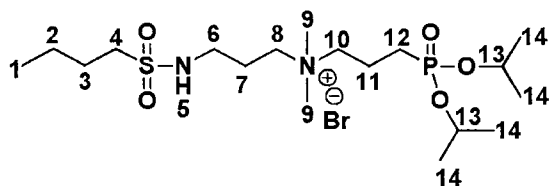
This compound was synthesized using *N*-(3-(dimethylamino)propyl)naphthalene-1-sulfonamide (0.50 g, 4.13 mmol) and diisopropyl (3-bromopropyl)phosphonate (0.50 mL, 3.42 mmol, 1 eq.) in ACN (3 mL) for 5.5 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as pale yellow fluffy/gummy powder after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 77.4 % (0.77 g). ¹H NMR (CDCl₃, 400 MHz, δ): 8.82 (d, 1H, *J*₈₋₇ = 8.7 Hz, H8), 8.20 (d, 1H, *J*₆₋₇ = 7.3 Hz, H6), 8.02 (d, 1H, *J*₁₋₂ = 8.3 Hz, H1), 7.92 – 7.84 (m, 2H, H4 & H11), 7.73 – 7.62 (m, 1H, H7), 7.57 – 7.48 (m, 2H, H3 & H2), 4.69 – 4.50 (m, 2H, H19), 3.62 – 3.47 (m, 4H, H14 & H16), 3.12 (s, 6H, H15), 3.03 (dd, 2H, *J*₁₂₋₁₁ = 11.2 Hz, *J*₁₂₋₁₃ = 5.6 Hz, H12), 2.08 – 1.82 (m, 7H, (ACN, H13 & H17)), 1.71 (dt, 2H, *J*_{18-P} =

17.5 Hz, $J_{18-17} = 7.2$ Hz, H18), 1.12 (t, 12H, $J_{20-19} = 6.0$ Hz, H20) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 134.63 (C9), 134.18 (C5), 13.14 (C1), 129.37 (C6), 128.92 (C4), 128.63 (C7), 128.03 (C10), 127.08 (C3), 125.17 (C8), 124.36 (C2), 70.80 (d, $^2J_{19-P} = 6.7$ Hz, C19), 63.60 (d, $^3J_{16-P} = 15.1$ Hz, C16), 62.36 (C14), 51.14 (C15), 39.74 (C12), 24.12 (d, $J_{20-P} = 4.5$ Hz, C20), 23.99 (d, $J_{20-P} = 4.0$ Hz, C20), 23.74 & 22.31 (d, $J_{18-P} = 144.5$ Hz, C18), 22.68 (C13), 16.65 (d, $^2J_{17-P} = 144.3$ Hz, C17) ppm. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121.45 MHz, δ): 27.19 ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Br}^-]$ calculated for $\text{C}_{24}\text{H}_{40}\text{N}_2\text{O}_5\text{P}_1\text{S}_1$, 499.2390, found, 499.2385.



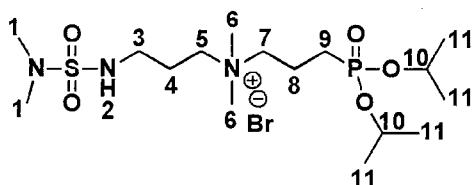
Example 21 - 3-(diisopropoxyphosphoryl)-N-(3-(ethylsulfonamido)propyl)-N,N-dimethylpropan-1-aminium bromide (7b):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)ethanesulfonamide (0.25 g, 1.29 mmol) and diisopropyl (3-bromopropyl)phosphonate (0.30 mL, 1.29 mmol, 1 eq.) in ACN (3 mL) for 5 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as white gummy powder after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 86.0 % (0.53 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.08 (t, 1H, $J_{3-4} = 5.8$ Hz, H3), 4.76 – 4.54 (m, 2H, H11), 3.74 (t, 2H, $J_{6-5} = 7.6$ Hz, H6), 3.63 (t, 2H, $J_{8-9} = 7.9$ Hz, H8), 3.35 – 3.16 (m, 8H, H7 & H4), 3.07 (q, 2H, $J_{2-1} = 7.4$ Hz, H2), 2.27 – 2.13 (m, 2H, H5), 2.12 – 1.96 (m, 2H, H9), 1.82 (dt, 2H, $J_{10-P} = 17.4$ Hz, $J_{10-9} = 7.2$ Hz, H10), 1.44 – 1.24 (m, 15H, H1 & H12) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 70.74 (d, $^2J_{11-P} = 6.7$ Hz, C11), 63.75 (d, $^3J_{8-P} = 15.7$ Hz, C8), 62.36 (C6), 51.20 (C7), 46.22 (C2), 39.97 (C4), 24.12 (d, $J_{12-P} = 4.5$ Hz, C12), 23.98 (d, $J_{12-P} = 4.0$ Hz, C12), 23.86 & 22.43 (d, $^2J_{10-P} = 144.3$ Hz, C10), 23.36 (C5), 16.74 (C9), 8.24 (C1) ppm. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121.45 MHz, δ): 27.05 ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Br}^-]$ calculated for $\text{C}_{16}\text{H}_{38}\text{N}_2\text{O}_5\text{P}_1\text{S}_1$, 401.2234, found, 401.2235.



Example 22 - 3-(butylsulfonamido)-N-(3-(diisopropoxyphosphoryl)propyl)-N,N-dimethylpropan-1-aminium bromide (8b):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)butane-1-sulfonamide (0.50 g, 2.25 mmol) and diisopropyl (3-bromopropyl)phosphonate (0.60 mL, 2.25 mmol, 1 eq.) in ACN (3 mL) for 3 hours resulting in viscous golden yellow brown solution. The product was purified using Et₂O (10 mL X 3) and obtained as pale yellow gummy powder after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 82.0 % (0.94 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.07 (t, 1H, *J*₃₋₄ = 6.1 Hz, H5), 4.69 (qd, 2H, *J*_{13-P} = 12.4 Hz, *J*₁₃₋₁₄ = 6.2 Hz, H13), 3.78 (t, 2H, *J*₈₋₇ = 7.8 Hz, H8), 3.66 (t, 2H, *J*₁₀₋₁₁ = 8.4 Hz, H10), 3.33 (s, 6H, H9), 3.28 (dd, 2H, *J*₆₋₅ = 12.0 Hz, *J*₆₋₇ = 6.0 Hz, H6), 3.29 (t, 2H, *J*₄₋₃ = 8.4 Hz, H4), 2.24 – 2.15 (m, 2H, H7), 2.15 – 2.03 (m, 2H, H11), 1.89 – 1.75 (m, 4H, H3 & H12), 1.45 (dq, 2H, *J*₂₋₃ = 14.7, *J*₂₋₁ = 7.3, H2), 1.38 – 1.29 (m, 12H, H14), 0.96 (t, 3H, *J*₁₋₂ = 7.4 Hz, H1) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 70.77 (d, ²*J*_{13-P} = 6.7 Hz, C13), 63.73 (d, ³*J*_{10-P} = 15.5 Hz, C10), 62.36 (C8), 51.72 (C4), 51.25 (C9), 39.98 (C6), 25.35 (C3), 24.14 (d, *J*_{14-P} = 4.5 Hz, C14), 24.00 (d, *J*_{14-P} = 4.0 Hz, C14), 23.87 & 22.43 (d, *J*_{12-P} = 144.4 Hz, C12), 23.37 (C7), 21.51 (C2), 16.73 (d, ²*J*_{11-P} = 4.2 Hz, C11), 13.62 (C1) ppm. ³¹P{¹H} NMR (CDCl₃, 121.45 MHz, δ): 27.22 ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Br⁻] calculated for C₁₈H₄₂N₂O₅P₁S₁, 429.2547, found, 429.2543.

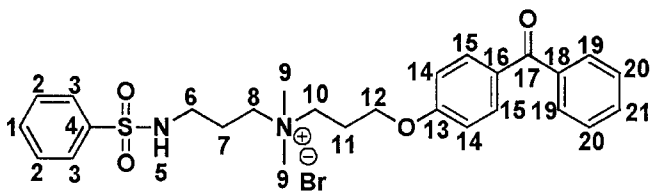


Example 23 - 3-(diisopropoxyphosphoryl)-N-(3-((N,N-dimethylsulfamoyl)amino)propyl)-N,N-dimethylpropan-1-aminium bromide (9b):

This compound was synthesized using *N*-(2-(dimethylamino)propyl)-N,N-Dimethyl-sulfamide (0.50 g, 2.39 mmol) and diisopropyl (3-bromopropyl)phosphonate (0.6 mL, 2.39 mmol, 1 eq.) in ACN (3 mL) for 3 hours resulting in viscous pale yellow solution. The product was purified using

Et₂O (10 mL X 3) and obtained as pale yellow fluffy/gummy powder after drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 91.7 % (1.09 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.02 (t, 1H, *J*₂₋₃ = 5.9 Hz, H2), 4.62 (qd, 2H, *J*_{10-P} = 12.4 Hz, *J*₁₀₋₁₁ = 6.2 Hz, H10), 3.66 (t, 2H, *J*₅₋₄ = 7.9 Hz, H5), 3.59 (t, 2H, *J*₇₋₈ = 8.2 Hz, H7), 3.26 (s, 6H, H6), 3.14 (dd, 2H, *J*₃₋₂ = 12.0 Hz, *J*₃₋₄ = 6.0 Hz, H3), 2.75 (s, 6H, H1), 2.20 – 2.06 (m, 2H, H4), 2.05 – 1.97 (m, 2H, H8), 1.78 (dt, 2H, *J*_{9-P} = 17.4 Hz, *J*₉₋₈ = 7.2 Hz, H9), 1.31 – 1.20 (m, 12H, H11) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 70.78 (d, ²*J*_{10-P} = 6.6 Hz, C10), 63.74 (d, ³*J*_{7-P} = 15.4 Hz, C7), 62.44 (C5), 51.24 (C6), 40.19 (C6), 38.15 (C1), 24.13 (d, *J*_{11-P} = 4.5 Hz, C11), 24.06 (d, *J*_{11-P} = 4.0 Hz, C11), 23.87 & 22.44 (d, *J*_{9-P} = 144.0 Hz, C9). 22.84 (C4), 16.74 (C8) ppm. ³¹P {¹H} NMR (CDCl₃, 121.45 MHz, δ): 27.27 ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Br⁻] calculated for C₁₆H₃₉N₃O₅P₁S₁, 416.2343, found, 416.2341.

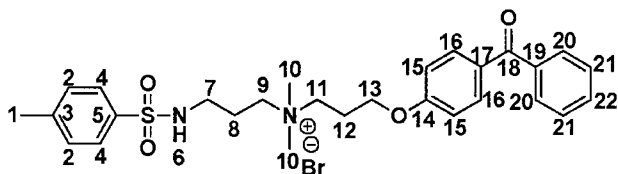
Synthesis of Benzophenone based QAC



Example 24 - 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(phenylsulfonamido)propyl)propan-1-aminium bromide (1c):

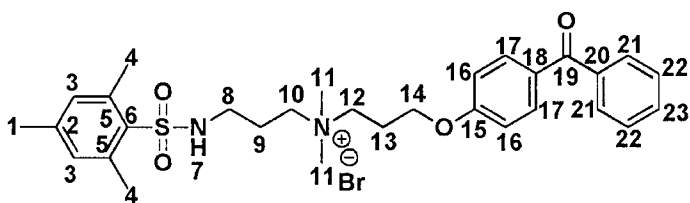
This compound was synthesized using *N*-(3-(dimethylamino)propyl)phenylsulfonamide (0.921 g, 3.8 mmol) and 4-(3-bromopropoxy)benzophenone (1.29 g, 4.0 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy pale yellow powder after washing with Et₂O (10 mL X 3) and drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 82% (1.74 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.96 – 7.89 (m, 2H, H3), 7.86 – 7.77 (m, 1H, H5), 7.74 – 7.62 (m, 4H, H15 & H19), 7.57 – 7.49 (m, 1H, H21), 7.49 – 7.37 (m, 5H, (H1, H2, & H20)), 6.89 (d, 2H, *J*₁₄₋₁₅ = 8.9 Hz, H14), 4.11 (t, *J*₁₂₋₁₁ = 5.3 Hz, H12), 3.79 – 3.56 (m, 4H, H8 & H10), 3.27 (s, 6H, H9), 3.06 – 2.92 (m, 2H, H6), 2.36 – 2.19 (m, 2H, H11), 2.19 – 1.97 (m, 2H, H7) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 195.58 (C17), 161.80 (C13), 139.64 (C1), 137.99 (C4), 132.71 (C18), 132.51 (C15), 132.19 (C21), 130.60 (C16), 139.75 (C2), 129.32 (C19), 128.35 (C20), 127.22 (C3), 114.31 (C14), 64.68 (C12), 62.44 (C8), 62.06 (C10), 39.98 (C6), 23.08 (C11), 22.75 (C7) ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Br⁻] calculated for

C₂₇H₃₃N₂O₄S, 481.2156; found 481.2155.



