European Journal of Medicinal Chemistry 45 (2010) 4199–4208

Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

Original article

Synthesis, structure and *in vitro* antibacterial activities of new hybrid disinfectants quaternary ammonium compounds: Pyridinium and quinolinium stilbene benzenesulfonates

Kullapa Chanawanno [a], Suchada Chantrapromma [a,*], Theerasak Anantapong [b], Akkharawit Kanjana-Opas [b], Hoong-Kun Fun [c]

[a] Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand
[b] Department of Industrial Biotechnology, Faculty of Agro-Industry, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand
[c] X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM Penang, Malaysia

ARTICLE INFO

Article history:
Received 18 February 2010
Received in revised form
7 June 2010
Accepted 9 June 2010
Available online 17 June 2010

Keywords:
Antibacterial
Disinfectants
Pyridinium
Quaternary ammonium compounds (QACs)
Quinolinium
Stilbene

ABSTRACT

The series of pyridinium (**1**–**10**) and quinolinium (**11**–**20**) stilbene benzenesulfonates have been synthesized and their structures were investigated by UV–vis, FT-IR and ^{1}H NMR spectroscopy. In addition, compound **5** was also determined by single crystal X-ray diffraction technique. The antibacterial activity of the synthesized compounds against both Gram-positive and Gram-negative bacteria has been determined. The quinolinium derivatives exhibited two very potent characteristic activities, namely, (i) specific activity to Methicillin-Resistant *Staphylococcus aureus* and (ii) with broad band spectrum activity. Compounds **11**, **13** and **14** are the most active showing broad spectrum antibacterial activity against Gram-positive (Methicillin-Resistant *S. aureus, S. aureus, Bacillus subtilis,* Vancomycin-Resistant *Enterococcus faecalis* and *E. faecalis*) and Gram-negative bacterium (*Shigella sonnei*). The MICs of these compounds were found to be better than that of Benzalkonium chloride (BZK), the commercially used disinfectant.

1. Introduction

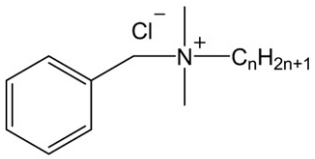
The discovery of an alarming growth rate of bacterial resistance phenomena against common antibacterial agents has limited the use of commercial disinfectants [1]. In the field of synthetic chemistry, numerous studies of the synthesis and antimicrobial characteristics of quaternary ammonium compounds (QACs) have been used since 1935 [2]. Among these compounds, pyridinium and quinolinium salts represent the important groups of chemicals widely used as biocides, drugs and herbicides [3,4]. Disinfectants based on this class are widely used in hospital environments and in the food industry due to their low toxicity to humans and animals and to their wide antimicrobial spectra [5,6]. Benzalkonium chloride (BZK; Fig. 1) is the quaternary ammonium disinfectant which consisted of a mixture of alkylbenzyldimethylammonium chlorides of various alkyl chain lengths and usually used as a biocide. BZK solutions are rapidly-acting biocidal agents with a moderately long duration of action. They are mostly active against bacteria, viruses, fungi, and protozoa. Gram-positive bacteria are generally more susceptible to BZK than Gram-negative [7]. However, the allergic problems reported worldwide [8,9] and the BZK-resistant bacteria [10–14] have restricted the use of this agent.

Among the various structure types of QAC, stilbene derivative seem to be an effective candidate according to the literature which suggested that the aminated stilbenes possess some pharmacological properties and biological role in plant defense against pathogens [15]. Moreover, introducing new molecular parameters such as heteroatoms [16], chemical functions [17,18] and aromatics [19] may lead to potential compounds which can overcome the increasing resistance phenomenon. There are numerous reports on antibacterial agents containing dimethylamino [20,21] and ethoxy [22,23] groups so these two groups were applied to our designed compounds.

In addition, the well-known antibacterial drugs sulfonamides also represented wide application in synthetic bioactive compounds for a long period of time [24,25]. These interesting features of QAC and sulfonamides led us to design and synthesize the hybrid disinfectant between QAC (pyridinium and quinolinium

* Corresponding author. Tel.: +66 7428 8447; fax: +66 7421 2918.
E-mail address: suchada.c@psu.ac.th (S. Chantrapromma).

0223-5234/$ – see front matter © 2010 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.ejmech.2010.06.014



n = 8, 10, 12, 14, 16, 18

Fig. 1. The structure of the well-known quaternary ammonium disinfectant Benzalkonium chloride (BZK).

stilbene) and sulfonamide-like skeletons in order to study their antibacterial activities.

