Synthesis and Biocidal Efficacy of Self-Spreading Polydimethylsiloxane Oligomers Possessing Oxyethylene-Functionalized Quaternary Ammoniums

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ABSTRACT: In an effort to develop a more versatile creeping biocide that is capable of self-spreading and self-decontaminating of pathogenic bacteria, we report the development of two new homologous series of hybrid PDMS molecules. These oligomers were synthesized with terminal quaternary ammonium functionalities bearing variable length oxyethylene moieties. It is shown that the ionic interaction of the ammonium groups with the surface onto which it spreads can be tempered by the oxyethylene segments through close association of the polar chains with the cationic centers within the hydrophobic PDMS environment, thereby promoting self-spreading of the molecule. Once the compounds spread to a humid environment, the oxyethylene chains "blossom" and subsequently expose the biocidal centers, at which point, function as broad spectrum versatile antimicrobials. While biological evaluation showed antimicrobial activity against both Gram-positive and Gram-negative bacteria for all samples, one series was found to be much more effective due to lower steric hindrance surrounding the biocidal cationic termini. However, this increased exposure of the cationic center also altered the physical properties of the compounds except those isolated as a waxy solid. Self-spreading abilities with increasing oxyethylene chain length correlating to a decreasing spread rate. The decontaminating ability of the two most active compounds was demonstrated by allowing samples to spread to pools of water contaminated with *S. aureus*, yielding log reductions as high as 5.7 in less than two hours without external influences. © 2009 Wiley Periodicals, Inc.† J Appl Polym Sci 113: 2397–2403, 2009

Key words: synthesis; silicone; self-spreading; quaternary ammoniums; poly(ethylene glycol); polydimethylsiloxanes

INTRODUCTION

Quaternary ammonium salts (QAS) are amphiphilic surfactants widely employed for control of bacterial growth in clinical and industrial environments for half a century.[1,2] They are reported to kill bacteria and fungi through interaction with the cell envelop, leading to weakening of the cytoplasmic membrane and ultimately resulting in the loss of cytoplasm constituents due to changes in osmotic pressure.[3] Likewise, siloxanes possessing quaternary ammonium functionalities have received considerable attention due to widespread application as foaming agents,[4] fire depression surfactants,[5] anticarcinogenics[6,7] and skin conditioning agents.[8]

Polydimethylsiloxanes (PDMS) have been utilized in a variety of applications due to their unique physical properties including low surface energy, the ability to wet a variety of surfaces, chemical inertness, low dielectric constants and low coefficients of friction.[9–12] Furthermore, methyl terminated PDMS have previously been reported to have a high rate of spread in comparison to other liquids such as vegetable oil, motor oil and water.[13] This observation is attributed to a combination of low surface energy and flexible siloxane backbone.

A recent report from our laboratory details the development of trialkylammonium-terminated polydimethylsiloxanes that were found to be an effective class of mobile antimicrobials when blended with unfunctionalized PDMS for increased mobility.[13] However, the hydrophobicity of these compounds prevents use in many areas where bacteria growth is likely to occur, such as damp surfaces and standing water. Utility of amphiphilic quaternary ammoniums have shown mobility within coatings to surface segregate; however, possessed no mobility.[14] In an ongoing effort to develop a more versatile creeping biocide that is capable of self-spreading and self-decontaminating pathogenic bacteria, we report the development of two novel homologous series of hybrid PDMS molecules. These oligomers were synthesized with terminal quaternary ammonium functionalities bearing variable length oxyethylene moieties. It was believed that the ionic interaction of the ammonium groups with the surface onto which it spreads could be tempered by the oxyethylene segments through close

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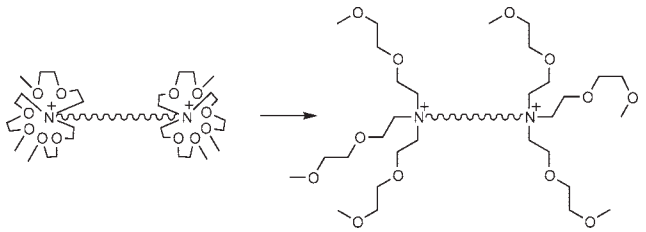

Figure 1 Conformational changes of the oxyethylene-functionalized ammonium groups upon transitioning from a nonpolar (left) to aqueous polar environment (right).

association of the polar chains with the cationic centers within the hydrophobic PDMS environment, thereby promoting self-spreading of the molecule. However, once the compounds spread to a humid environment, the oxyethylene chains would "blossom" and expose the biocidal centers as depicted in Figure 1. Moreover, polyoxyethylene compounds themselves have been reported to possess antimicrobial activities,[15,16] and it was believed that this functionality would provide increased synergistic antimicrobial activity with quaternary ammonium groups.