Example 25 - 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(4-methylphenylsulfonamido)propyl)propan-1-aminium bromide (2c):

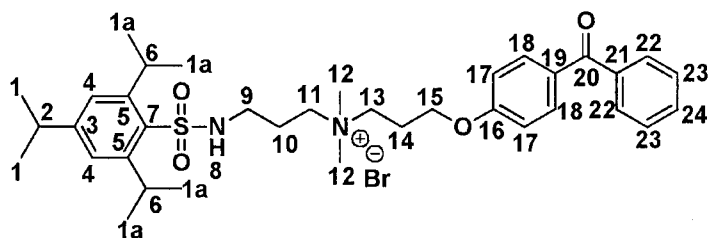
This compound was synthesized using *N*-(3-(dimethylamino)propyl)-4-methylphenylsulfonamide (1.05 g, 4.1 mmol) and 4-(3-bromopropoxy)benzophenone (1.417 g, 4.44 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy pale yellow powder after washing with Et₂O (10 mL X 3) and drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 80 % (1.88 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.80 (d, 2H, *J*₄₋₂ = 8.2 Hz, H4), 7.73 – 7.65 (m, 4H, H16 & H20), 7.56 – 7.59 (m, 1H, H22), 7.42 (t, *J*₄₋₂ = 7.2 Hz 2H, H22), 7.21 (d, 2H, *J*₂₋₄ = 8.2 Hz, H2), 6.89 (d, 2H, *J*₁₅₋₁₆ = 8.8 Hz, H15), 4.12 (t, 2H, *J*₁₃₋₁₂ = 5.4 Hz, H13), 3.79 – 3.59 (m, 4H, H9 & H11), 3.29 (s, 6H, H10), 3.07 – 2.90 (m, 2H, H7), 2.35 – 2.23 (m, 5H, H1 & H12), 2.19 – 2.03 (m, 2H, H8) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 195.57 (C18), 161.82 (C14), 143.50 (C3), 138.05 (C5), 136.53 (C19), 132.54 (C16), 132.19 (C22), 130.69 (C17), 129.90 (C20), 129.80 (C2), 128.36 (C21), 127.34 (C4), 114.32 (C15), 64.71 (C13), 62.53 (C9), 62.11 (C11), 51.62 (C10), 40.01 (C7), 23.15 (C12), 22.75 (C8), 21.57 (C1) ppm. HRMS-ESI-TOF (*m/z*): [M⁺ - Br⁻] calculated for C₂₈H₃₅N₂O₄S, 495.2312; found 495.2319.



Example 26 - 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide (3c):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)-2,4,6-trimethylphenylsulfonamide (0.853 g, 3.0 mmol) and 4-(3-bromopropoxy)benzophenone (1.0 g,

3.13 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy white powder after washing with Et₂O (10 mL X 3) and drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 67 % (1.20 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.76 (d, 2H, *J*₁₇₋₁₆ = 8.7 Hz, H17), 7.72 (d, 2H, *J*₂₁₋₂₂ = 7.2 Hz, H21), 7.56 (t, 2H, *J*₂₃₋₂₂ = 7.4 Hz, H23), 7.49 – 7.41 (m, 2H, H22), 7.22 (t, 1H, *J*₄₋₂ = 6.2 Hz, H7), 6.94 (t, 2H, *J*₁₆₋₁₇ = 6.0 Hz, H16), 6.90 (s, 2H, H3), 4.21 (t, 2H, *J*₁₄₋₁₃ = 5.4 Hz, H14), 3.90 – 3.80 (m, 2H, H10), 3.80 – 3.68 (m, 2H, H12), 3.37 (s, 6H, H11), 3.04 (dd, 2H, *J*₈₋₇ = 11.4 Hz, *J*₈₋₉ = 5.7 Hz, H8), 2.63 (s, 6H, H4), 2.43 – 2.32 (m, 2H, H13), 2.25 (s, 3H, H1), 2.23 – 2.13 (m, 2H, H9) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 195.63 (C19), 161.81 (C15), 142.40 (C5), 139.24 (C2), 138.15 (20), 133.41 (C6), 132.66 (C17), 132.22 (C23), 132.18 (C3), 130.91 (C18), 129.90 (C21), 128.39 (C22), 64.72 (C14), 62.68 (C10), 62.29 (C12), 51.77 (C11), 39.36 (C8), 23.42 (C4), 23.27 (C13), 23.05 (C9), 21.03 (C1) ppm. HRMS-ESI-TOF (*m/z*): [*M*⁺ - Br⁻] calculated for C₃₀H₃₉N₂O₄S, 523.2625; found 523.2636.

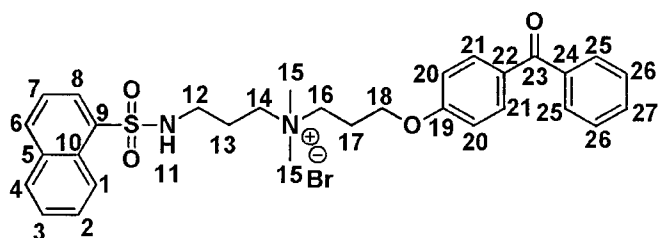


Example 27 - 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-triisopropylphenyl)sulfonamido)propylpropan-1-aminium bromide (4c):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)-2,4,6-triisopropylbenzenesulfonamide (0.379 g, 1.03 mmol) and 4-(3-bromopropoxy)benzophenone (0.329 g, 1.03 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy pale white powder after washing with Et₂O (10 mL X 3) and drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 92% (0.65 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.78 – 7.65 (m, 4H, H18 & H22), 7.57 – 7.49 (m, 1H, H24), 7.43 (t, 2H, *J*₂₃₋₂₂ = 7.5 Hz, H23), 7.12 (s, 2H, H4), 7.06 (t, 1H, *J*₈₋₉ = 6.1 Hz, H8), 6.93 (d, 2H, *J*₁₇₋₁₈ = 8.9 Hz, H17), 4.20 (t, 2H, *J*₁₅₋₁₄ = 5.5 Hz, H15), 4.16 – 4.05 (m, 2H, H6), 3.90 – 3.81 (m, 2H, H11), 3.80 – 3.69 (m, 2H, H13), 3.39 (s, 6H, H12), 3.10 (dd, 1H, *J*₉₋₈ = 11.3 Hz, *J*₉₋₁₀ = 5.7 Hz, H9), 2.91 – 2.79 (m, 2H, H2), 2.45 – 2.31 (m, 2H, H14), 2.28 – 2.14 (m, 2H, H10), 1.21 (dd, 18H, *J*₁₋₂ = 6.8 Hz, *J*_{1a-6} = 2.3 Hz, H1 & H1a) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 195.55 (C20), 161.75 (C16), 152.76 (C3), 150.33

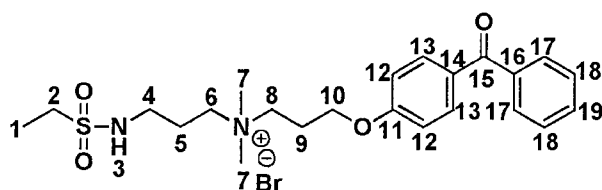
(C7), 138.01 (C21), 132.50 (C18), 132.06 (C24), 131.96 (C5), 130.66 (C19), 129.74 (C22), 128.24 (C23), 123.88 (C4), 114.22 (C17), 64.67 (C15), 62.49 (C11), 62.03 (C13), 51.66 (C12), 39.47 (C9), 34.10 (C2), 29.54 (C6), 25.12 (C1), 23.14 (C14), 23.07 (C10) ppm. HRMS-ESI-TOF (m/z): $[M^+ - Br^-]$ calculated for $C_{36}H_{51}N_2O_4S$, 607.3564; found 607.3555.

5



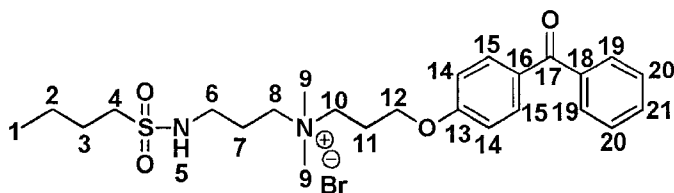
Example 28 - 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide (5c):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)naphthalene-1-sulfonamide (0.584 g, 2.0 mmol) and 4-(3-bromopropoxy)benzophenone (0.702 g, 2.2 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy white powder after washing with Et_2O (10 mL X 3) and drying under 10^{-3} mm Hg vacuum at room temperature. Yield: 82 % (1.0 g). ^1H NMR ($CDCl_3$, 400 MHz, δ): 8.80 (d, 1H, $J_{1-2} = 8.7$ Hz, H1), 8.15 (d, 1H, $J_{8-7} = 7.3$ Hz, H8), 7.96 (s, 1H, H11), 7.91 (d, 1H, $J_{6-7} = 8.3$ Hz, H6), 7.78 (d, 1H, $J_{4-3} = 8.2$ Hz, H4), 7.70 – 7.55 (m, 4H, (H2, H25, & H21)), 7.51 (t, 2H, $J_{27-26} = 7.4$ Hz, H27), 7.46 – 7.34 (m, 4H, (H3, H26, & H7)), 6.77 (d, 2H, $J_{20-21} = 8.7$ Hz, H20), 4.00 – 3.85 (m, 2H, H18), 3.59 – 3.37 (m, 4H, H14 & H16), 3.19 – 2.91 (m, 8H, H15 & H12), 2.17 – 1.99 (m, 2H, H17), 1.97 – 1.76 (m, 2H, H13) ppm. ^{13}C { ^1H } NMR ($CDCl_3$, 100 MHz, δ): 195.59 (C23), 161.77 (C19), 138.04 (C24), 134.85 (C9), 134.21 (C6), 132.50 (C25), 132.20 (C27), 130.56 (C10), 129.80 (C2), 129.36 (C8), 129.05 (C4), 128.76 (C21), 128.37 (C7), 128.00 (C22), 127.18 (C3), 125.20 (C1), 124.52 (C26), 114.25 (C20), 64.59 (C18), 62.42 (C14), 62.10 (C16), 51.42 (15), 39.83 (C12), 22.92 (C17 & C13) ppm. HRMS-ESI-TOF (m/z): $[M^+ - Br^-]$ calculated for $C_{31}H_{35}N_2O_4S$, 531.2312; found 531.2328.