In this study, the series of twenty pyridinium (**1**–**10**) and quinolinium (**11**–**20**) stilbene benzenesulfonates (see Fig. 2) were designed and synthesized on the basis of the combination of two efficient chemophores which were (i) stilbene-QAC and (ii) sulfonamide-like structures. The purpose of this investigation was to elucidate the influence of the presence of pyridinium and quinolinium rings, as well as the ethoxy and dimethylamino substituents in the phenyl ring on the antibacterial activities of these compounds in order to acquire further information on the structural characteristics enhancing their activities. The antibacterial activities of the compounds have been screened *in vitro* against the tested pathogenic bacteria by microliter plate colorimetric assay.

2. Chemistry

2.1. Materials

Melting points were determined on the Fisher-Johns melting point apparatus. UV–vis spectra were obtained in the methanol solutions with a SPECORD S100 (Analytikjena) spectrometer in the range of 200–800 nm. FT-IR spectra were recorded in the 4000–400 cm^{-1} region with a PerkinElmer FT-IR System Spectrum BX spectrophotometer using KBr pellets. Elemental analyses were performed with a CE Instruments Flash 1112 Series EA CHNS-O Analyzer and were consistent with theoretical values within ±0.4%.

^{1}H NMR spectra were recorded on a 300 MHz Bruker FT-NMR Ultra Shield™ spectrometers in DMSO-d_6 and $CDCl_3$ mixed solvent with TMS as the internal standard. Chemical shifts are reported in δ (ppm) and coupling constants (J) are expressed in Hertz.

All chemicals and solvents used for the synthesis were of reagent grade and used as received.

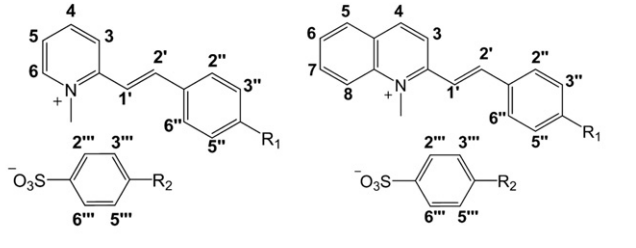


Fig. 2. Structure and ^{1}H designation of the synthesized pyridinium (**1**–**10**) and quinolinium (**11**–**20**) stilbene benzenesulfonates.

2.2. Synthesis of all pyridinium and quinolinium stilbene derivatives

The synthesis of compounds **PAM**, **PET**, **QAM**, **QET** and **1**–**20** are as following (Fig. 3).

2.2.1. (E)-2-(4-(dimethylamino)styryl)-1-methylpyridinium iodide (*PAM*)

(*E*)-2-(4-ethoxystyryl)-1-methylquinolinium iodide was synthesized by mixing a solution (1:1:1 mole ratio) of 1,2-dimethylpyridinium iodide (2.00 g, 8.5 mmol) which was synthesized by the previous method [26], 4-dimethylaminobenzaldehyde (1.27 g, 8.5 mmol) and piperidine (0.84 ml, 8.5 mmol) in hot methanol. The resulting red solution was refluxed for 6 h under nitrogen atmosphere. The resultant red solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 273–274 °C, 1.92 g (61%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 219.0, 281.0, 461.0; IR (KBr, cm^{-1}): νC=C; 1559 s, νC–N; 1370 s; ^{1}H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.20 (*s*, 1-CH_3), 8.17 (*d*, J = 7.5, H-3), 8.27 (*d*, J = 7.5, H-4), 7.54 (*d*, J = 7.5, H-5), 8.63 (*d*, J = 7.5, H-6), 7.06 (*d*, J = 15.6, H-1′), 7.71 (*d*, J = 15.6, H-2′), 7.55 (*d*, J = 8.4, H-2″, H-6″), 6.60 (*d*, J = 8.4, H-3″, H-5″), 2.95 (*s*, N-$(CH_3)_2$). Anal. calcd. for $C_{16}H_{19}IN_2$: C, 52.47; H, 5.23; N, 7.65. Found: C, 52.31; H, 5.18; N, 7.88.