Ideally, the desired molecules would be capable of creeping distances on the order of multiple feet as inert molecules within a time period of several days, encounter damp bacteria infested areas, molecularly reorient itself, uncloaking and presenting the active biocidal moiety and subsequently neutralizing any pathogenic bacteria present, on the order of seven logs, rendering a healthier environment. Because of relatively low molecular weight, these novel molecules should be capable of penetrating into traditionally inaccessible crevices whereby they could function as self-cleaning antimicrobials. Possible applications include but are not limited to air-ducts, berthing areas, kitchens, automobiles and other inaccessible compartments.

EXPERIMENTAL

General methods

All purchased chemicals were reagent grade and were used without further purification. Moisture sensitive reactions were conducted in oven-dried glassware under a nitrogen atmosphere. External elemental analyses were performed by Atlantic Microlab, Inc. Norcross, GA 30,091. Unless otherwise noted, ^{1}H and ^{13}C NMR were taken in $CDCl_3$ at 300 and 75 MHz respectively, with a tetramethylsilane (TMS) internal standard. Chemical shifts are reported in units downfield from TMS. Coupling constants, *J*, are reported in units of Hertz (Hz).

General procedure for the preparation of (2)

In a 25-mL round bottomed flask, equipped with magnetic stir bar, addition funnel and positive flow of nitrogen were placed 15.60 mmol of ethylene glycol monomethyl ether. The solution was stirred for 15 min in an ice bath before the drop wise addition of phosphorous tribromide (7.81 mmol) over a 10 min period. The solution was allowed to slowly warm to room temperature (rt) and stirred for 14 hrs, over which time it changed to a red color. The solution was then heated in a 90°C oil bath for 1 hr, at which time the solution turned yellow. The solution was then allowed to cool to rt, poured onto 30 g of ice/water mixture, and made slightly basic with dropwise addition of a 10% solution of $NaHCO_3$ ($\sim$ 6 mL). Subsequent extraction with diethyl ether (3×30 mL), followed by drying of combined ether layers over $MgSO_4$, and removal of volatiles *in vacuo* afforded colorless oils in sufficient purity (>95%) for use in subsequent reactions.

1-Bromo-2-(2-(2-methoxy-ethoxy)-ethoxy) ethane (**2c**) was afforded in a 65% yield as a colorless liquid; b.p. 198–201°C. Spectroscopic data correlated with that previously reported.[17]

1-Bromo-2-(2-(2-(2-methoxy-ethoxy)-ethoxy)-ethoxy) ethane (**2d**) was afforded in a 63% yield as a colorless liquid; b.p. 237–239°C. Spectroscopic data correlated with that previously reported.[18]

1-Bromo-(2-(methoxy-ethoxy)-ethoxy)) ethane (**2e**) was afforded in a 66% yield as a colorless waxy solid. FTIR: 2902, 2737, 1454, 1343, 1258, 1250, 1127, 850 cm^{-1}. ^{1}H NMR ($CDCl_3$): 3.82 (t, $J = 5.8$, 2H), 3.70–3.61 (m, 60H), 3.48–3.44 (t, $J = 6$, 2H), 3.37 δ (s, 3H).

General procedure for the preparation of tri(oxyethylene)-functionalized ionic silicones (3)

Into a 50-mL round bottomed flask equipped with reflux condenser and magnetic stir bar were placed 2.0 mmol of primary amino PDMS (MW 900–1000) (**1**) and 12.5 mmol of (**2**). To the mixture was added 25 mL of methanol, and the resulting solution was allowed to reflux for 18 hrs under nitrogen. Upon completion, volatiles were removed *in vacuo* to afford the desired product in significant purity. If desired, additional purification is accomplished by titration with ethyl ether (15 mL).

Bis (tri-(2-methoxyethyl)-*N*-propyl-ammonium terminated) polydimethyl siloxane dibromide **(3a)**

FTIR: 3414, 2965, 2894, 2802, 1400, 1262, 1092, 1023, 800, 707 cm^{-1}. ^{1}H NMR ($CDCl_3$): 3.79 (m, 12H), 3.63 (m, 12H), 3.36 (s, 18H), 3.15 (m, 4H), 1.82 (m, 4H), 0.65–0.52 (m, 4H), 0.15–0.11 δ (m, 72H). Product was afforded as a colorless viscous liquid in 85% yield. Anal. Calcd. Range: C, 38.61–38.43; H, 8.59–8.32; N, 1.93–1.86. Found: C, 38.27; H, 8.41; N, 1.89.