Example 29 - 3-(4-benzoylphenoxy)-N-(3-(ethylsulfonamido)propyl)-N,N-dimethylpropan-1-aminium bromide (7c):

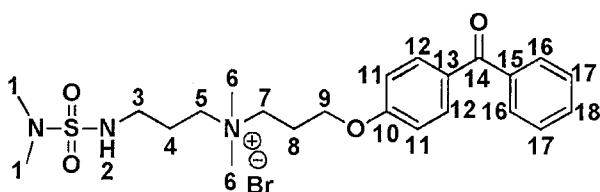
This compound was synthesized using *N*-(3-(dimethylamino)propyl)ethanesulfonamide (0.250 g, 1.29 mmol) and 4-(3-bromopropoxy)benzophenone (0.411 g, 1.29 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy pale yellow powder after washing with Et₂O (10 mL X 3) and drying under 10⁻³ mm Hg vacuum at room temperature. Yield: 77% (0.52 g). ¹H NMR (CDCl₃, 400 MHz, δ): 7.78 (d, 2H, *J*₁₃₋₁₂ = 8.7 Hz, H13), 7.72 (d, 2H, *J*₁₇₋₁₈ = 7.4 Hz, H17), 7.56 (t, 2H, *J*₁₉₋₁₈ = 7.4 Hz, H19), 7.50 – 7.40 (m, 2H, H18), 7.12 (t, 1H, *J*₃₋₄ = 6.0 Hz, H3), 6.98 (d, 2H, *J*₁₂₋₁₃ = 8.8 Hz, H12), 4.21 (t, 2H, *J*₁₀₋₉ = 5.3 Hz, H10), 3.86 – 3.75 (m, 2H, H6), 3.75 – 3.65 (m, 2H, H8), 3.35 (s, 6H, H7), 3.31 – 3.22 (m, 2H, H4), 3.07 (q, 2H, *J*₂₋₃ = 7.3 Hz, H2), 2.43 – 2.29 (m, 2H, H9), 2.27 – 2.13 (m, 2H, H5), 1.34 (t, 3H, *J*₂₋₃ = 7.4 Hz, H1) ppm. ¹³C {¹H} NMR (CDCl₃, 100 MHz, δ): 195.55 (C15), 161.66 (C11), 137.94 (C16), 132.55 (C13), 132.16 (C19), 130.83 (C14), 129.78 (C17), 128.29 (C18), 114.22 (C12), 64.57 (C10), 62.46 (C6), 62.17 (C8), 51.61 (C7), 46.44 (C2), 39.95 (C4), 23.64 (C5), 23.11 (C9), 8.27 (C1) ppm. HRMS-ESI-TOF (*m/z*): [*M*⁺ - Br⁻] calculated for C₂₃H₃₃N₂O₄S, 433.2156; found 433.2153.



Example 30 - 3-(4-benzoylphenoxy)-N-(3-(butylsulfonamido)propyl)-N,N-dimethylpropan-1-aminium bromide (8c):

This compound was synthesized using *N*-(3-(dimethylamino)propyl)butane-1-sulfonamide (0.324 g, 1.46 mmol) and 4-(3-bromopropoxy)benzophenone (0.466 g, 1.46 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy pale yellow powder after washing with Et₂O (10 mL X 3) and drying under 10⁻³ mm Hg vacuum at room

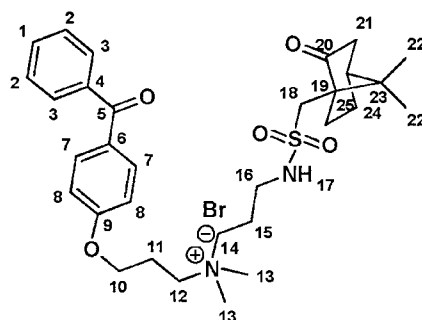
temperature. Yield: 73% (0.58 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.74 (d, 2H, $J_{15-14} = 8.7$ Hz, H15), 7.69 (d, 2H, $J_{19-20} = 7.1$ Hz, H19), 7.54 (t, 1H, $J_{21-20} = 7.4$ Hz, H21), 7.47 – 7.38 (m, 2H, H20), 7.10 (t, 1H, $J_{5-6} = 5.6$ Hz, H5), 6.96 (d, 2H, $J_{14-15} = 8.8$ Hz, H14), 4.18 (t, 1H, $J_{12-11} = 5.2$ Hz, H12), 3.79 – 3.61 (m, 2H, H8 & H10), 3.33 (s, 6H, H9), 3.27 – 3.20 (m, 2H, H6), 3.10 – 2.96 (m, 2H, H4), 2.42 – 2.25 (m, 2H, H11), 2.25 – 2.07 (m, 2H, H7), 1.80 – 1.65 (m, 2H, H3), 1.38 (dq, 2H, $J_{2-3} = 14.6$ Hz, $J_{2-1} = 7.4$ Hz, H2), 0.87 (t, 3H, $J_{1-2} = 7.3$ Hz, H1) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 195.56 (C17), 161.17 (C13), 137.89 (C18), 132.50 (C15), 132.16 (C21), 130.62 (C16), 129.71 (C19), 128.29 (C20), 114.27 (C14), 64.67 (C12), 62.30 (C8), 61.96 (C10), 51.79 (C4), 51.56 (C9), 25.37 (C3), 23.55 (C7), 23.05 (C11), 21.51 (C2), 13.64 (C1) ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Br}^-]$ calculated for $\text{C}_{25}\text{H}_{37}\text{N}_2\text{O}_4\text{S}$, 461.2469; found 461.2458.



Example 31 - 3-(4-benzoylphenoxy)-N-(3-((N,N-dimethylsulfamoyl)amino)propyl)-N,N-dimethylpropan-1-aminium bromide (9c):

This compound was synthesized using *N*-(2-(dimethylamino)propyl)-*N,N*-Dimethyl-sulfamide (0.232 g, 1.11 mmol) and 4-(3-bromopropoxy)benzophenone (0.354 g, 1.11 mmol) in ACN (10 mL) for 48 hours; yielding in viscous pale yellow solution. The product was obtained as fluffy pale yellow powder after washing with Et_2O (10 mL X 3) and drying under 10^{-3} mm Hg vacuum at room temperature. Yield: 60 % (0.36 g). ^1H NMR (CDCl_3 , 400 MHz, δ): 7.70 (d, 2H, $J_{12-11} = 8.7$ Hz, H12), 7.65 (d, 2H, $J_{16-17} = 7.2$ Hz, H16), 7.51 (t, 1H, $J_{18-17} = 7.4$ Hz, H18), 7.44 – 7.36 (m, 2H, H17), 7.03 – 6.87 (m, 3H, H11 & H2), 4.15 (t, 2H, $J_{9-8} = 4.7$ Hz, H9), 3.71 – 3.53 (m, 4H, H5 & H7), 3.28 (s, 6H, H6), 3.20 – 3.12 (m, 2H, H3), 2.72 (s, 6H, H1), 2.37 – 2.22 (m, 2H, H8), 2.19 – 2.02 (m, 2H, H4) ppm. ^{13}C $\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, δ): 195.62 (C14), 161.88 (C9), 137.87 (C15), 132.50 (C12), 132.17 (C18), 130.49 (C13), 129.73 (C16), 128.30 (C17), 114.35 (C11), 64.82 (C9), 62.24 (C5), 61.76 (C7), 51.62 (C6), 40.18 (C3), 38.15 (C1), 23.06 (C4), 22.97 (C8) ppm. HRMS-ESI-TOF (m/z): $[\text{M}^+ - \text{Br}^-]$ calculated for $\text{C}_{23}\text{H}_{34}\text{N}_3\text{O}_4\text{S}$, 448.2265; found 448.2262.

Example 31A - N-(3-(4-benzoylphenoxy)propyl)-3-((7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methylsulfonamido)-N,N-dimethylpropan-1-amine-1-aminium, bromide salt:



- 5 This compound was synthesized using 1-(7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-(3-(dimethylamino)propyl)methanesulfonamide (1.32 g, 4.187 mmol) and 4-(3-bromopropoxy)benzophenone (1.403 g, 4.39 mmol, 1.05 eq.) in refluxing EtOAc (10 mL) for 3 hours; yielding a viscous pale yellow oil. The product was obtained as fluffy white powder after purification. Yield: 58% (1.535 g), Mp = 33-34 °C. ¹H NMR (CDCl₃, 400 MHz, δ): δ 7.80 – 7.73 (m, 2H, H3), 7.73 – 7.58 (m, 2H, H7), 7.48 (s, 1H, H1), 7.43 – 7.37 (m, 2H, H2), 7.09 – 6.95 (m, 2H, H8), 4.04 – 4.00 (m, 2H, H10), 3.69 (s, 1H, H18), 3.54 – 3.39 (m, 5H, H18, H12, H14), 3.36 – 3.32 (m, 6H, H13), 2.76 (d, *J* = 7.4 Hz, 2H, H16), 2.36 (s, 1H,), 2.22 – 2.18 (m, 2H, H11), 2.11 (s, 1H,), 2.03 (dd, *J* = 19.1, 0.6 Hz, 4H), 1.83 (s, 1H, H25), 1.59 (s, 1H, H24), 1.34 (s, 1H, H24), 1.11 (s, 3H, H22), 1.08 (m, 3H, H22) ppm.

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Example 32 – Application and Curing of Benzophenone-Anchored Antimicrobials to Test Surfaces

- 1% (w/v) solutions of the benzophenone-anchored sulfonamide quaternary ammonium cation (QUAT) antimicrobials were prepared by dissolving the desired antimicrobial compound within a range of ethanol:water mixture between 10:90 to 40:60, depending on the solubility of the antimicrobial compound. An emphasis was made to reduce ethanol content where applicable. Coating of the test samples, which consisted of 25 mm (± 5 mm) x 25 mm (± 5 mm) x 1 mm coupons of each plastic material, was performed via an ESS AD-LG electrospray apparatus set to 150 kPa that applied the compound uniformly over the test surfaces. After application, the coated

surfaces were allowed to air-dry before proceeding to a UV curing step which involved exposing the surfaces to 5000mW intensity UV light for 1 minute. This coating and curing sequence was repeated a second time to ensure adequate coverage of the compound, as confirmed with bromophenol blue staining which allowed for visualization of the surface-bound sulfonamide QUAT compound. Stock polystyrene and polyethylene material was supplied by VWR International, polyvinyl chloride was sourced from Home Depot and polyether ether ketone was sourced from Drake Plastics. **Figure 1** shows the treated versus untreated samples.

Example 33 – Application and Curing of Silicone-Anchored Antimicrobials to Test Surfaces

1% (w/v) solutions of the silane-anchored sulfonamide QUAT antimicrobials were prepared in a range of methanol:water mixtures between 30:70 to 70:30, depending on the solubility of the antimicrobial compound. An emphasis was made to reduce methanol content where applicable. Coating of the test samples was performed via gently heating and agitating cotton samples at 40°C within the coating solution for 5 minutes. After application, the coated surfaces were allowed to air-dry before rinsing with water. Coating quality of the treated cotton samples was confirmed with bromophenol blue staining, which allowed for visualization of the surface-bound sulfonamide QUAT compound. Stock cotton fabric was supplied by META Labware. **Figure 2** shows the treated versus untreated cotton samples.

Example 34 – Testing Antimicrobial Efficacy at Solid-Air Interfaces

Large-droplet inoculation method (Ronan E. et al, *Biofouling* 2013,29, 1087-1096)

Many pathogens are able to remain viable during extended periods of desiccation on inanimate surfaces. Long-term survival of pathogens in the inanimate environment pose a significant risk for infection transmission and contamination in high-risk environments such as hospital rooms or food-processing plants. The large-droplet inoculation method was developed to simulate the deposition of bacterial species onto exposed surfaces and to determine the ability of these cells to survive desiccation.

For these tests, small surface coupons were first coated with the antimicrobial using the method described above. Bacterial test species were grown overnight in a shaking incubator and cultures

were washed twice to replace the growth media with sterile water. 100µL aliquots of the prepared culture were then inoculated onto multiple coated surfaces and allowed to air-dry within a biological safety cabinet. Drying typically occurred 2-3 hours after inoculation, and surviving cells were enumerated immediately and 24 hours after drying. For enumeration, inoculated coupons were sacrificed in triplicate and placed inside separate tubes containing 5mL of a 0.9% saline collection liquid. Each coupon was agitated vigorously for 1 minute with a bench-top vortex to transfer cells from the test surface to the collection liquid. Plate counts were then performed on serial dilutions of the collection liquid, and colony counts from triplicate treated surfaces were averaged and compared to colony counts from tests of untreated control surfaces carried out in parallel.