*2.2.1.1. (E)-2-(4-(dimethylamino)styryl)-1-methylpyridinium 4-methylbenzenesulfonate **(1)**.* A 0.26 g (0.71 mmol) solution of **PAM** in hot methanol (50 ml) was mixed with 0.20 g (0.71 mmol) of silver (I) 4-methylbenzenesulfonate in hot methanol (50 ml). The mixture turned to deep red and cloudy immediately. After stirring for 30 min, the precipitate of silver iodide was filtered and the filtrate was evaporated to give a deep red solid. The resultant yellow solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 195–196 °C, 0.21 g (71%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 219.0, 284.0, 462.0; IR (KBr, cm^{-1}): νC=C; 1591 s, νC–N; νS = O; 1195 s; 1440 s; ^{1}H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.34 (*s*, 1-CH_3), 8.28 (*d*, J = 7.2, H-3), 8.25 (*t*, J = 7.2, H-4), 7.73 (*d*, J = 7.2, H-5), 8.78 (*d*, J = 7.2, H-6), 7.77 (*d*, J = 15.3, H-1′), 7.13 (*d*, J = 15.3, H-2′), 7.65 (*d*, J = 7.5, H-2″, H-6″), 7.10 (*d*, J = 7.5, H-3″, H-5″), 3.10 (*s*, N-$(CH_3)_2$), 7.70 (*d*, J = 7.8, H-2‴, H-6‴), 6.70 (*d*, J = 7.8, H-3‴, H-5‴), 2.32 (*s*, 4‴-CH_3). Anal. calcd. for $C_{23}H_{26}N_2O_3S$: C, 67.29; H, 6.38; N, 6.82; S, 7.82; O, 11.69. Found: C, 67.09; H, 6.48; N, 7.00; S, 7.72; O, 11.71.

Compounds **2**–**5** were synthesized with identical procedure of **1** by replacing silver (I) 4-methylbenzenesulfonate with silver (I) 4-methoxybenzenesulfonate (for **2**), silver (I)4-bromobenzenesulfonate (for **3**), silver (I) 4-chlorobenzenesulfonate (for **4**), and silver (I) 4-aminobenzenesulfonate (for **5**). All of the resulting solids were further purified by recrystallization whereas silver (I) 4-substituted-benzenesulfonates were synthesized according to previously reported procedure [26–29].

*2.2.1.2. (E)-2-(4-(dimethylamino)styryl)-1-methylpyridinium 4-methoxybenzenesulfonate **(2)**.* M.p. 175–176 °C, 0.25 g (89%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 229.0, 273.0, 461.0; IR (KBr, cm^{-1}): νC=C; 1596 s, νC–N; 1207 s, νS = O; 1189 s; ^{1}H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.33 (*s*, 1-CH_3), 8.40 (*d*, J = 8.1, H-3), 8.29 (*t*, J = 8.1, H-4), 7.70 (*d*, J = 8.1, H-5), 8.77 (*d*, J = 8.1, H-6), 7.20 (*d*, J = 15.6, H-1′), 7.85 (*d*, J = 15.6, H-2′), 7.65 (*d*, J = 8.7, H-2″, H-6″), 7.64 (*d*, J = 8.7, H-3″, H-5″), 3.08 (*s*, N-$(CH_3)_2$), 6.81 (*d*, J = 8.1, H-2‴, H-6‴), 6.74 (*d*, J = 8.1, H-3‴, H-5‴), 3.78 (*s*, 4‴-OCH_3). Anal. calcd. for $C_{23}H_{26}N_2O_4S$: C, 64.77; H, 6.14; N, 6.57; S, 7.52; O, 15.00. Found: C, 64.84; H, 6.20; N, 6.55; S, 7.50; O, 14.91.

*2.2.1.3. (E)-2-(4-(dimethylamino)styryl)-1-methylpyridinium 4-bromobenzenesulfonate **(3)**.* M.p.(decompose) 280–281 °C, 0.25 g

