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Polysiloxane cationic biocides with imidazolium salt (ImS) groups, synthesis and antibacterial properties

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ABSTRACT

Novel polysiloxanes with pendant biocidal *N,N′*-dialkylimidazolium salt (ImS) groups were synthesized and compared with polysiloxanes bearing conventional biocidal quaternary ammonium salt (QAS) groups. The bacteriostatic power of these polymers was tested and compared under the same conditions in aqueous solution against two common strains of Gram positive bacteria and three strains of Gram negative bacteria. These new ImS containing polymers exhibited high antibacterial potency against all bacteria studied, similar to those substituted with QAS groups. The advantage of the imidazolium substituted polysiloxane stems from its higher thermal stability, as compared with the quaternary alkylammonium functionalized polymer, as demonstrated by thermogravimetric studies.

1. Introduction

Interest in polymeric biocides is rapidly increasing for their potential use in human and animal health care as well as in the protection of materials against biocorrosion and surface fouling. There is a broad class of polymer biocides having biocidal groups permanently bonded to their chains. These can effectively inhibit the growth of bacteria and other microbes without releasing low molecular weight toxic products to the environment [1–4]. When covalently attached to the surfaces of a variety of materials they are able to kill bacteria on contact, and their antimicrobial activity is durable and sustainable [4–8]. With these polymers there is no problem of residual toxicity [4–8], by contrast to the group of antimicrobial polymers releasing the low MW biocides in a controlled way to their surroundings [1–4]. In addition, the common bacterial strains, *Escherichia coli* and *Staphylococcus aureus* do not appear to develop resistance against polymeric biocides [9]. Biocidal polymers of polycationic structure, in particular those having quaternary tetraalkylammonium (QAS) [5–18], tetraalkylphosphonium [19–21] and *N*-alkylpyridinium salt groups [5,10,22–26] pendant to the polymer chain have been developed. These polycations bearing considerable positive charge may destructively interact through electrostatic forces with the negatively charged bacteria walls and membranes leading to the death of the bacteria [2,27]. This destructive action is known to be strengthened by hydrophobic moieties (typically, C_8–C_{16} hydrocarbon chains) bonded to the nitrogen of the biocidal group. Amongst the polycationic antimicrobial agents organosilicon polymers, polysiloxanes [8,28–31] and polysilsesquioxanes [32] have been used. Polysiloxanes are particularly attractive as they show exceptionally high static and dynamic flexibility of their polymer chains, which gives them high solubility in many solvents, high permeability, and unusual surface properties [33]. All these features facilitate the contact of the biocidal polymer with the bacterial wall and its diffusion to cytoplasmic

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membranes. Polysiloxanes with pendant quaternary ammonium salt groups (QAS) show high biocidal potency [8,28,29]. Polysiloxane biocides bearing halamine groups were also synthesized [34–36]. These polymers are very effective in killing bacteria by direct contact with oxidative halogen chemically bonded to the polymer and find variety of uses such as in water disinfection.

In the search for new, active biocidal polymers we focused our attention on polysiloxanes with imidazolium salt (ImS) groups as some antibacterial effect of the uncharged imidazole ring attached to organic polymers has been observed recently [37,38].

This paper is devoted to the synthesis of polysiloxanes with the ImS groups pendant to polymer chain and to the comparison of their antibacterial activity and thermal stability with those of polysiloxanes bearing QAS groups. We designed these new polysiloxane biocides to be more thermally stable than the QAS substituted polysiloxanes in which the QAS groups readily undergo decomposition by the Hoffman elimination at elevated temperatures. To assure the reproducibility and reliability of the measured antibacterial activity–structure relationships, comparative studies were performed with aqueous solutions of biocidal polymers. The antibacterial potency of various polymeric biocides bonded to surfaces could not be adequately compared in this way because the antibacterial activity on a surface depends additionally on other factors.

2. Experimental

2.1. Chemicals

Reagent grade chemicals: 1-allylimidazole, Across Organics 97%; *N*,*N*-dimethyl-*N*-*n*-octylamine, Aldrich 95%; *n*-octyl chloride, Fluka, 98%; *n*-octyl bromide, Aldrich 99%; dimethyldichlorosilane, ABCR 98%; methyldichlorosilane, ABCR 99%; (3-chloropropyl)methyldichlorosilane, ABCR 97% were used without purification. *N*,*N*-Dimethylformamide (DMF), POCh pure, was dried over $MgSO_4$ for 1 day and distilled under reduced pressure. Toluene, POCh analytical grade, was shaken with concentrated H_2SO_4, washed with $NaHCO_3$ water solution and dried over $MgSO_4$ prior to distillation from sodium. 2-(3-*N*-imidazolopropyl)-2,4,4,6,6-pentamethyl-cyclotrisiloxane was synthesized and purified as described earlier [39]. Methyldiethoxysilane was obtained by the reaction of methyldichlorosilane with dried ethanol in a hexane solution in the presence of pyridine. (3-Imidazolopropyl)methyldichlorosilane hydrochloride and 1,1,3,3-tetramethyldisiloxane were synthesized as described elsewhere [39]. Their high purity was confirmed by ^{1}H NMR.