A range of bacterial species were used in these tests. *Arthrobacter* spp., a gram-positive lab strain originally isolated from indoor air was used in the bulk of the testing, as it is known to be highly resistant to desiccation and therefore was used as a model for desiccation-tolerant pathogens. Efficacy tests were also carried out against, for example, gram-negative *Escherichia coli* (*E. coli*) and gram-positive *Staphylococcus aureus* (*S. aureus*), since they all contain pathogenic strains and have been implicated in major nosocomial outbreaks. **Figure 3** shows that 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl) propan-1-aminium bromide treated polystyrene and N,N-dimethyl-3-(4-methylphenyl sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride treated cotton demonstrated within three hours excellent activity against *Arthrobacter* spp. The following are the tabulated bacterial reduction data:

Polystyrene Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	1.28E+08	1.28E+08	1.28E+08		1.28E+08	0.00E+00
3 hours	9.75E+06	7.65E+06	8.60E+06		8.67E+06	1.05E+06
24 hours	7.75E+03	9.10E+03	2.50E+02		5.70E+03	4.77E+03
Polystyrene Mesityl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	1.28E+08	1.28E+08	1.28E+08		1.28E+08	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
Cotton Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	1.28E+08	1.28E+08	1.28E+08		1.28E+08	0.00E+00

3 hours	2.20E+06	1.65E+06	2.75E+06		2.20E+06	5.50E+05
24 hours	5.60E+05	2.65E+05	3.10E+05		3.78E+05	1.59E+05
Cotton Tosyl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	1.28E+08	1.28E+08	1.28E+08		1.28E+08	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

Figure 4 shows that N,N-dimethyl-3-(phenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride, N,N-dimethyl-3-(trimethoxysilyl)-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium chloride and N,N-dimethyl-3-(naphthalene-1-sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride treated cotton demonstrated within three hours excellent activity against *Arthrobacter* spp. The following are tabulated bacteria reduction data:

Cotton Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	4.04E+07	4.04E+07	4.04E+07		4.04E+07	0.00E+00
3 hours	1.76E+03	1.92E+04	7.60E+03		9.50E+03	8.85E+03
24 hours	1.20E+02	0.00E+00	0.00E+00		4.00E+01	6.92E+01
Cotton Mesityl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	4.04E+07	4.04E+07	4.04E+07		4.04E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
Cotton Tosyl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	4.04E+07	4.04E+07	4.04E+07		4.04E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
Cotton Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	6.10E+07	6.10E+07	6.10E+07		6.10E+07	0.00E+00
3 hours	8.75E+04	2.70E+05	3.15E+05		2.24E+05	1.20E+05
24 hours	6.95E+04	5.85E+04	7.15E+04		6.65E+04	7.00E+03
Cotton Benzyl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	6.10E+07	6.10E+07	6.10E+07		6.10E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
Cotton Naphthyl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	6.10E+07	6.10E+07	6.10E+07		6.10E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
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Figure 5 shows that 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide and 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(phenyl sulfonamido)propyl)propan-1-aminium bromide treated polyethylene demonstrated within three hours excellent activity against *Arthrobacter* spp. The following are tabulated bacteria reduction data:

Polyethylene Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	2.70E+07	2.70E+07	2.70E+07		2.70E+07	0.00E+00
3 hours	1.80E+04	7.00E+06	9.00E+05		2.64E+06	3.80E+06
24 hours	4.00E+02	7.00E+02	5.00E+02		5.33E+02	1.53E+02
Polyethylene Naphthyl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	2.70E+07	2.70E+07	2.70E+07		2.70E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
Polyethylene Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	2.70E+07	2.70E+07	2.70E+07		2.70E+07	0.00E+00
3 hours	1.80E+04	7.00E+06	9.00E+05		2.64E+06	3.80E+06
24 hours	4.00E+02	7.00E+02	5.00E+02		5.33E+02	1.53E+02
Polyethylene Phenyl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	2.70E+07	2.70E+07	2.70E+07		2.70E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

Figure 6 shows that 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenyl sulfonamido)propyl)propan-1-aminium bromide treated polyethylene demonstrated within three hours excellent activity against *E. coli* and *S. aureus*. The following are tabulated bacteria reduction data:

<i>E. coli</i> Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	5.05E+07	5.05E+07	5.05E+07		5.05E+07	0.00E+00
3 hours	5.00E+02	2.50E+02	4.50E+02		4.00E+02	1.32E+02
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
<i>E. coli</i> Mesityl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours	5.05E+07	5.05E+07	5.05E+07		5.05E+07	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
<i>S. aureus</i> Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	8.30E+05	8.30E+05	8.30E+05		8.30E+05	0.00E+00
3 hours	1.10E+04	7.50E+03	8.00E+03		8.83E+03	1.89E+03
24 hours	1.14E+04	3.20E+03	1.95E+03		5.52E+03	5.13E+03
<i>S. aureus</i> Mesityl	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	8.30E+05	8.30E+05	8.30E+05		8.30E+05	0.00E+00
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
24 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

Figure 7 shows the inclusion of a trace amount (0.05% w/v) of a fluorophore demonstrated that a polyethylene sample was coated with 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide. **Figure 8** shows that 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide containing 0.05% w/v fluorophore demonstrated within three hours excellent activity against *Arthrobacter* spp. The following are tabulated bacteria reduction data:

Polyethylene Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	4.63E+08	4.63E+08	4.63E+08		4.63E+08	0
3 hours	4.20E+06	8.55E+06	9.10E+06		7.28E+06	2.68E+06
Polyethylene Treated	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	4.63E+08	4.63E+08	4.63E+08		4.63E+08	0
3 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0

Example 34 – Testing Antimicrobial Efficacy at Static Solid-Liquid Interfaces*Static biofilm tests*

The interior of polyethylene test tubes was coated with the sulfonamide QUAT antimicrobial similarly as in Example 32. Tubes were filled with 2.7mL of growth media (3g/L TSB) into which 300µL of *Arthrobacter* spp. bacterial culture was inoculated. Planktonic cells were sampled after 48 hours of incubation and agitation by removing 100µL aliquots from each tube. After 48 hours, the liquid in each tube was removed completely so that biofilm attachment to the interior of the tubes could be assessed. To test for biofilm attachment the tubes were first gently rinsed in a saline solution to remove any loosely attached or residual planktonic cells. Next, 1mL of saline solution was added to each tube before the tubes were vortexed vigorously for 1 minute to transfer biofilm cells to the collection liquid. Plate counts were then performed on serial dilutions of this collection liquid. Planktonic and biofilm colony counts from triplicate coated tubes were averaged and compared to colony counts from tests of uncoated control tubes carried out in parallel.

After 14 days of exposure to ambient air, the tubes used in the above test were subjected to a second static biofilm test as described above, without reapplying the antimicrobial. This test was performed to determine whether the antimicrobial effects of the coating persisted following repeated exposures.

Figure 9 shows that 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenyl sulfonamido)propyl)propan-1-aminium bromide treated polyethylene test tubes inoculated with *Arthrobacter* spp. demonstrated within 48 hours excellent activity against planktonic cells. The following are tabulated bacteria reduction data:

Initial Planktonic Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	7.75E+08	7.75E+08	7.75E+08		7.75E+08	0.00E+00
48 hours	1.48E+08	1.58E+08	1.59E+08		1.55E+08	6.08E+06
Initial Planktonic Treated	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	7.75E+08	7.75E+08	7.75E+08		7.75E+08	0.00E+00
48 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

Rechallenge Planktonic Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	8.00E+08	8.00E+08	8.00E+08		8.00E+08	0.00E+00
48 hours	2.88E+08	1.61E+09	2.93E+09		1.61E+09	1.32E+09
Rechallenge Planktonic Treated	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	8.00E+08	8.00E+08	8.00E+08		8.00E+08	0.00E+00
48 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

Figure 10 shows that 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenyl sulfonamido)propyl)propan-1-aminium bromide treated polyethylene test tubes inoculated with *Arthrobacter* spp. demonstrated within excellent activity against biofilm development. The

5 following are tabulated bacteria reduction data:

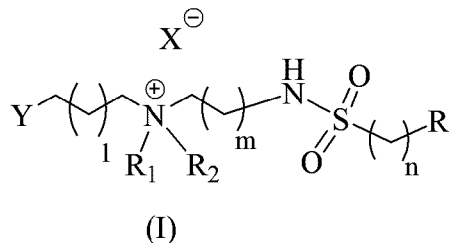
Initial Biofilm Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	7.75E+08	7.75E+08	7.75E+08		7.75E+08	0.00E+00
48 hours	9.00E+04	1.10E+05	6.20E+05		2.73E+05	3.00E+05
Initial Biofilm Treated	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	7.75E+08	7.75E+08	7.75E+08		7.75E+08	0.00E+00
48 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00
Rechallenge Biofilm Control	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	8.00E+08	8.00E+08	8.00E+08		8.00E+08	0.00E+00
48 hours	8.90E+06	7.20E+06	6.70E+06		7.60E+06	1.15E+06
Rechallenge Biofilm Treated	A (cfu)	B (cfu)	C (cfu)		Average	Deviation
0 hours (Load)	8.00E+08	8.00E+08	8.00E+08		8.00E+08	0.00E+00
48 hours	0.00E+00	0.00E+00	0.00E+00		0.00E+00	0.00E+00

As many changes can be made to the preferred embodiment of the above without departing from the scope thereof, it is intended that all matter contained herein be considered illustrative and not in a limiting sense.

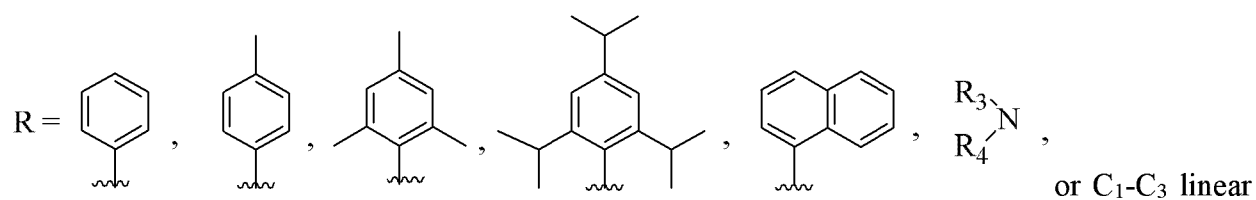
CLAIMS

We claim:

1. A quaternary ammonium sulfonamide compound of formula (I):



wherein



or branched alkyl,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

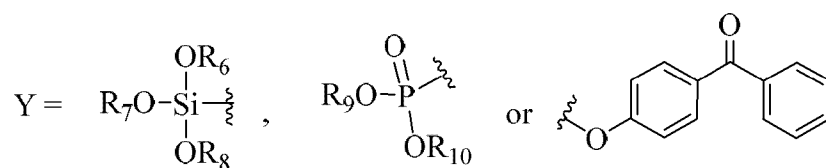
R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃ or OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

X = halogen, and

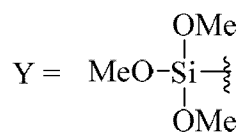


wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or

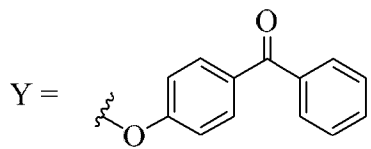
branched alkyl and wherein when , Y may be substituted or

unsubstituted, and when R is aryl, it is substituted or unsubstituted and when R is naphthyl, the aryl group is not substituted.