Bis(tri-(2-(2-methoxy-ethoxy)-ethyl))-*N*-propyl-ammonium terminated) polydimethylsiloxane dibromide **(3b)**

FTIR: 3410, 2964, 2891, 2821, 2725, 1601, 1443, 1416, 1350, 1269, 1008, 796 cm^{-1}. ^1H NMR ($CDCl_3$): 3.81–3.76 (m, 12H), 3.68–3.64 (m, 12H), 3.57–3.52 (m, 12H), 3.48–3.36 (m, 12H), 3.36 (s, 18H), 3.03–2.98 (m, 4H), 1.81 (m, 4H), 0.59 (m, 4H), 0.14–0.04 δ (m, 72H). Product was afforded as a colorless viscous liquid in 87% yield. Anal. Calcd. Range: C, 40.84–40.79; H, 8.63–8.43; N, 1.67–1.56. Found: C, 40.82; H, 8.61; N, 1.63.

Bis(tri-(2-(2-(2-methoxy-ethoxy)-ethoxy)-ethyl))-*N*-propyl-ammonium terminated) polydimethylsiloxane dibromide **(3c)**

FTIR: 3358, 2956, 2880, 1450, 1416, 1355, 1264, 1097, 1025, 801 cm^{-1}. ^1H NMR ($CDCl_3$): 3.82–3.78 (m, 12H), 3.68–3.63 (m, 24H), 3.56–3.53 (m, 12H), 3.49–3.44 (m, 24H), 3.37 (s, 18H), 2.89 (m, 4H), 1.79 (m, 4H), 0.61–0.55 (m, 4H), 0.11–0.04 δ (m, 72H). Product was afforded as a colorless viscous liquid in 83% yield. Anal. Calcd. Range: C, 42.82–42.77; H, 8.69–8.56; N, 1.41–1.36. Found: C, 42.79; H, 8.59; N, 1.40.

Bis(tri(2-(2-(2-(2-methoxy-ethoxy)-ethoxy)-ethoxy-ethyl))-*N*-propyl-ammonium terminated) polydimethylsiloxane dibromide **(3d)**

FTIR: 3358, 2956, 2880, 1450, 1416, 1355, 1264, 1097, 1025, 801 cm^{-1}. ^1H NMR ($CDCl_3$): 3.83–3.81 (m, 12H), 3.72–3.62 (m, 48H), 3.57–3.56 (m, 12H), 3.54–3.45 (m, 24H), 3.38 (s, 18H), 2.98–2.96 (m, 4H), 1.76–1.74 (m, 4H), 0.59–0.53 (m, 4H), 0.12–0.05 δ (m, 72H). Product was afforded as a colorless viscous liquid in 87% yield. Anal. Calcd. Range: C, 43.99–43.71; H, 8.77–8.63; N, 1.31–1.26. Found: C, 43.64; H, 8.62; N, 1.30.

Bis(tri(2-(poly-(methoxy-ethoxy)-ethyl))-*N*-propyl-ammonium terminated) polydimethylsiloxane dibromide **(3e)**

FTIR: 3364, 2964, 2875, 1443, 1350, 1258, 1100, 1023, 804 cm^{-1}. ^1H NMR ($CDCl_3$): 3.83–3.81 (m, 12H), 3.70–3.58 (m, 300H), 3.52–3.58 (m, 12H), 3.40 (s, 18H), 2.99–2.96 (m, 4H), 1.82–1.80 (m, 4H), 0.63–0.58 (m, 4H), 0.13–0.02 δ (m, 72H). Product was afforded as a colorless waxy solid in a 77% yield.

General procedure for the preparation of bis(oxyethylene)-functionalized nonionic silicones (4)

Into a 50-mL round bottomed flask equipped with reflux condenser and magnetic stir bar were placed 2.0 mmol of primary amino PDMS (MW 900–1000) (**1**) and 8.0 mmol of (**2**). To the mixture was added 25 mL of methanol and the resulting solution was allowed to reflux for 18 hrs under nitrogen. Upon completion, volatiles were removed *in vacuo*, and the product was precipitated from Et_2O (15 mL). Product was afforded as a viscous liquid in 81% yield. FTIR: 2967, 2881, 1587, 1453,1412, 1256, 1051, 842, 796 cm^{-1}. ^1H NMR ($CDCl_3$): 3.83–3.79 (m, 8H), 3.39 (s, 12H), 3.21–3.19 (m, 8H), 3.04–3.02 (m, 4H), 1.86–1.82 (m, 4H), 0.65–0.62 (m, 4H), 0.17–0.08 δ (m, 72H).