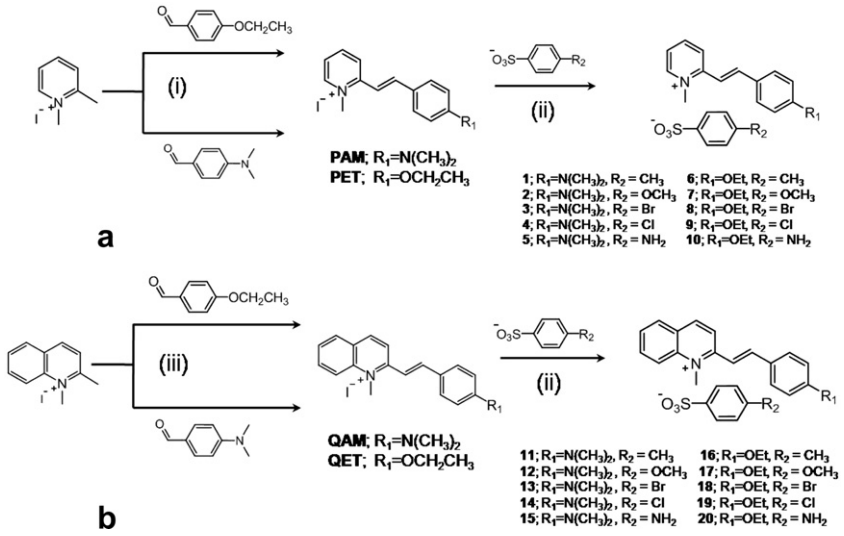


Fig. 3. Synthesis scheme of pyridinium stilbene derivatives (a) and quinolinium stilbene derivatives (b); (i)=MeOH, reflux, 50–55 °C, 4 h, N_2 atmosphere (**PET**) and 6 h (**PAM**), (ii)=MeOH, stir, 50 °C, 0.5 h (iii)=MeOH, reflux, 50–55 °C, 6 h, N_2 atmosphere (both **QET** and **QAM**).

(91%) yield. UV (CH_3OH) λ_{max} (nm): 203.0, 223.0, 461.0; IR (KBr, cm^{-1}): νC=C; 1636 s, νC–N; 1191 s, νS = O; 1191 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.30 (*s*, 1-CH_3), 8.17 (*d*, *J* = 7.5, H-3), 8.17 (*d*, *J* = 7.5, H-4), 7.54 (*d*, *J* = 7.5, H-5), 8.66 (*d*, *J* = 7.5, H-6), 7.02 (*d*, *J* = 15.6, H-1′), 7.71 (*d*, *J* = 15.6, H-2′), 7.49 (*d*, *J* = 8.4, H-2″, H-6″), 6.60 (*d*, *J* = 8.4, H-3″, H-5″), 2.94 (*s*, N-$(CH_3)_2$), 7.56 (*d*, *J* = 8.7, H-2‴, H-6‴), 6.82 (*d*, *J* = 8.7, H-3‴, H-5‴). Anal. calcd. for $C_{22}H_{23}BrN_2O_3S$: C, 55.58; H, 4.88; N, 5.89; S, 6.74; O, 10.10. Found: C, 55.42; H, 4.89; N, 5.89; S, 6.70; O, 10.21.

*2.2.1.4. (E)-2-(4-(dimethylamino)styryl)-1-methylpyridinium 4-chlorobenzenesulfonate **(4)**.* M.p. 243–244 °C, 0.22 g (79%) yield. UV (CH_3OH) λ_{max} (nm): 201.0, 223.0, 284.0, 462.0; IR (KBr, cm^{-1}): νC=C; 1683 s, νC–N; 1198 s, νS = O; 1198 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.35 (*s*, 1-CH_3), 8.24 (*d*, *J* = 8.1, H-3), 8.30 (*t*, *J* = 8.1, H-4), 7.70 (*t*, *J* = 8.1, H-5), 8.74 (*d*, *J* = 8.1, H-6), 7.77 (*d*, *J* = 15.6, H-1′), 7.12 (*d*, *J* = 15.6, H-2′), 7.64 (*d*, *J* = 8.7, H-2″, H-6″), 6.73 (*d*, *J* = 8.7, H-3″, H-5″), 3.11 (*s*, N-$(CH_3)_2$), 7.78 (*d*, *J* = 8.4, H-2‴, H-6‴), 7.28 (*d*, *J* = 8.4, H-3‴, H-5‴). Anal. calcd. for $C_{22}H_{23}ClN_2O_3S$: C, 61.31; H, 5.38; N, 6.50; S, 7.44; O, 11.14. Found: C, 61.35; H, 5.36; N, 6.43; S, 7.49; O, 11.12.

*2.2.1.5. (E)-2-(4-(dimethylamino)styryl)-1-methylpyridinium 4-aminobenzenesulfonate **(5)**.* M.p. 257–258 °C, 0.19 g (66%) yield. UV (CH_3OH) λ_{max} (nm): 204.0, 253.0, 461.0; IR (KBr, cm^{-1}): νC=C; 1611 s, νC–N; 1297 s, νS = O; 1195 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.32 (*s*, 1-CH_3), 8.42 (*d*, *J* = 8.7, H-3), 8.31 (*t*, *J* = 8.7, H-4), 7.69 (*d*, *J* = 8.7, H-5), 8.77 (*d*, *J* = 8.7, H-6), 7.87 (*d*, *J* = 15.9, H-1′), 7.22 (*d*, *J* = 15.9, H-2′), 7.69 (*d*, *J* = 8.4, H-2″, H-6″), 7.37 (*d*, *J* = 8.4, H-3″, H-5″), 3.07 (*s*, N-$(CH_3)_2$), 6.75 (*d*, *J* = 8.1, H-2‴, H-6‴), 6.48 (*d*, *J* = 8.1, H-3‴, H-5‴), 5.00 (*br s*, 4‴-NH_2). Anal. calcd. for $C_{22}H_{25}N_3O_3S$: C, 64.21; H, 6.12; N, 10.22; S, 7.79; O, 11.66. Found: C, 64.31; H, 6.09; N, 10.18; S, 7.90; O, 11.52.

