Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Fluorine Chemistry 124 (2003) 89–91
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/jfluchem

Synthesis and antimicrobial activity of a perfluoroalkyl-containing quaternary ammonium salt

Hui Shao[a], Li Jiang[a], Wei-Dong Meng[a], Feng-Ling Qing[a,b,*]

[a]College of Chemistry and Chemical Engineering, Donghua University, 1882 West Yanan Road, Shanghai 200051, China
[b]Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

Received 9 May 2003; received in revised form 4 July 2003; accepted 9 July 2003

Abstract

A novel perfluoroalkyl-containing quaternary ammonium salt **5** was designed and synthesized. Consequently, the antimicrobial activities of compound **5** were measured with *Escherichia coli* 8099 as a Gram-negative strain and *Staphylococcus aureus* ATCC 6538 as a Gram-positive strain. Both the minimum inhibitory concentration (MIC, the lowest concentration of compound **5** that inhibits microbial growth) values of quaternary ammonium salt **5** against *Escherichia coli* 8099 and *Staphylococcus aureus* ATCC 6538 were 7.8 μg/ml.

Keywords: Perfluoroalkyl-containing quaternary ammonium salt; Textile finishing; Antimicrobial activity

1. Introduction

Textile materials are excellent media for growing microorganisms. In the last few decades, the prevention of microbial attack on textile and wearers of textile materials has become increasingly important to consumers and textile producers [1]. A market study in Germany revealed a steady increase in the demand for antimicrobial fabrics. The potential market for antimicrobial fabrics is 28,000 t in Europe and 40,000 t in the United States and Japan [2]. So far, various antimicrobial agents have been applied to impart antimicrobial properties to textile [3–6]. Among them, the quaternary ammonium halide cationic surfactants are widely used in antimicrobial finishing of textile, since Domagk developed an important class of antimicrobial agents based on quaternary ammonium salts in 1935 [7]. Quaternary ammonium salts exhibit marked antimicrobial activity against a wide range of bacteria, fungi, and viruses [8]. The introduction of unsaturated alkyl groups into quaternary ammonium salts can enhance its antimicrobial activity [9].

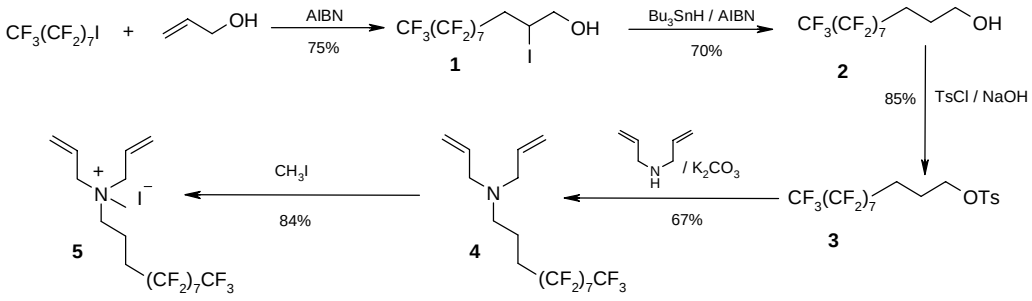
Hospital materials such as theater drapes, gowns, mask, sheets, and pillowcases are known to be major sources of cross-infection, so all textile materials used in hospitals should prevent to minimize infection or transmission of disease [10]. Especially for surgical gowns, there is an increasing need to protect medical staff from infection by blood borne pathogens such as HIV and HBV [11]. Gowns should be able to prevent ''strike through'' of ''wetting out'' of the fabric, and so surgical gown materials should have not only antimicrobial properties but also blood barrier properties [12].

Perfluoroalkyl-containing chemicals and fluoropolymers most abundantly used as repellent agents in textile finishing, not only satisfy the demand for high water repellency but also impart oil and soil repellency to finished textiles. Water and oil repellency is achieved by reducing the critical surface energy of fabrics [13].