General procedure for the preparation of functionalized ionic silicones (6)

Into a 50-mL round bottomed flask equipped with reflux condenser and magnetic stir bar were placed 2.0 mmol of secondary amino PDMS (MW 800–900) (**5**) and 8.5 mmol of (**2**). To the mixture was added 25 mL of methanol, and the resulting solution was allowed to reflux under a nitrogen atmosphere for 18 h. Upon completion, volatiles were removed *in vacuo*, and the product was precipitated from Et_2O (15 mL).

Bis(ethyl-di(2-methoxyethyl)-*N*-isobutyl ammonium terminated) polydimethyl siloxane dibromide **(6a)**

FTIR: 3726, 2952, 2798, 1447, 1416, 1269, 1108, 1015, 807cm^{-1}. ^1H NMR ($CDCl_3$): 3.51–3.48 (m, 8H), 3.36 (s, 12H), 3.07–3.03 (m, 8H), 2.82–2.76 (m, 8H), 2.51 (m, 2H), 1.56–1.52 (m, 6H), 1.22–1.18 (d, $J = 7$, 6H), 1.02–0.92 (m, 4H), 0.21–0.02 δ (m, 66H). Product was afforded as a colorless waxy solid in 82% yield. Anal. Calcd. Range: C, 40.32–39.92; H, 8.75–8.66; N, 1.17–1.06. Found: C, 40.22; H, 8.65; N, 1.09.

Bis(ethyl-di(2-(2-methoxy-ethoxy)-ethyl))-*N*-isobutyl ammonium terminated) polydimethyl siloxane dibromide **(6b)**

FTIR: 3376, 2960, 2898, 2802, 1454, 1393, 1258, 1085, 1031, 807 cm^{-1}. ^1H NMR ($CDCl_3$): 3.67–3.65 (m, 8H), 3.63–3.60 (m, 8H), 3.56–3.53 (m, 8H), 3.36 (s, 12H), 3.16–3.07 (m, 8H), 2.87–2.71 (m, 8H), 2.38 (m, 2H), 1.51–1.50 (m, 6H), 1.22 (d, $J = 6$, 6H), 0.61–0.56 (m, 4H), 0.17–0.02 δ (m, 66H). Product was afforded as a colorless waxy solid in 81% yield. Anal. Calcd. Range: C, 41.98–41.62; H, 8.79–8.67; N, 1.97–1.86. Found: C, 41.69; H, 8.72; N, 1.88.

Bis(ethyl-di(2-(2-(2-methoxy-ethoxy)-ethoxy)-ethyl))-*N*-isobutyl ammonium terminated) polydimethylsiloxane dibromide **(6c)**

FTIR: 3356, 2964, 2879, 1456, 1408, 1262, 1115, 1015, 796 cm^{-1}. ^1H NMR ($CDCl_3$): 3.80–3.79 (m, 8H), 3.72–3.66 (m, 32H), 3.39 (s, 12H), 3.16–3.07 (m, 8H), 2.83–2.76 (m, 8H), 2.38–2.34 (m, 2H), 1.50 (m, 6H), 1.28–

1.26 (m, 6H), 0.81–0.79 (m, 4H), 0.18–0.01 δ (m, 66H). Product was afforded as a colorless waxy solid in 84% yield. Anal. Calcd. Range: C, 43.76–43.12; H, 8.95–8.86; N, 1.67–1.61. Found: C, 43.01; H, 8.82; N, 1.67.

Bis(ethyl-di(2-(2-(2-(2-methoxy-ethoxy)-ethoxy)-ethoxy-ethyl))-*N*-isobutyl ammonium terminated) polydimethylsiloxane dibromide **(6d)**

FTIR: 3341, 2956, 2867, 1454, 1347, 1262, 1104, 1031, 815 cm^{-1}. ^1H NMR ($CDCl_3$): 3.85–3.81 (m, 8H), 3.79–3.76 (m, 48H), 3.36 (s, 12H), 3.02–3.98 (m, 8H), 2.84–2.81 (m, 8H), 2.49 (m, 2H), 1.52–1.50 (m, 6H), 1.23 (d, $J = 6$, 6H), 0.64–0.62 (m, 4H), 0.19–0.01 δ (m, 66H). Product was afforded as a colorless waxy solid in 86% yield. Anal. Calcd. Range: C, 44.26–44.19; H, 8.91–8.81; N, 1.63–1.59. Found: C, 44.13; H, 8.85; N, 1.56.