*2.2.2. (E)-2-(4-ethoxystyryl)-1-methylpyridinium iodide **(PET)***

(*E*)-2-(4-ethoxystyryl)-1-methylpyridinium iodide was synthesized by mixing a solution (1:1:1 mole ratio) of 1,2-dimethylpyridinium iodide (2.00 g, 8.5 mmol) which was synthesized by the previous method [26], 4-ethoxybenzaldehyde (1.16 ml, 8.5 mmol) and piperidine (0.84 ml, 8.5 mmol) in hot methanol. The resulting deep yellow solution was refluxed for 4 h under nitrogen atmosphere. The resultant yellow solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 208–210 °C, 2.08 g (66%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 218.0, 366.0; IR (KBr, cm^{-1}): νC=C; 1601 s, νC = O; 1237 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.44 (*s*, 1-CH_3), 8.40 (*d*, *J* = 8.7, H-3), 8.46 (*t*, *J* = 8.7, H-4), 7.74 (*t*, *J* = 8.7, H-5), 8.95 (*d*, *J* = 8.7, H-6), 7.41 (*d*, *J* = 15.9, H-1′), 7.85 (*d*, *J* = 15.9, H-2′), 7.80 (*d*, *J* = 8.7, H-2″, H-6″), 6.98 (*d*, *J* = 8.7, H-3″, H-5″), 4.12 (*q*, *J* = 6.9, O–CH_2), 1.43 (*t*, *J* = 6.9, CH_3). Anal. calcd. for $C_{16}H_{18}INO$: C, 52.33; H, 4.94; N, 3.81; O, 4.36. Found: C, 52.28; H, 4.92; N, 3.92; O, 4.30.

*2.2.2.1. (E)-2-(4-ethoxystyryl)-1-methylpyridinium 4-methylbenzenesulfonate **(6)**.* A 0.22 g (0.58 mmol) solution of **PET** in hot methanol (50 ml) was mixed with 0.20 g (0.58 mmol) of silver (I) 4-methylbenzenesulfonate in hot methanol (50 ml). The mixture turned to yellow and cloudy immediately. After stirring for 30 min, the precipitate of silver iodide was filtered and the filtrate was evaporated to give a yellow solid. The resultant yellow solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 171–172 °C, 0.26 g (88%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 246.0, 366.0; IR (KBr, cm^{-1}): νC=C; 1597 s, νC = O; 1220 s, νS = O; 1180 s; δ ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.44 (*s*, 1-CH_3), 8.42 (*d*, *J* = 8.4, H-3), 8.49 (*t*, *J* = 8.4, H-4), 7.78 (*t*, *J* = 8.4, H-5), 8.98 (*d*, *J* = 8.4, H-6), 7.41 (*d*, *J* = 15.9, H-1′), 7.85 (*d*, *J* = 15.9, H-2′), 7.80 (*d*, *J* = 8.7, H-2″, H-6″), 6.98 (*d*, *J* = 8.7, H-3″, H-5″), 4.13 (*q*, *J* = 6.9, O–CH_2), 1.41 (*t*, *J* = 6.9, CH_3), 7.79 (*d*, *J* = 8.7, H-2‴, H-6‴), 6.98 (*d*, *J* = 8.7, H-3‴, H-5‴), 2.32 (*s*, 4‴-CH_3). Anal. calcd. for $C_{23}H_{25}NO_4S$: C, 67.14; H, 6.12; N, 3.40; S, 7.79; O, 15.55. Found: C, 66.11; H, 6.09; N, 3.41; S, 7.81; O, 15.58.

Compounds **7**–**10** were synthesized with identical procedure of **6** by replacing silver (I) 4-methylbenzenesulfonate with silver (I) 4-methoxybenzenesulfonate (for **7**), silver (I) 4-bromobenzenesulfonate (for **8**), silver (I) 4-chlorobenzenesulfonate (for **9**), and silver (I) 4-aminobenzenesulfonate (for **10**). All of the resulting solids were further purified by recrystallization.