In the light of the facts above mentioned, we envisaged that a novel quaternary ammonium salt, which contains both perfluoroalkyl group and diallyl groups, should be suitable a finishing agent for providing the fabrics with barriers against microorganisms, water, oil, soil and blood. Moreover, the introduction of diallyl groups into the quaternary ammonium salt not only can enhance the antimicrobial activity, but also extend its application fields. It can be applied in two categories of antimicrobial finishes: one category is part of the fiber-forming process and the other category is the one incorporated in the finishing process. It can also be used as a perfluoroalkyl-containing monomer in the polymer field, which is a convenient method incorporating perfluoroalkyl chain in the polymer. We describe herein the synthesis and

* Corresponding author. Tel.: +86-216-416-3300; fax: +86-216-416-6128.
E-mail address: flq@pub.sioc.ac.cn (F.-L. Qing).

0022-1139/$ – see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S0022-1139(03)00193-3



Scheme 1.

antimicrobial activity of a perfluoroalkyl-containing quaternary ammonium salt.

2. Results and discussion

The target molecule **5** was designed to be a multifunctional textile finishing agent capable of being attached to fiber by ionic interactions and providing them with barriers against microorganisms, water, oil, soil and blood. The synthesis of **5** was outlined in Scheme 1. The first step proceeded by a free radical addition of a perfluorooctyl iodide to allyl alcohol that was initiated with AIBN to provide the perfluoroalkylated iodohydrin **1** in 75% yield. Compound **1** was then reduced to the perfluoroalkyl alcohol **2** in 70% yield by using tributyltin hydride [14]. Subsequent tosylation of compound **2** provided the intermediate **3** in 85% yield. The alkylation of diallylamine with **3** in the presence of K_2CO_3 afforded the key material **4** in 67% yield [15]. Finally, treatment of **4** with CH_3I in anhydrous CH_3CN gave the target molecular **5** in 84% yield. The perfluoroalkyl-containing quaternary ammonium salt **5** is soluble in water.

Consequently, the antimicrobial activities of the target molecule **5** were measured with *Escherichia coli* 8099 as a Gram-negative strain and *Staphylococcus aureus* ATCC 6538 as a Gram-positive strain on the basis of MIC values, defined as the lowest concentration of antimicrobial agent that results in inhibiting of growth of the test organism after 24 h of incubation at 37 °C. The MIC values were shown in the Table 1. This result showed compound **5** possessed good antimicrobial activities against both Gram-positive *S. aureus* and Gram-negative *E. coli*.

In conclusion, we have designed and synthesized a novel perfluoroalkyl-containing diallyl quaternary ammonium salt **5**. It shows good antimicrobial activities against both Gram-positive *S. aureus* and Gram-negative *E. coli*. The application of the compound **5** for textile multifunctional finishing and polymerization will be reported in due course.

Table 1
The minimum inhibitory concentration (MIC) for compound **5**

Bacterium	Gram	MIC (μg/ml)
Staphylococcus aureus ATCC 6538	(+)	7.8
Escherichia coli 8099	(−)	7.8

3. Experimental section

Melting points were determined on a Pai-ke melting point apparatus and were uncorrected. ^{1}HNMR spectra were recorded on a Bruker AM 300 (300 MHz) spectrometer with Me_4Si as internal standard. ^{19}F NMR spectra were obtained on Bruker AM 300 (282 MHz) spectrometer in $CDCl_3$ with $CFCl_3$ as external standard, downfield shifts being designated as negative. All chemical shifts (δ) are expressed in ppm, coupling constants (J) are given in Hz. Mass spectra were recorded on a Finnigan-MAT-8430 instrument using EI ionization at 70 eV. IR spectra were recorded on a Shimadzu IR-440 spectrometer.