2.2. Synthesis of (3-N-imidazolopropyl)methyldiethoxysilane

In a Schlenck reactor were placed: *N*-allylimidazole (6.8 g, 6.3×10^{-2} mol), toluene (10 ml) and Karstedt catalyst (0.0427 g of the solution in xylene containing 4.8×10^{-5} mol of Pt). The mixture was stirred at room temperature for 0.5 h. Then methyldiethoxysilane (14.0 g, 7.9×10^{-2} mol) was introduced. The mixture was stirred at 90 °C for 3 days. Distillation of the post-reaction mixture gave 9.18 g of the pure product identified as (3-*N*-imidazolopropyl)methyldiethoxysilane, yield 60% relatively to *N*-allylimidazole used, B.p. 95 °C/0.24 mmHg. Elemental analysis: C 53.1% (th 54.5%), H 9.32% (th 9.09%), N 12.12% (th 11.6%). ^{1}H NMR ($CDCl_3$) in ppm: 0.05 [s, Si**H$_3$**], 0.45–0.52 [m, Si**H$_2$**], 1.08–1.18 [t, OCH_2C**H$_3$**], !.71–1.87 [m, $SiCH_2$**H$_2$**], 3.63-3.75 [q, O**H$_2$**CH_3], 3.84–3.93 [t, CH_2**H$_2$**N], 6.86 [s, C**H**NCH_2], 6.98 [s, NC**H**CH], 7.44 [s, NC**H**N]. ^{29}Si NMR ($CDCl_3$) in ppm −7.23.

2.3. Synthesis of poly(3-N-imidazolopropyl)methylsiloxane

(3-*N*-Imidazolopropyl)methyldiethoxysilane (5.52 g, 2.28×10^{-2} mol), dioxane (15 ml) and 25% aqueous solution of ammonia (2 ml) were placed in a three neck round–bottomed flask equipped with a reflux condenser. The mixture was stirred at 50 °C for 2 days. Then volatile components were removed by evaporation. After washing with water and drying under vacuum, 3.5 g, yield 91%, of the crude polymer product was obtained. The polymer was dissolved in a methanol–water 1:3 vol/vol mixture (20 mL). The solution was placed in a tubular bag of a Spectrum Laboratories Inc. 6 Spectra/Por Dialysis Membrane, MWCO: 1000, wet in 0.1% sodium azide. The membrane bag filled with the polymer solution was placed in a 2 L beaker filled with distilled water and kept in an ambient temperature for 3 days. The polymer fraction remaining in the bag (polymer **1**), 3.2 g was isolated by evaporation of solvents and characterized by ^{1}H NMR (Fig. 1) and SEC: Mn = 1700 g/mol, Mw = 2200 g/mol.

2.4. Synthesis of poly[(3-N-imidazolopropyl)methylsiloxane-co-bisdimethylsiloxane]

In a reactor installed on a high vacuum line (hvl), purged with argon, 2[3(*N*-imidazolo)propyl]2,4,4,6,6-pentamethylcyclotrisiloxane (2.3 g, 7.3×10^{-3} mol) was placed. The reactor was evacuated and 3 ml of THF was distilled to it on hvl from a Na–K alloy. After the reactor was filled again with argon 2,6-di-*tert*-butylpyridine (0.17 g, 8.9×10^{-4} mol) and butyl lithium (0.050 mL of the 2.5 M solution in *n*-hexane containing 1.25×10^{-4} mol of *n*-BuLi) were introduced together with a known amount of *n*-dodecane as GC standard. The polymerization was carried out in ambient temperature and was monitored by GC. The reaction was quenched with an excess of Me_3SiCl at a monomer conversion of 93%. Volatile components of the post-reaction mixture were removed by distillation in vacuum and the polymer was heated in 60 °C under vacuum of 10^{-3} Torr for 8 h. 1.93 g of the product (polymer **2**) was obtained, yield 84%. The SEC analysis performed using DMF (70 °C) as eluent and polystyrene as standard gave Mn = 4700 g/mol, Mw/Mn = 1.50. ^{1}H NMR (solvent CD_3OD, in ppm): 0.02–1.2 (s, C**H$_3$**Si); 0.35–0.55 (b.s. C**H$_2$**Si); 1.67–1.90 (b.s. C**H$_2$**CH_2Si); 3.92–4.07 (b.s. C**H$_2$**N); 6.98, 7.10 (2 × s. C**H**CH); 6.50 (s. NC**H**N). ^{29}Si NMR (solvent CD_3OD, in ppm): –(20.3–21.9) (m. CH_2CH_3**Si**O); –(21.9–23.8) (m. $(CH_3)_2$**Si**O).