*2.2.2.2. (E)-2-(4-ethoxystyryl)-1-methylpyridinium 4-methoxybenzenesulfonate **(7)**.* M.p. 153–155 °C, 0.21 g (72%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 230.0, 271.0, 366.0; IR (KBr, cm^{-1}): νC=C; 1618 s, νC = O; 1230 s, νS = O; 1183 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.40 (*s*, 1-CH_3), 8.46 (*d*, *J* = 8.4, H-3), 8.40 (*t*, *J* = 8.4, H-4), 7.78 (*d*, *J* = 8.4, H-5), 8.90 (*d*, *J* = 8.4, H-6), 7.41 (*d*, *J* = 15.9, H-1′), 7.85 (*d*, *J* = 15.9, H-2′), 7.66 (*d*, *J* = 8.4, H-2″, H-6″), 6.97 (*d*, *J* = 8.4, H-3″,

H-5″), 4.11 (*q*, *J* = 6.9, O–CH_2), 1.41 (*t*, *J* = 6.9, CH_3), 7.66 (*d*, *J* = 8.7, H-2‴, H-6‴), 6.82 (*d*, *J* = 8.7, H-3‴, H-5‴), 3.78 (*s*, 4‴-OCH_3). Anal. calcd. for $C_{23}H_{25}NO_5S$: C, 64.62; H, 5.89; N, 3.28; S, 7.50; O, 18.71. Found: C, 64.55; H, 6.10; N, 3.20; S, 7.49; O, 18.66.

2.2.2.3. (E)-2-(4-ethoxystyryl)-1-methylpyridinium 4-bromobenzenesulfonate ***(8)***. M.p. 190–193 °C, 0.20 g (73%) yield. UV (CH_3OH) λ_{max} (nm): 210.0, 266.0, 366.0; IR (KBr, cm^{-1}): νC=C; 1595 s, νC = O; 1224 s, νS = O; 1179 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.40 (*s*, 1-CH_3), 8.42 (*d*, *J* = 8.7, H-3), 8.51 (*t*, *J* = 8.7, H-4), 7.64 (*t*, *J* = 8.7, H-5), 8.91 (*d*, *J* = 8.7, H-6), 7.41 (*d*, *J* = 15.9, H-1′), 7.85 (*d*, *J* = 15.9, H-2′), 7.80 (*d*, *J* = 8.7, H-2″, H-6″), 6.91 (*d*, *J* = 8.7, H-3″, H-5″), 4.12 (*q*, *J* = 6.9, O–CH_2), 1.43 (*t*, *J* = 6.9, CH_3), 7.86 (*d*, *J* = 8.7, H-2‴, H-6‴), 6.98 (*d*, *J* = 8.7, H-3‴, H-5‴). Anal. calcd. for $C_{22}H_{22}BrNO_4S$: C, 55.47; H, 4.65; N, 2.94; S, 6.73; O, 13.43. Found: C, 55.44; H, 4.60; N, 2.87; S, 6.61; O, 13.69.

2.2.2.4. (E)-2-(4-ethoxystyryl)-1-methylpyridinium 4-chlorobenzenesulfonate ***(9)***. M.p. 185–186 °C, 0.24 g (85%) yield. UV (CH_3OH) λ_{max} (nm): 202.0, 222.0, 366.0; IR (KBr, cm^{-1}): νC=C; 1627 s, νC = O; 1230 s, νS = O; 1179 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.40 (*s*, 1-CH_3), 8.42 (*d*, *J* = 7.5, H-3), 8.30 (*t*, *J* = 7.5, H-4), 7.77 (*d*, *J* = 7.5, H-5), 8.90 (*d*, *J* = 7.5, H-6), 7.41 (*d*, *J* = 15.9, H-1′), 7.84 (*d*, *J* = 15.9, H-2′), 7.71 (*d*, *J* = 8.4, H-2″, H-6″), 6.98 (*d*, *J* = 8.4, H-3″, H-5″), 4.12 (*q*, *J* = 6.9, O–CH_2), 1.42 (*t*, *J* = 6.9, CH_3), 7.72 (*d*, *J* = 8.4, H-2‴, H-6‴), 7.30 (*d*, *J* = 8.4, H-3‴, H-5‴). Anal. calcd. for $C_{22}H_{22}ClNO_4S$: C, 61.18; H, 5.13; N, 3.24; S, 7.42; O, 14.82. Found: C, 60.95; H, 5.09; N, 3.22; S, 7.43; O, 15.11.