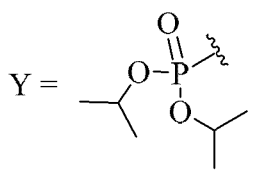
2. The compound of claim 1 wherein the X is Br.
3. The compound of claim 1 wherein the X is Cl.
4. The compound of claim 1 wherein l is 1, m is 2 and n is 0.
5. The compound of claim 1 wherein R₁ and R₂ are the same and methyl.
6. The compound of any one of claims 1 to 5 wherein



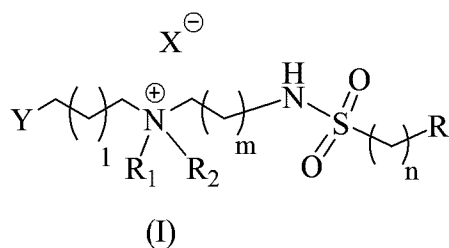
7. The compound of any one of claims 1 to 5 wherein



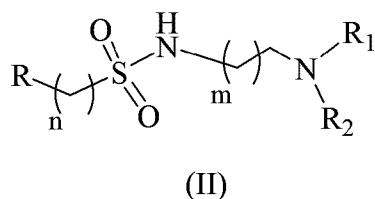
8. The compound of any one of claims 1 to 5 wherein



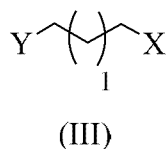
9. A process for preparing a quaternary ammonium sulfonamide of formula (I):



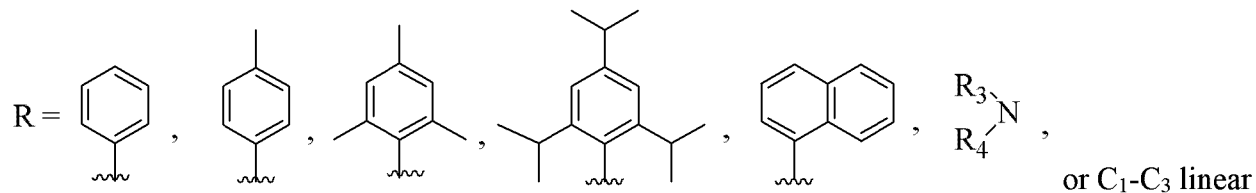
comprising reacting a compound of formula (II)



with an alkyl halide of formula (III)



wherein



or branched alkyl,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, or

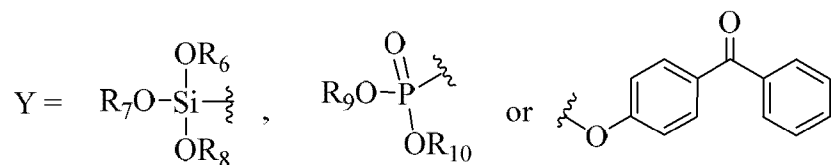
OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

X = halogen, and

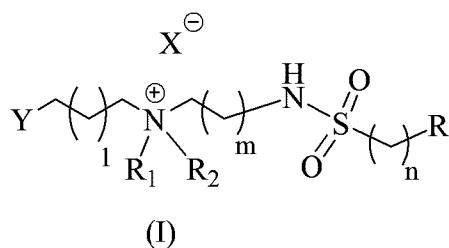


wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or

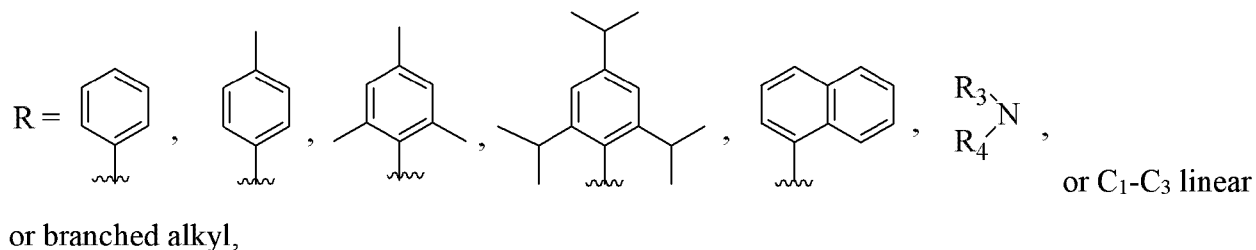
branched alkyl and wherein when $Y = \text{---O}-\text{C}_6\text{H}_4-\text{C}(=\text{O})-\text{C}_6\text{H}_5$, Y may be substituted or unsubstituted, and wherein when R is aryl, it is substituted or unsubstituted and when R is naphthyl, the aryl group is not substituted.

10. The process of claim 9 wherein X is Cl.
11. The process of claim 9 wherein X is Br.
12. The process of claim 9 wherein l is 1, m is 2 and n is 0.
13. The process of claim 9 wherein R₁ and R₂ are the same and methyl.
14. The process of any one of claims 9 to 13 wherein the aryl group of R is naphthyl is unsubstituted.
15. The process of any one of claims 9 to 14 wherein the reaction is carried out in at least one polar, aprotic solvent.
16. The process of claim 15 wherein said at least one polar, aprotic solvent is selected from the group consisting of dimethylformamide, tetrahydrofuran and acetonitrile.
17. The process of claim 16 wherein the solvent is acetonitrile.
18. The process of claim 15, 16 or 17 wherein the reaction is carried out at a refluxing temperature of the polar, aprotic solvent.
19. The process of any one of claims 9 to 18 wherein the reaction has a duration of from about 2 to about 8 hours.

20. An antimicrobial substrate treating composition comprising a compound of formula (I)



wherein



R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

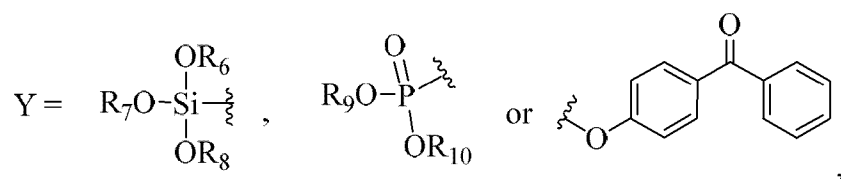
R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, or OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

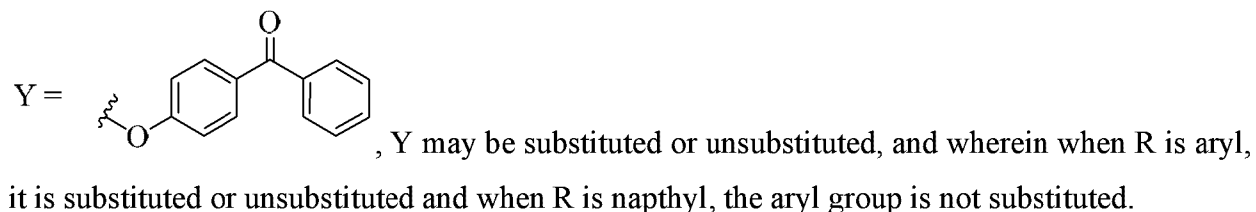
m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

X = halogen, and

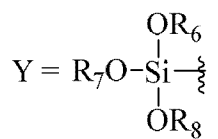


wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl, and an environmentally friendly carrier and wherein when

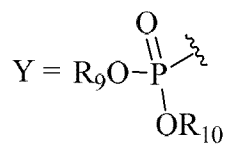


21. The composition of claim 20 wherein X is Cl.

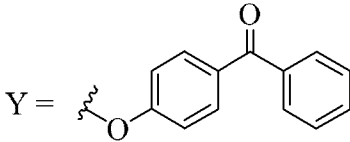
22. The composition of claim 20 wherein X is Br.
23. The composition of claim 20 wherein l is 1, m is 2 and n is 0.
24. The composition of claim 20 wherein R₁ and R₂ are the same and methyl.
25. The composition of claim 20 wherein the aryl group of R is naphthyl is unsubstituted.
26. The composition of any one of claims 20 to 25 wherein



27. The composition of claim 26 wherein R₆, R₇ and R₈ are the same and methyl.
28. The composition of any one of claims 20 to 25 wherein



29. The composition of claim 28 wherein R₉ and R₁₀ are the same and isopropyl.

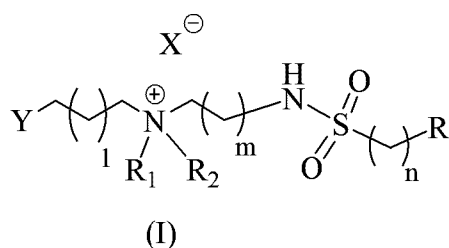
30. The composition of any one of claims 20 to 25 wherein  and Y may be substituted or unsubstituted.

31. The composition of any one of claims 20 to 30 wherein the carrier comprises water or a mixture of water and at least one alkanol.
32. The composition of claim 31 wherein the alkanol is a lower alkanol selected from methanol or ethanol.
33. The composition of claim 31 wherein the carrier comprises a mixture of alkanol and water.

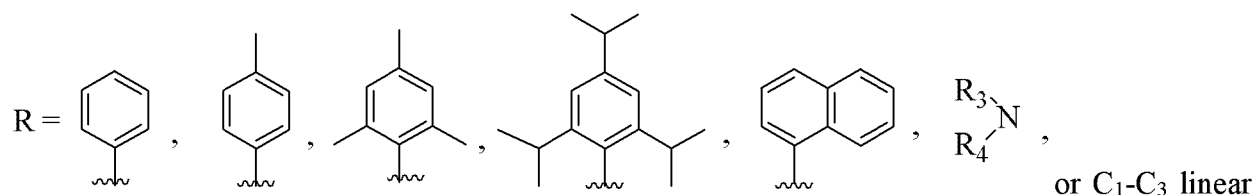
34. The composition of claim 33 wherein the mixture of alkanol and water has a ratio of alkanol to water from about 5:95 to about 80:20.

35. A process for treating a substrate with an antimicrobial, said process comprising the steps of:

i) contacting the substrate with an antimicrobial composition comprising at least one compound of formula (I)



wherein



or branched alkyl, wherein when R is aryl, it is substituted or unsubstituted and when R is naphthyl, the aryl group is not substituted,

R_1 and R_2 are the same or different and selected from C_1 to C_{18} linear or branched alkyl,

R_3 and R_4 are the same or different and selected from C_1 to C_4 linear or branched alkyl, CF_3 , or OR_5 where R_5 is C_1 to C_8 linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

$\text{X} = \text{halogen}$, and

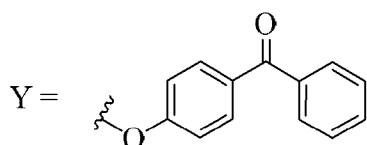
R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, or OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

X = halogen, and



and Y may be substituted or unsubstituted, and an environmentally friendly carrier,

(ii) drying the coated substrate passively or actively, and

(iii) irradiating the coated substrate wherein said environmentally friendly carrier is selected from the group consisting of water and a mixture of water and at least one alkanol.

39. The process of claim 38 wherein l is 1, m is 2 and n is 0.

40. The process of claim 39 wherein R₁ and R₂ are the same and methyl.

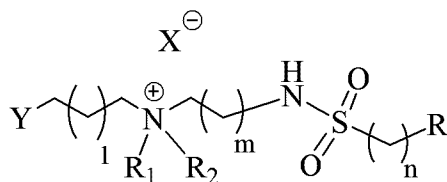
41. The process of claim 39 wherein the aryl group of R is naphthyl is unsubstituted.

42. The process of any one of claims 39 to 41 wherein the substrate is a polymer.

43. The process of claim 42 wherein the polymer is selected from the group consisting of polyethylene, polypropylene, acrylonitrile-butadiene-styrene, polyurethane, polyvinyl chloride and nylon.