Bis(ethyl-di(2-((methoxy-poly-ethoxy)-ethyl))-*N*-isobutyl ammonium terminated) polydimethylsiloxane dibromide **(6e)**

FTIR: 3480, 2960, 2871, 1454, 1350, 1262, 1146, 1027, 946, 800 cm^{-1}. ^1H NMR ($CDCl_3$): 3.86–3.84 (m, 8H), 3.74–3.69 (m, 200H), 3.36 (s, 12H), 3.02–2.99 (m, 8H), 2.87–2.84 (m, 8H), 2.39–2.37 (m, 2H), 1.57–1.56 (m, 6H), 1.29–1.27 (m, 6H), 0.81–0.80 (m, 4H), 0.18–0.02 δ (m, 66H). Product was afforded as a colorless waxy solid in a 79% yield.

General procedure for the preparation of functionalized nonionic silicones (7)

Into a 50-mL round bottomed flask equipped with reflux condenser and magnetic stir bar were placed 2.0 mmol of secondary amino PDMS (MW 800–900) (**5**) and 4.0 mmol of (**2**). To the mixture was added 25 mL of methanol, and the resulting solution was allowed to reflux under a nitrogen atmosphere for 18 h. Upon completion, volatiles were removed *in vacuo*, and the product was precipitated from Et_2O (15 mL). Product was afforded as a waxy solid in 80% yield. FTIR: 2960, 2879, 1593, 1416, 1266, 1054, 792 cm^{-1}. ^1H NMR ($CDCl_3$): 3.47–3.43 (m, 4H), 3.39 (s, 6H), 2.81–2.76 (m, 4H), 2.67–2.63 (m, 4H), 2.27–2.25 (m, 4H), 2.14 (m, 2H),1.56–1.52 (m, 6H), 1.19–1.17 (d, $J = 5$, 6H), 1.09–1.04 (m, 4H), 0.23–0.01 δ (m, 66H).

General techniques for monitoring movement of antimicrobial liquids

Movement of all liquids in this study were monitored optically with the use of an Intel-QX5 microscope at a magnification power of 10×. In all cases, photos were captured every twenty seconds for fifteen minutes. All liquid movement measurements were made on precleaned glass microscope slides. Microscope slide pretreatment was removed by soaking in chloroform, followed by a soak in an alcoholic potassium hydroxide solution for two hours. After base treatment, the slides were washed with copious amounts of deionized water prior to drying in an oven. Care was taken not to store cleaned substrates for prolong periods of time in order to prevent contamination by ambient organics or dust particles. A 1-μL aliquot of each liquid was placed on the center of the microscope slide using a calibrated micropipette. A millimeter-scale ruler was placed beneath the microscope slide to measure distance. Use of a second microscope slide as a protective cover along with spacers was necessary to prevent contamination from airborne dust particles present in the laboratory. Spacers prevented capillary effect, while permitting air currents to affect the sample as in an open ambient environment. The use of an additional external light source was necessary in order to better visualize the advancing edge of the thinning liquid.

After liquids were allowed to spread, video was analyzed and the average diameter of the advancing edges was measured. The movement of all liquids reported is the average of three trials. All data were normalized to the initial liquid drop size at T_0. In those examples where the spread was not perfectly circular, multiple measurements of diameters were made and the average of those obtained was used for plotting.

General bacterial challenge preparations

Bacteria and media

Luria-Bertani (LB) media (Difco Laboratories, Detroit, MI) was used as a bacterial growth medium for all procedures, and was prepared according to the manufacturer's specifications. *Staphylococcus aureus* (ATCC 25,923) and *Escherichia coli* (ATCC 11,105) were used for all bacterial challenges. Both were grown according to standard microbiological practices.

Determination of minimum inhibitory concentration

Liquid biocides were diluted at 1 : 500, 1 : 1000, 1 : 2000, 1 : 5000, and 1 : 10000 into LB media. The media were then inoculated with 2×10^6 *S. aureus* or *E. coli* from a fresh overnight culture. The cultures were grown at 37°C overnight and examined visually for growth. Waxy solid biocides were blended with liquid unfunctionalized PDMS (MW 1250) and tested as described above, taking only the biocidal component into account for concentration values

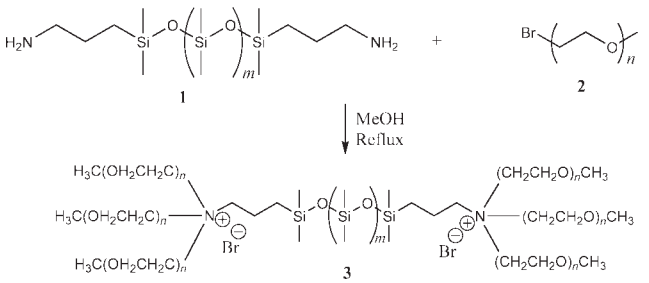

Figure 2 Synthetic scheme for tri(oxyethylene) ammonium-terminated PDMS **(3)**.