2.2.2.5. (E)-2-(4-ethoxystyryl)-1-methylpyridinium 4-aminobenzenesulfonate ***(10)***. M.p. 216–218 °C, 0.20 g (68%) yield. UV (CH_3OH) λ_{max} (nm): 204.0, 252.0, 366.0; IR (KBr, cm^{-1}): νC=C; 1603 s, νC = O; 1230 s, νS = O; 1179 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.40 (*s*, 1-CH_3), 8.43 (*d*, *J* = 8.4, H-3), 8.39 (*t*, *J* = 8.4, H-4), 7.94 (*d*, *J* = 8.4, H-5), 8.89 (*d*, *J* = 8.4, H-6), 7.39 (*d*, *J* = 15.9, H-1′), 7.82 (*d*, *J* = 15.9, H-2′), 7.76 (*d*, *J* = 8.4, H-2″, H-6″), 6.98 (*d*, *J* = 8.4, H-3″, H-5″), 4.12 (*q*, *J* = 6.9, O–CH_2), 1.43 (*t*, *J* = 6.9, CH_3), 7.46 (*d*, *J* = 8.4, H-2‴, H-6‴), 6.52 (*d*, *J* = 8.4, H-3‴, H-5‴), 4.72 (*br s*, 4‴-NH_2). Anal. calcd. for $C_{22}H_{24}N_2O_4S$: C, 64.06; H, 5.86; N, 6.79; S, 7.77; O, 15.52. Found: C, 64.00; H, 6.11; N, 6.70; S, 7.69; O, 15.50.

2.2.3. (E)-2-(4-(dimethylamino)styryl)-1-methylquinolinium iodide ***(QAM)***

(*E*)-2-(4-(dimethylamino)styryl)-1-methylquinolinium iodide was synthesized by mixing a solution (1:1:1 mole ratio) of 1,2-dimethylquinolinium iodide (2.00 g, 7.01 mmol) 4-dimethylaminobenzaldehyde (1.05 g, 7.01 mmol) and piperidine (0.69 ml, 7.01 mmol) in hot methanol (50 ml). The resulting solution was refluxed for 6 h under a nitrogen atmosphere. The resulting solid was filtered off, washed with methanol, dried in vacuo and recrystallized from methanol to give green crystals. M.p. 218–219 °C, 2.52 g (89%) yield. UV (CH_3OH) λ_{max} (nm): 205.3, 221.9, 280.9, 326.8, 521.1; IR (KBr, cm^{-1}): νC=C; 1600 s, νC–N; 1280 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.50 (*s*, 1-CH_3), 3.15 (*s*, *N*-$(CH_3)_2$), 8.40 (*d*, *J* = 9.0, H-3), 8.70 (*d*, *J* = 9.0, H-4), 8.14 (*d*, *J* = 7.8, H-5), 7.80 (*t*, *J* = 7.8, H-6), 8.01 (*t*, *J* = 7.8, H-7), 8.31 (*d*, *J* = 7.5, H-8), 7.50 (*d*, *J* = 15.3, H-1′), 8.05 (*d*, *J* = 15.3, H-2′), 7.78 (*d*, *J* = 8.7, H-2″, H-6″), 6.80 (*d*, *J* = 8.7, H-3″, H-5″). Anal. calcd. for $C_{20}H_{21}IN_2$: C, 57.70; H, 5.08; N, 6.74. Found: C, 57.65; H, 5.10; N, 6.90.

2.2.3.1. (E)-2-(4-(dimethylamino)styryl)-1-methylquinolinium 4-methylbenzenesulfonate ***(11)***. A 0.23 g (0.58 mmol) solution of **QAM** in hot methanol (50 ml) was mixed with 0.20 g (0.58 mmol) of silver (I) 4-methylbenzenesulfonate in hot methanol (50 ml). The mixture turned to green and cloudy immediately. After stirring for 30 min, the precipitate of silver iodide was filtered and the filtrate was evaporated to give a yellow solid. The resultant yellow solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 218–219 °C, 0.20 g (89%) yield. UV (CH_3OH) λ_{max} (nm): 328.6, 521.1; IR (KBr, cm^{-1}): νC=C; 1600 s, νC–N; 1280 s, νS = O s; 1167; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.50 (*s*, 1-CH_3), 3.15 (*s*, *N*-$(CH_3)_2$), 8.42 (*d*, *J* = 9.0, H-3), 8.71 (*d*, *J* = 9.0, H-4), 8.35 (*d*, *J* = 7.8, H-5), 7.80 (*t*, *J* = 7.8, H-6), 8.12 (*t*, *J* = 7.8, H-7), 8.35 (*d*, *J* = 7.8, H-8), 7.60 (*d*, *J* = 15.6, H-1′), 8.00 (*d*, *J* = 15.6, H-2′), 7.73 (*d*, *J* = 8.7, H-2″, H-6″), 6.80 (*d*, *J* = 8.7, H-3″, H-5″), 7.10 (*d*, *J* = 8.1, H-2‴, H-6‴), 7.55 (*d*, *J* = 8.1, H-3‴, H-5‴), 2.28 (*s*, 4‴-CH_3). Anal. calcd. for $C_{27}H_{28}N_2O_3S$: C, 70.71; H, 6.13; N, 6.08; S, 6.96; O, 10.42. Found: C, 70.49; H, 6.26; N, 6.19; S, 6.94; O, 10.12.