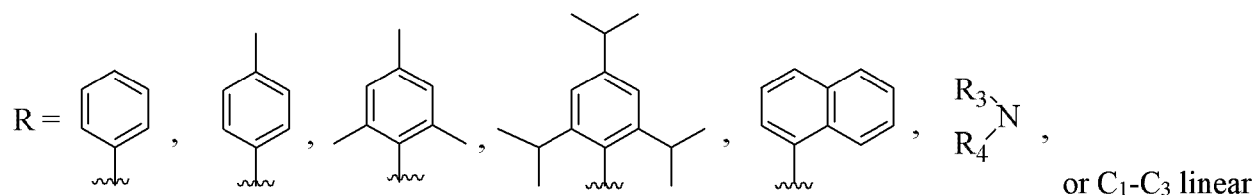
44. A process for treating a substrate with an antimicrobial, said process comprising the steps of:

i) contacting the substrate with an antimicrobial comprising a compound of formula (I)



(I)

wherein



or branched alkyl, wherein when R is aryl, it is substituted or unsubstituted and when R is naphthyl, the aryl group of R is not substituted,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

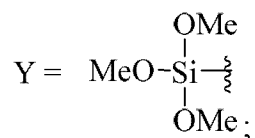
R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, or OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

X = halogen, and



ii) drying the substrate; and

iii) washing the treated substrate.

45. The process of claim 44 wherein l is 1, m is 2 and n is 0.

46. The process of claim 44 wherein R₁ and R₂ are the same and methyl.

47. The process of claim 44 wherein the aryl group of R is naphthyl is unsubstituted.

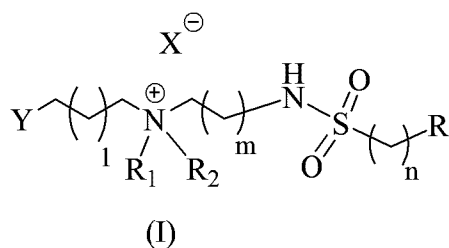
48. The process of any one of claim 44 to 47 wherein the substrate is a cellulosic material.

49. The process of claim 48 wherein the cellulosic material is cotton.

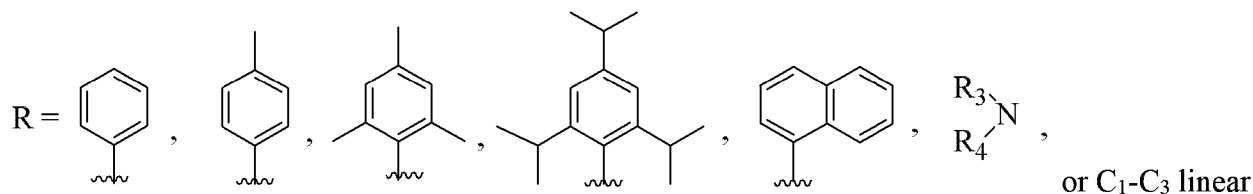
50. The process of any one of claims 44 to 47 wherein the substrate is a glass.

51. A process for treating a substrate with an antimicrobial coating, said process comprising the steps of:

i) contacting a heated substrate with a compound of formula (I)



wherein



or branched alkyl, wherein when R is aryl, it is substituted or unsubstituted and when R is naphthyl, the aryl group of R is not substituted,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

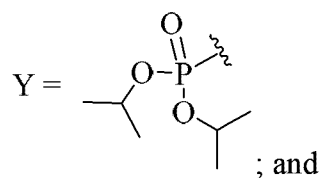
R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, or OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18,

X = halogen, and



ii) drying the substrate.

52. The process of claim 51 wherein l is 1, m is 2 and n is 0.

53. The process of claim 51 wherein R₁ and R₂ are the same and methyl.

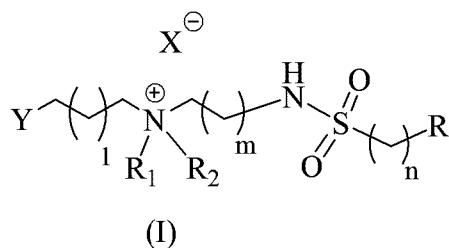
54. The process of claim 51 wherein the aryl group of R is naphthyl is unsubstituted.

55. The process of any one of claims 51 to 54 wherein the substrate is selected from the group consisting of a mineral, a metal, a metal oxide and a metal alloy.
56. The process of claim 55 wherein the substrate is a metal.
57. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial composition of any one of claims 20 to 34.
58. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium bromide.
59. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(4-methylphenylsulfonamido)propyl)propan-1-aminium bromide.
60. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(phenylsulfonamido)propyl)propan-1-aminium bromide.
61. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising 3-(4-benzoylphenoxy)-N,N-dimethyl-N-(3-(naphthalene-1-sulfonamido)propyl)propan-1-aminium bromide.
62. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising N,N-dimethyl-3-(trimethoxysilyl)-N-(3-(2,4,6-trimethylphenylsulfonamido)propyl)propan-1-aminium chloride.
63. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising N,N-dimethyl-3-(4-methylphenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride.
64. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising N,N-dimethyl-3-(phenylsulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride.

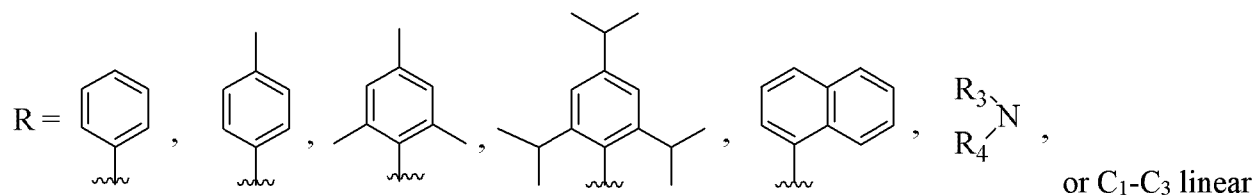
65. A method of reducing growth of at least one microbe on a substrate comprising treating said substrate with an antimicrobial comprising N,N-dimethyl-3-(naphthalene-1-sulfonamido)-N-(3-(trimethoxysilyl)propyl)propan-1-aminium chloride.

66. The method of any one of claims 57 to 65 wherein the at least one microbe is selected from the group consisting of *Listeria monocytogenes*, *Arthrobacter*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* and combinations thereof.

67. Use of an antimicrobial compound of formula (I):



wherein



or branched alkyl,

R₁ and R₂ are the same or different and selected from C₁ to C₁₈ linear or branched alkyl,

R₃ and R₄ are the same or different and selected from C₁ to C₄ linear or branched alkyl, CF₃, or

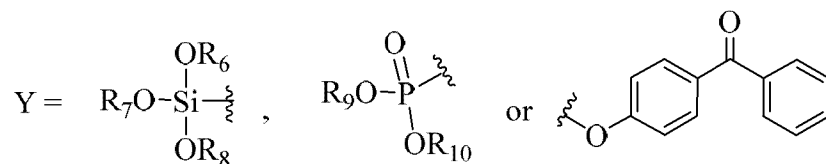
OR₅ where R₅ is C₁ to C₈ linear or branched alkyl or polyethylene oxide,

l is 1, 2, 3, 4, 5, 6, 7 or 8,

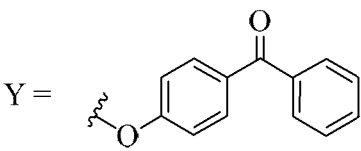
m is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17,

n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, wherein when R is aryl, it is substituted or unsubstituted and when R is naphthyl, the aryl group of R is unsubstituted,

X = halogen, and



wherein R₆, R₇, R₈, R₉ and R₁₀ are the same or different and selected from C₁ to C₆ linear or branched alkyl, to protect a substrate from a bio-fouling comprising treating said substrate with

said antimicrobial; and wherein when  Y may be substituted or unsubstituted.

68. The use of claim 67 wherein the halogen is Cl.

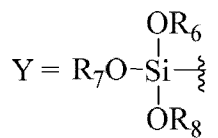
69. The use of claim 67 wherein the halogen is Br.

70. The use of claim 67 wherein l is 1, m is 2 and n is 0.

71. The use of claim 67 wherein R₁ and R₂ are the same and methyl.

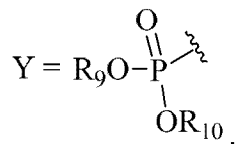
72. The use of claim 67 wherein the aryl group of R is naphthyl is unsubstituted.

73. The use of any one of claims 67 to 72 wherein

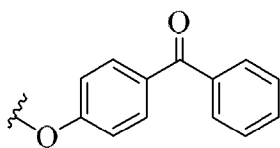


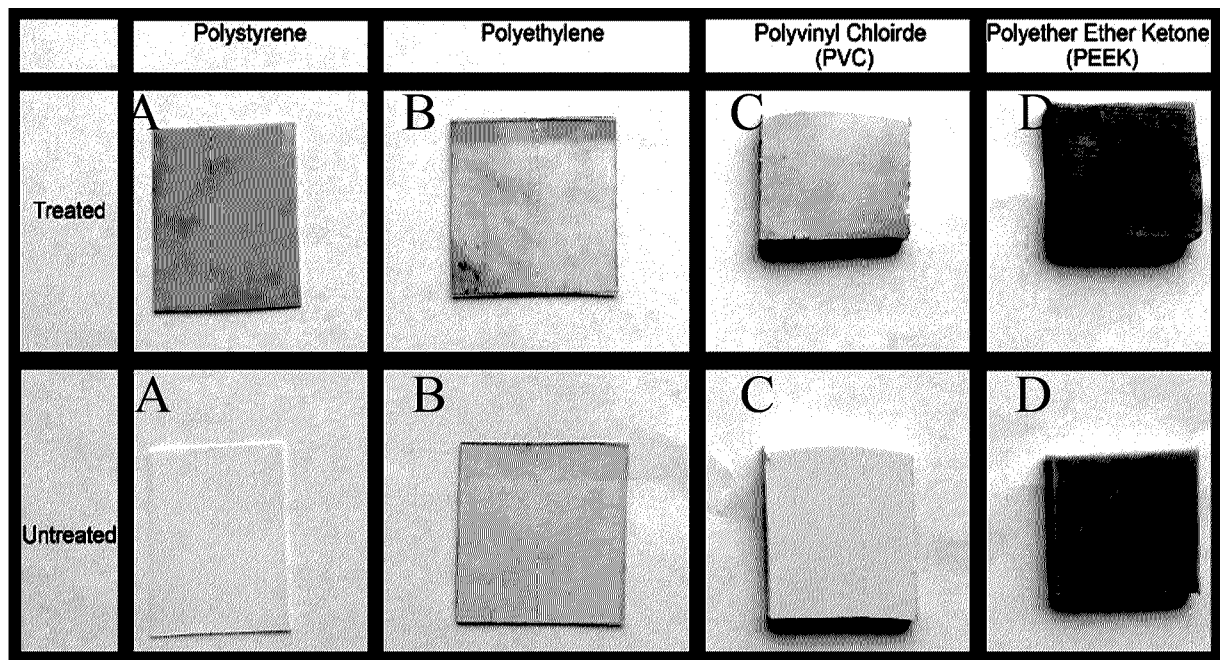
74. The use of claim 73 wherein R₆, R₇ and R₈ are the same and methyl.

75. The use of any one of claims 67 to 72 wherein



76. The use of claim 75 wherein R₉ and R₁₀ are the same and isopropyl.

77. The use of any one of claims 67 to 72 wherein $Y =$  and Y may be substituted or unsubstituted.
78. The use of any one of claims 67 to 77 wherein the bio-fouling is caused by a biofilm.
79. The use of the compound of claim 1 for reducing bacterial growth on a solid/air interface.
80. The process of any one of claims 44-50 further comprising stirring and heating in step i).
81. The process of claim 80 wherein the stirring has a duration of from about 3 minutes to about 5 minutes.
82. The process of claim 80 or 81, wherein the heating is from about 30°C to about 80°C.
83. The composition of any one of claims 20-34 wherein said environmentally friendly carrier is a mixture of water and at least one alkanol.
84. The composition of any one of claims 31 and 83 wherein said water is distilled water and said at least one alkanol is selected from the group consisting of methanol, ethanol, isopropanol and combinations thereof.
85. The process of any one of claims 35-43 wherein said environmentally friendly carrier is a mixture of water and at least one alkanol.
86. The process of any one of claims 35-43 and 85 wherein said water is distilled water and said at least one alkanol is selected from the group consisting of methanol, ethanol, isopropanol and combinations thereof.