(pure unfunctionalized PDMS was not found to be antimicrobial at concentrations as high as 50 mg/mL). Minimum inhibitory concentration (MIC) was determined by the formula, [(highest dilution with no bacterial growth/culture volume) × mg/μL of the biocide]/culture volume.

Creeping decontamination test

A 13 mm thick aluminum plate was drilled with 12 mm diameter wells 10 mm deep. Each well was charged with 300 μL of aqueous solution containing 10^9 *S. aureus* bacteria. Immediately adjacent, approximately 1 mm from the edge, to these wells were placed 5.0 μL samples of biocide that were allowed to spread and subsequently contaminate the wells. A 3.0 μL aliquot was taken from each well at described time intervals and serially diluted 7 times in media containing Letheen, then allowed to grow overnight at 37°C. Log kill is determined by the number of the last tube in a series that shows bacterial growth.

RESULTS AND DISCUSSION

The synthesis was conducted starting with the primary amino-terminated PDMS oligomer (**1**); reacting with various oxyethylene bromides (**2**) resulted in the formation of the corresponding oxyethylene quaternary ammonium PDMS molecule (**3**), as shown in Figure 2 and summarized in Table I. The series of molecules were synthesized in 77–87 % yield, and could be easily purified by precipitation from ether. Compounds **3a–d** were isolated as viscous liquids, with increasing oxyethylene chain length correlating to increasing viscosity. The molecule bearing the longest oxyethylene chains, (**3e**,$n = \sim 18$) was found to be a waxy solid. A charge-neutral analog (**4**) with only two oxyethylene units on each terminus was synthesized as a control sample (Fig. 3) for **3**, in order to determine the effects of the cationic quaternary ammonium termini on creep and bioactivity.

TABLE I
Results of Antimicrobial Evaluation

Compound	Oxyethylene chain length (*n*)	MIC (mg/mL)	
		S. aureus (G+)	*E. coli* (G–)
3a	1	0.310	1.000
3b	2	0.290	2.300
3c	3	0.0064	1.280
3d	4	0.0074	1.480
3e	~ 18	5.000	5.000
4	1	2.000	2.000
6a	1	0.011	0.420
6b	2	0.024	0.470
6c	3	0.020	1.000
6d	4	0.015	0.610
6e	~ 18	0.013	0.510
7	1	<5[a]	>5[a]

[a] Not active up to 5 mg/mL.

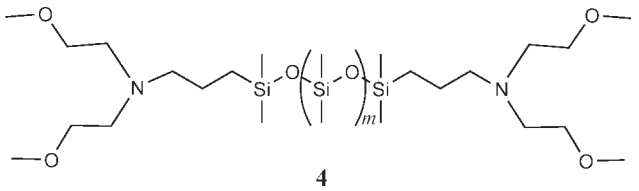

Figure 3 Structure of di(oxyethylene) amine-terminated PDMS **(4)**.

In an effort to probe the effects of decreased steric encumbrance around the ammonium center, a second series of PDMS with quaternary ammonium end-groups, this time featuring two oxyethylene chains and one ethyl group, was synthesized (Fig. 4). It was envisioned that the reduction of steric hindrance surrounding the ammonium would result in enhanced antimicrobial activity by increasing exposure of the cationic center. The secondary diamino PDMS (**5**) was reacted with excess **2**, resulting in formation of **6** in 79–86 % yields. The effects of replacing one oxyethylene chain with an ethyl group on the physical properties was immediately evident, as each derivative of **6** was isolated as a waxy solid, not capable of self-spreading. Furthermore, these compounds displayed significantly lower water solubility than **3**. As in the previous series, a charge-neutral analog with amine termini bearing an ethyl group and a single oxyethylene chain, **7**, was synthesized for comparison (Fig. 5).

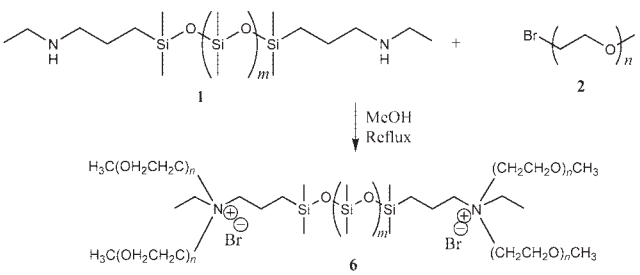

Figure 4 Synthetic scheme for ethyl di(oxyethylene) ammonium-terminated PDMS **(6)**.