3.1. 1H,1H,2H,2H,3H,3H-perfluoro-1-undecanol (2)

Allyl alcohol (3.73 g, 64.2 mmol) was added dropwise slowly to a mixture of perfluorooctyl iodide (27.1 g, 49.7 mmol) and AIBN (0.166 g, 1.01 mmol) at 95 °C. The reaction mixture was stirred for 24 h at 95 °C. Then the excessive allyl alcohol was removed in vacuo. Purification of the yellow residue by column chromatography on silica gel (petroleum ether:ethyl acetate = 10:1) gave compound **1** (22.5 g, 75% yield) as a white solid. Then to a mixture of **1** (22.0 g, 36.5 mmol) and AIBN (0.041 g, 0.24 mmol) was added dropwise tributyltin hydride (10.6 g, 36.5 mmol) at 100 °C for 4 h under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 24 h. The phase separation phenomenon occurred. The lower liquid phase was collected and chromatographed on silica gel (petroleum ether:ethyl acetate = 10:3) to afford compound **2** as a white solid (12.2 g, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70 (t, J = 6.0 Hz, 2H), 2.20 (m, 2H), 1.88 (m, 2H), 1.50 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ 80.72 (t, J = 9.9 Hz, 3F), 114.24 (m, 2F), 121.66–121.87 (m, 6F), 122.65 (s, 2F), 123.46 (s, 2F), 126.06 (s, 2F).

3.2. Toluene-4-sulfonic acid 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-undecyl ester (3)

Alcohol **2** (8.10 g, 16.9 mmol) and toluene-4-sulfonyl chloride (3.84 g, 20.2 mmol) were dissolved in CH_2Cl_2 (50 ml). A 50% (w/w) aqueous sodium hydroxide solution (25 ml) was then added, and the reaction mixture was heated

at 40 °C for 2 h. The suspension was cooled and decanted. The organic phase was washed three times with water (30 ml), brine, dried over anhydrous $MgSO_4$ and filtration, the solvent was removed in vacuo. Purification of the residue by column chromatography on silica gel (petroleum ether:-ethyl acetate = 10:1) gave compound **3** (9.07 g, 85% yield) as a white solid. m.p. 60 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99 (m, 2H), 2.22 (m, 2H), 2.46 (s, 3H), 4.12 (t, $J = 6.0$ Hz, 2H), 7.37 (d, $J = 8.1$ Hz, 2H), 7.80 (d, $J = 8.1$ Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ 80.75 (t, $J = 9.9$ Hz, 3F), 114.43 (m, 2F), 121.90–121.94 (m, 6F), 122.69 (s, 2F), 123.46 (s, 2F), 126.08 (s, 2F).

*3.3. N-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)-N,N-diallylamine **(4)***

A suspension of toluene-4-sulfonate **3** (7.00 g, 11.1 mmol), diallylamine (1.45 g, 14.9 mmol), and potassium carbonate (2.54 g, 18.4 mmol) in CH_3CN (35 ml) was heated to reflux for 24 h under nitrogen. The reaction mixture was filtered. The filtrates were concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether:ethyl acetate = 14:1) to give compound **4** (4.13 g, 67% yield) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75 (m, 2H), 2.08 (m, 2H), 2.50 (t, $J = 6.9$ Hz, 2H), 3.09 (d, $J = 6.9$ Hz, 4H), 5.16 (m, 4H), 5.84 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ 80.75 (t, $J = 9.9$ Hz 3F), 114.16 (m, 2F), 121.99–121.94 (m, 6F), 122.76 (s, 2F), 123.46 (s, 2F), 126.12 (s, 2F). IR (thin film) 3084, 2984, 2812, 1645, 1243, 1209, 1152, 1114, 997, 923, 705, 656 cm^{-1}. MS *m/z* 557 (3), 530 (6), 110 (100), 69 (11), 41 (51). Anal. Calcd. for $C_{17}H_{16}F_{17}N$: C, 36.64; H, 2.89; N, 2.51. Found: C, 36.57; H, 3.10; N, 2.67%.