A = Polystyrene, B = Polyethylene, C = Polyvinyl Chloride (PVC), D = Polyether ether ketone (PEEK)

Figure 1

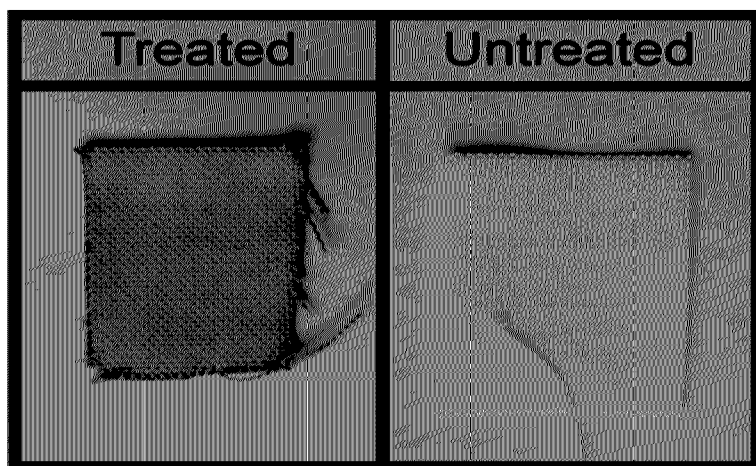


Figure 2

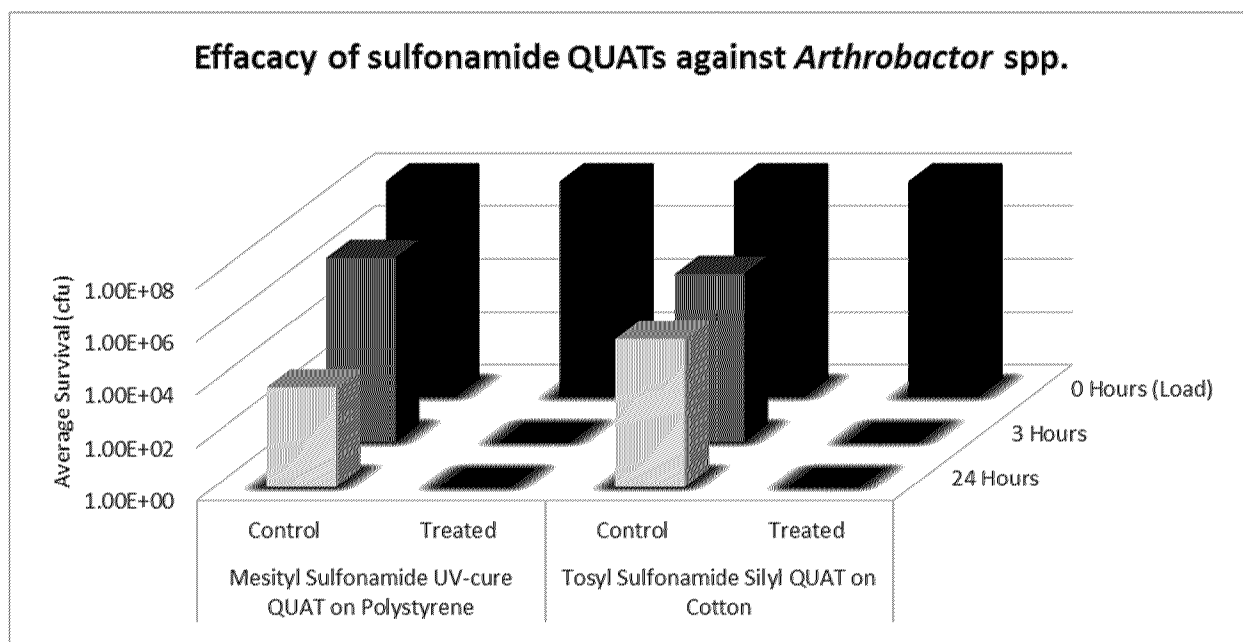


Figure 3

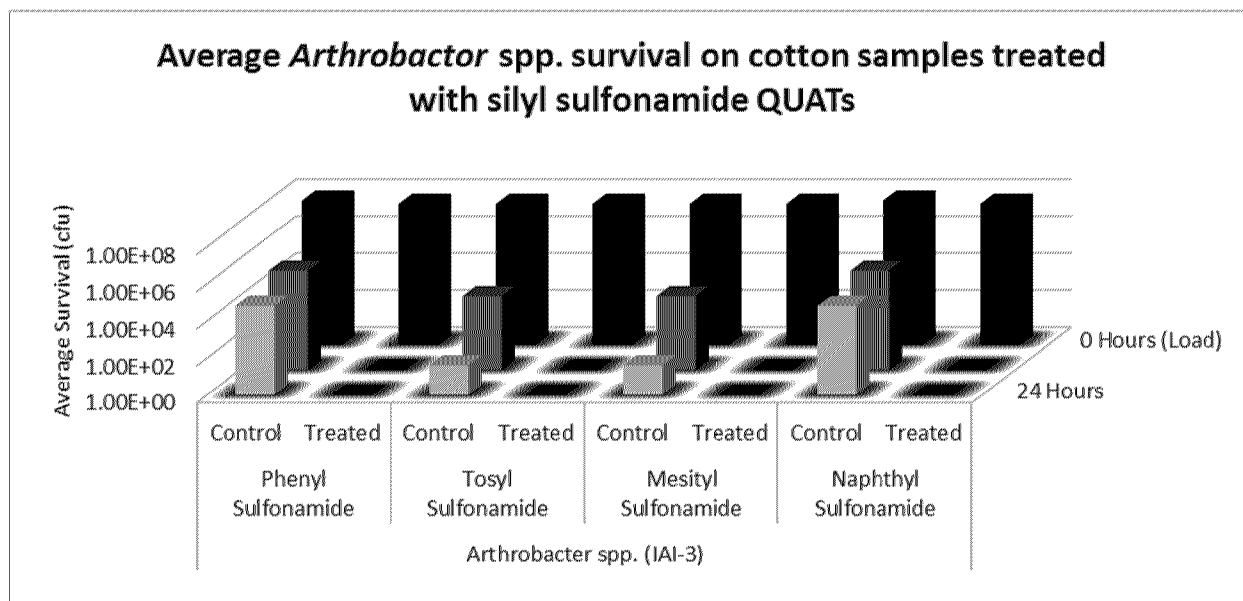


Figure 4

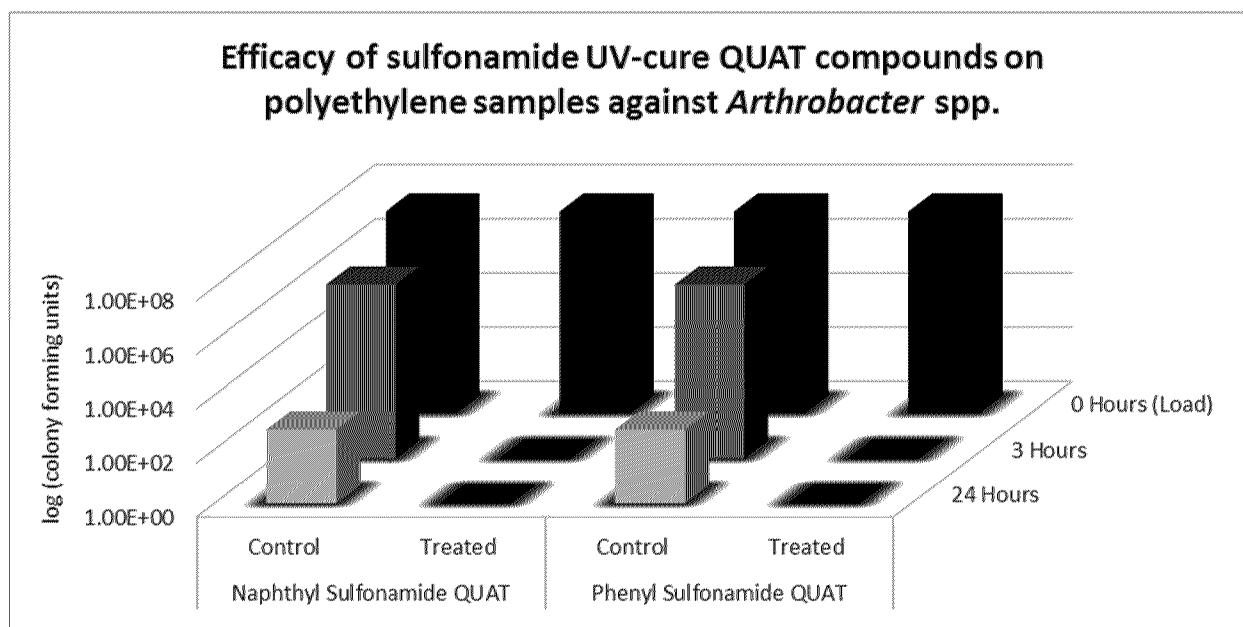


Figure 5