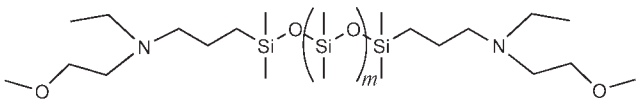

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Figure 5 Structure of ethyl oxyethylene amine-terminated PDMS **(7)**.

The self-spreading abilities of the homologous series **3a–d** and **4** were analyzed on a glass surface, and results are depicted in Figure 6. Compounds **3a** and **4** demonstrated the highest rates of spread, comparable to the unfunctionalized PDMS. The rates of spread were observed to decrease with increasing oxyethylene chain length, likely due to increased chain entanglement and polar surface interactions. Compound **3e**, a waxy solid that did not demonstrate self-spreading properties, was not included in Figure 6. It is further noted that the rate of spread after $\sim$ 200 seconds are approximately the same. This is believed to be attributed to the amount of liquid deposited on the substrate. As the liquid spreads, it approaches monolayer thicknesses the mechanism of spread is believed to change in addition to the fact that visualization becomes increasingly difficult. Utilization of elipsometry would be increasingly beneficial as the liquid approaches monolayer thicknesses; however, this technique does not present an accurate method of thickness with respect to distance travel, especially in real-time. As mentioned earlier, the mechanism of spread is believed to change as the liquid travels from a thick sample to that approaching monolayer thicknesses. The initial boost in transport is believed attributed to the spread/movement of liquid over liquid. As the liquid becomes thinner, the dominant forces become that of liquid with surface, resulting in a noticeable decrease in spread rate. The extremely thin films that are obviously present at the radial distances were shown to retain their biocidal activity.

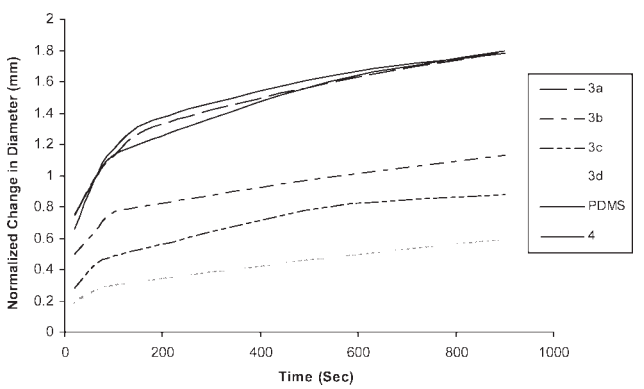

Figure 6 Spread of **3a–d**, **4**, and unfunctionalized PDMS on glass.

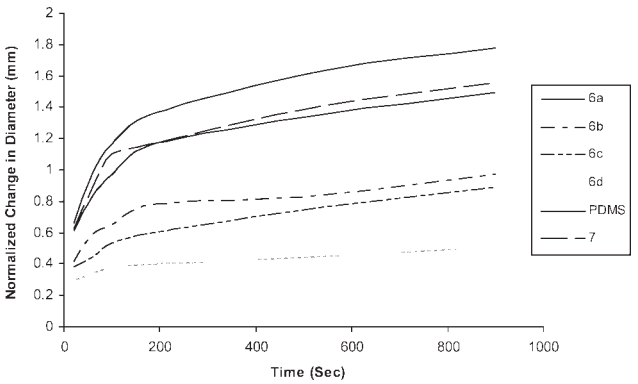

Figure 7 Spread of **6** blended with unfunctionalized PDMS (MW 1250) 60 : 40.

Analysis of creep of **6a–d** was performed in a similar manner to that used for series **3**; however, all compounds of the former series were obtained as waxy solids and displayed no tendency to spread on the glass surface. Thus, **6** and **7** were blended with unfunctionalized methyl-terminated PDMS (MW $\sim$ 1250) in a 60 : 40 ratio. The result of creep analysis of blended **6a–d** (Fig. 7) shows a similar trend to that exhibited by **3**; as the oxyethylene chain length is increased, the self-spreading characteristics of the mixtures decrease.