*3.4. N-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)-N,N-diallylmethyl ammonium iodide **(5)***

A mixture of compound **4** (0.794 g 1.42 mmol), CH_3I (0.206 g, 1.45 mmol) and anhydrous CH_3CN (2 ml) was refluxed for 24 h. The solvent was removed in vacuo. The residue was washed with anhydrous ether (3× 10 ml) to give quaternary ammonium salt **5** (0.833 g, 84% yield) as a pale yellow solid. m.p. 65–68 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18–2.40 (m, 4H), 3.34 (s, 3H), 3.71 (t, $J = 7.2$ Hz 2H), 4.30 (d, $J = 6.9$ Hz 4H), 5.83 (m, 4H), 6.03 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ 79.90 (t, $J = 9.9$ Hz 3F), 112.64 (m, 2F), 120.78–121.08 (m, 6F), 121.90 (s, 2F), 122.31 (s, 2F), 125.32 (s, 2F). IR (KBr) 3005, 2974, 1478, 1253, 1204, 1153, 1116, 954, 887, 703, 657 cm^{-1}; MS *m/z* 531(3 M^+–I–C_3H_5), 504 (7), 168 (5), 127 (3), 110 (5), 84 (100), 41 (31), 69 (9); Anal. Calcd. for $C_{18}H_{19}F_{17}NI$: C, 30.92; H, 2.74; N, 2.00. Found: C, 31.17; H, 2.74; N, 1.84%.

3.5. Antimicrobial activity

The antimicrobial activity was tested against *Escherichia coli* 8099 and *Staphylococcus aureus* ATCC 6538. The minimum inhibitory concentration (MIC) of compound **5** against selected bacterium was determined by a standard broth dilution method [16]. Bacterial suspensions (5×10^5 to 5×10^6 CFU/ml) were incubated for 24 h at 37 °C in the presence of different concentrations of compound **5**. The MIC values were defined as the lowest concentration of compound **5** that resulted in complete inhibition of growth of the test bacterium.

Acknowledgements

We thank the Ministry of Education of China for financial support.

References

[1] H.S. Seong, J.P. Kim, S.W. Ko, Textile Res. J. 69 (1999) 483–488.
[2] G. Tanchis, Tanctoria 99 (2002) 68–69.
[3] T. Nakashima, Y. Sakagami, H. Ito, M. Matsuo, Textile Res. J. 71 (2001) 688–694.
[4] K. Teraoka, T. Nonami, Y. Yokogawa, H. Taoda, T. Kameyama, J. Mater. Res. 15 (2000) 1243–1244.
[5] Y.H. Kim, G. Sun, Textile Res. J. 71 (2001) 318–323.
[6] Y.J. Jeong, S.Y. Cha, W.R. Yu, W.H. Park, Textile Res. J. 72 (2002) 70–76.
[7] M. Diz, M.R. Infante, P. Erra, Textile Res. J. 71 (2001) 695–700.
[8] D.L. Fredel, J. Cross, E.J. Singer, Surfactant Science Series, vol. 53, Marcel Dekker, NY, 1994.
[9] H. Kourai, Y. Manabe, E. Matsutan, Bokin Bobai 23 (1995) 271.
[10] T.L. Vigo, Textile Res. J. 51 (1981) 454–465.
[11] K.K. Leonas, INDA J. Nonwovens Res. 5 (1993) 22–26.
[12] E.A. McCullough, L.K. Schoenberger, INDA J. Nonwovens Res. 3 (3) (1991) 14–20.
[13] D. Lammermann, Melliand Textillber. Eng. Ed. 72 (1991) 380–383.
[14] J.M. Vincent, A. Rabion, V.K. Yachandra, R.H. Fish, Angew. Chem. Int. Ed. Engl. 36 (1997) 2346–2349.
[15] F.D. Campo, D. Lastécouères, J.M. Vincent, J.B. Verlhac, J. Org. Chem. 64 (1999) 4969–4971.
[16] Technical Standard For Disinfection, Broth Dilution Minimum Inhibitory Concentration Test, Ministry of Health, PR China, 2002.