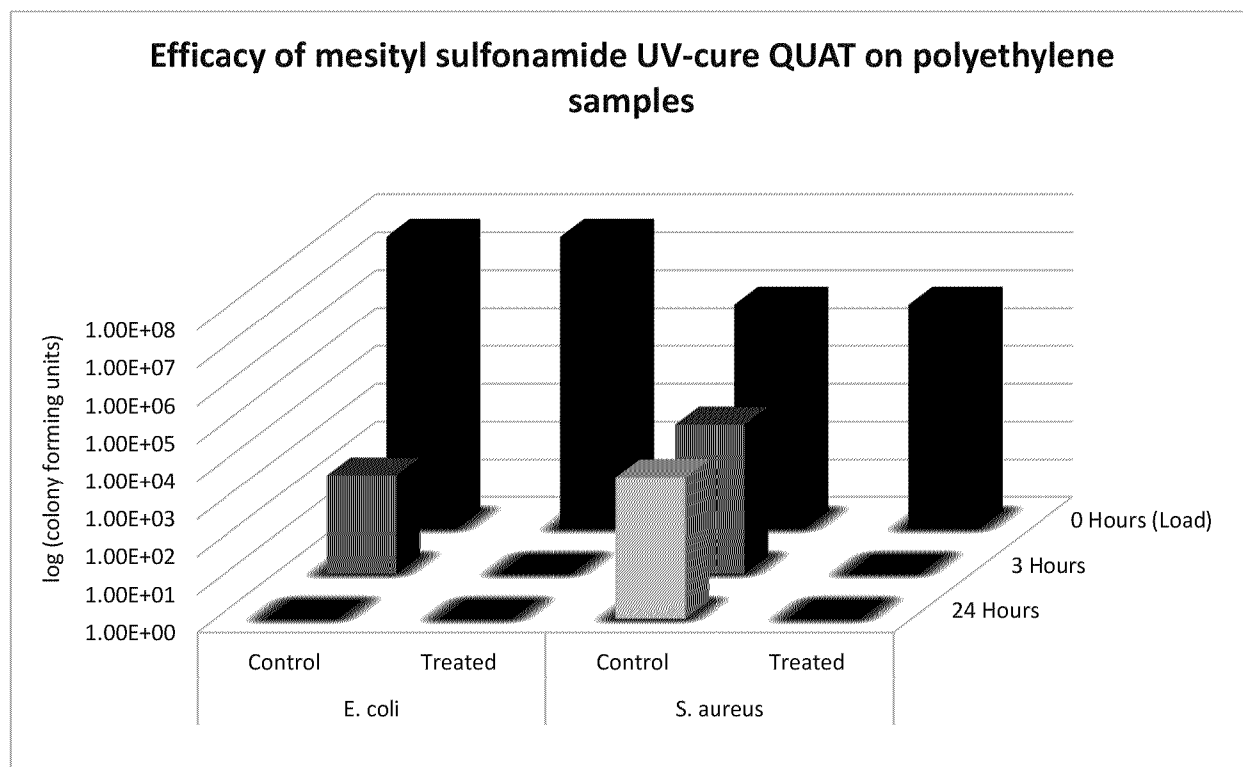


Figure 6

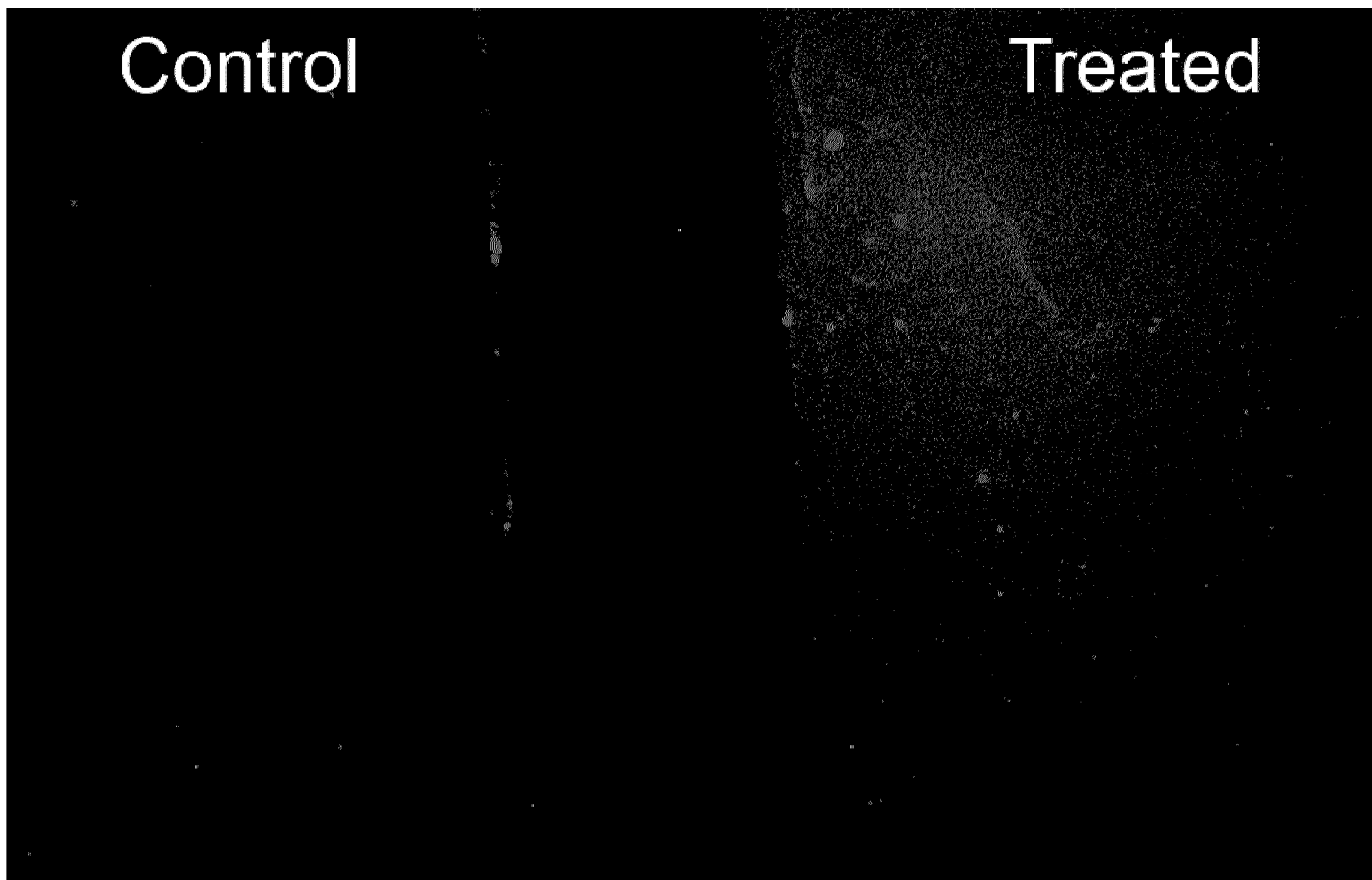


Figure 7

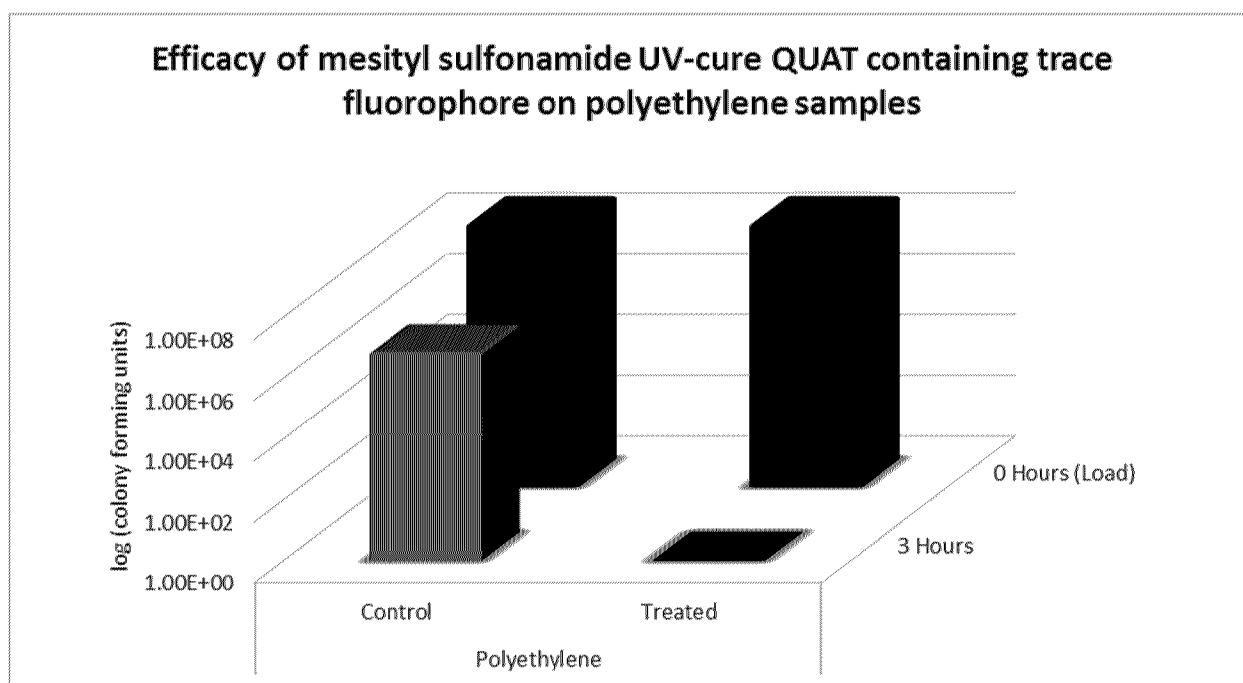


Figure 8

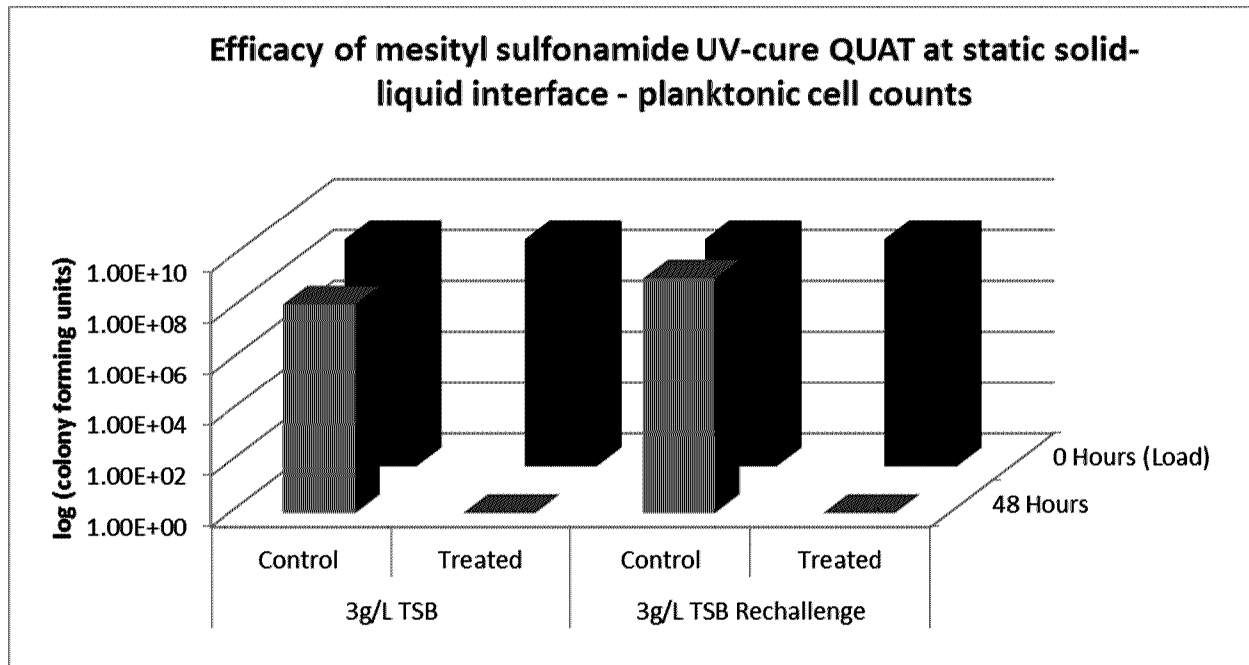


Figure 9

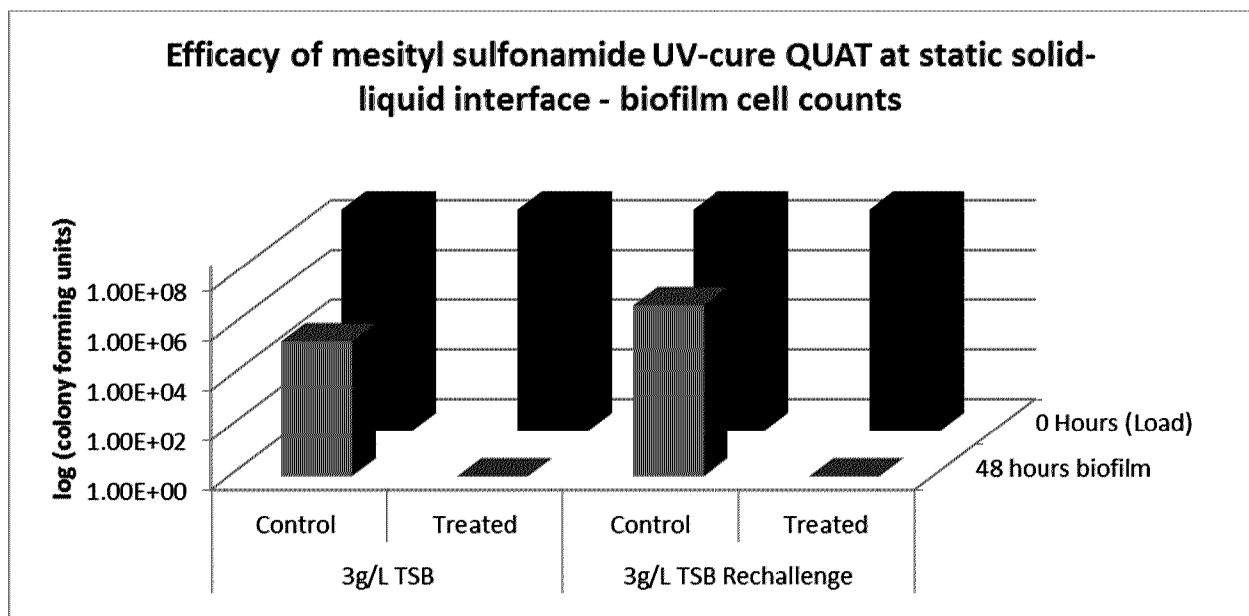
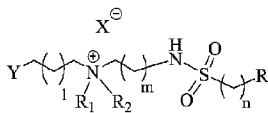


Figure 10



(I)