Series **3** and **6** were both evaluated for antimicrobial activity against both Gram-positive (*S. aureus*) and Gram-negative (*E. coli*) bacteria, MIC (Table I). All samples showed antimicrobial activity with greater effectiveness against *S. aureus* than *E. coli*. With respect to series **3**, it was found that **3c** and **3d** were 40–50 times more effective against *S. aureus* than **3a** and **3b**. However, **3a–d** were all comparably effective against *E. coli*, with significantly higher activity (i.e., **3c** and **3d** were 200 times more effective against *S. aureus* than *E. coli*, while **3a** and **3b** were 3.2 and 7.9, respectively). Compound **3e** ($n = \sim 18$) was found to be less effective against both bacteria than derivatives with shorter oxyethylene groups, dramatically so against *S. aureus*. This is likely due to the steric effects of the extremely long terminal oxyethylene tethers, serving to hinder access to the cationic biocidal moiety. Also, the charge-neutral compound **4** was less effective than **3a**, its quaternary cationic counterpart, against both types of bacteria.

As expected, **6a–e** were found to be more effective biocides than the analogous derivatives of **3**, with the exceptions of **3c** and **3d** against *S. aureus* only. The most extreme example of this trend was in the derivatives bearing the longest oxyethylene chains ($n = \sim 18$), in which **3e** had the highest MIC values of 5.0 mg/mL against both bacteria, while **6e** was one of the most effective at 0.013 and 0.510 mg/mL against *S. aureus* and *E. coli*, respectively. Clearly, the more

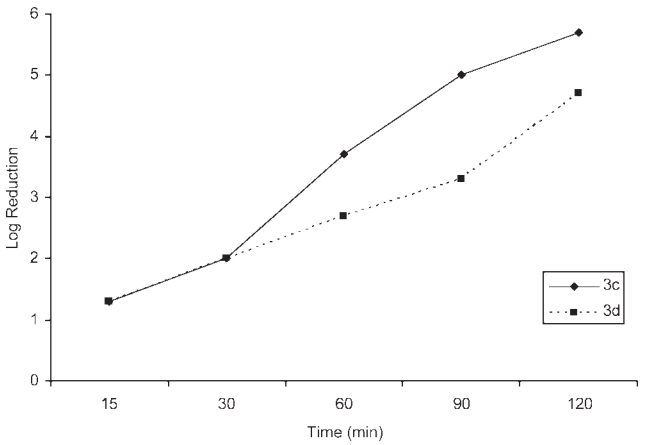

Figure 8 Log reduction of *S. aureus* bacteria in contaminated pools by self-spreading biocides.

exposed cationic center of **6** compared to **3** allows easier access of bacteria to the biocidal moieties, increasing effectiveness against both Gram-positive and Gram-negative bacteria. All derivatives of **6** were determined to be more effective against *S. aureus* than *E. coli*, although altering the length of the oxyethylene groups was not found to have a significant effect. Unlike **4**, the charge-neutral ethyl, monooxyethylene derivative **7** was not effective against either *S. aureus* or *E. coli* when tested as high as 5.0 mg/mL.

Having confirmed the antimicrobial activity of **3a–d** in solution, a test of the ability to decontaminate aqueous domains via self-spreading was necessary. An experiment was designed in which 5.0 μL samples of the best-performing liquid biocides, **3c** and **3d**, were placed adjacent to 0.300 mL pools of solution containing *S. aureus* bacteria. Once the biocides reached the pools, log-reduction was measured at increasing time intervals. Both samples diffused quickly throughout the aqueous pools, revealing bacteria reduction by over 90% after only 15 min of contact (Fig. 8). After 2 h, **3c** reduced bacterial contamination by 5.7 log, purely through its own spread and diffusion capabilities. Nearly as effective, **3d** reduced contamination by 4.7 log at 2 h (Table II).

TABLE II
Results of Mobile Decontamination Experiments

	Log reduction[a]	
Time (min)	**3c**	**3d**
15	1.3	1.3
30	2.0	2.0
60	3.7	2.7
90	5.0	3.3
120	5.7	4.7

[a] Average of three experiments.

CONCLUSIONS

In conclusion, two series of water soluble mobile antimicrobials were designed and synthesized. While biological evaluation showed antimicrobial activity against both Gram-positive and Gram-negative bacteria for all samples, **6** was found to be more effective than **3** due to lower steric hindrance surrounding the biocidal cationic termini. However, this increased exposure of the cationic center also altered the physical properties of the compounds; each derivative of **6** was isolated as a waxy solid that could only be employed as a self-spreading decontaminant when blended with liquid, unfunctionalized PDMS. Derivatives of **3**, with the exception of **3e**, displayed self-spreading abilities with increasing oxyethylene chain length correlating to a decreasing spread rate. The decontaminating ability of the two most active compounds, **3c** and **3d**, was demonstrated by allowing samples to spread to pools of water contaminated with *S. aureus*, yielding log reductions as high as 5.7 without any external spreading or mixing. Current efforts are underway towards further improving self-spreading and biocidal capabilities.

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