Compounds **12**–**15** were synthesized with identical procedure of **11** by replacing silver (I) 4-methylbenzenesulfonate with silver (I) 4-methoxybenzenesulfonate (for **12**), silver (I) 4-bromobenzenesulfonate (for **13**), silver (I) 4-chlorobenzenesulfonate (for **14**), and silver (I) 4-aminobenzenesulfonate (for **15**). All of the resulting solids were further purified by recrystallization.

2.2.3.2. (E)-2-(4-(dimethylamino)styryl)-1-methylquinolinium 4-methoxybenzenesulfonate ***(12)***. M.p. 279–281 °C, 0.26 g (81%) yield. UV (CH_3OH) λ_{max} (nm): 311.6, 524.5; IR (KBr, cm^{-1}): νC=C; 1568 s, νC–N; 1339 s, νS = O; 1162 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.50 (*s*, 1-CH_3), 3.13 (*s*, *N*-$(CH_3)_2$), 8.41 (*d*, *J* = 9.0, H-3), 8.70 (*d*, *J* = 9.0, H-4), 8.16 (*d*, *J* = 7.9, H-5), 7.81 (*t*, *J* = 7.9, H-6), 7.99 (*t*, *J* = 7.9, H-7), 8.31 (*d*, *J* = 7.9, H-8), 7.50 (*d*, *J* = 15.3, H-1′), 8.09 (*d*, *J* = 15.3, H-2′), 7.76 (*d*, *J* = 8.7, H-2″, H-6″), 6.80 (*d*, *J* = 8.7, H-3″, H-5″), 6.81 (*d*, *J* = 8.1, H-2‴, H-6‴), 7.69 (*d*, *J* = 8.1, H-3‴, H-5‴), 3.82 (*s*, 4‴-OCH_3). Anal. calcd. for $C_{27}H_{28}N_2O_4S$: C, 68.04; H, 5.92; N, 5.88; S, 6.73; O, 13.43. Found: C, 68.11; H, 5.89; N, 5.79; S, 6.76; O, 13.45.

2.2.3.3. (E)-2-(4-(dimethylamino)styryl)-1-methylquinolinium 4-bromobenzenesulfonate ***(13)***. M.p. 282–283 °C, 0.18 g (59%) yield. UV (CH_3OH) λ_{max} (nm): 289.5, 328.0, 522.2; IR (KBr, cm^{-1}): νC=C; 1569 s, νC–N; 1377 s, νS = O; 1189 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.52 (*s*, 1-CH_3), 2.50 (*s*, *N*-$(CH_3)_2$), 8.41 (*d*, *J* = 9.0, H-3), 8.84 (*d*, *J* = 9.0, H-4), 8.14 (*d*, *J* = 7.8, H-5), 7.88 (*t*, *J* = 7.8, H-6), 8.01 (*t*, *J* = 7.8, H-7), 8.37 (*d*, *J* = 7.8, H-8), 7.72 (*d*, *J* = 15.3, H-1′), 8.05 (*d*, *J* = 15.3, H-2′), 7.82 (*d*, *J* = 7.5, H-2″, H-6″), 6.74 (*d*, *J* = 7.5, H-3″, H-5″), 6.95 (*d*, *J* = 8.7, H-2‴, H-6‴), 7.63 (*d*, *J* = 8.7, H-3‴, H-5‴). Anal. calcd. for $C_{26}H_{25}BrN_2O_3S$: C, 59.43; H, 4.80; N, 5.33; S, 6.10; O, 9.13. Found: C, 59.24; H, 4.77; N, 5.51; S, 6.01; O, 9.17.

2.2.3.4. (E)-2-(4-(dimethylamino)styryl)-1-methylquinolinium 4-chlorobenzenesulfonate ***(14)***. M.p. 284–285 °C, 0.17 g (54%) yield. UV (CH_3OH) λ_{max} (nm): 289.5, 326.9, 522.8; IR (KBr, cm^{-1}): νC=C; 1570 s, νC–N; 1335 s, νS = O; 1164 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.50 (*s*, 1-CH_3), 3.12 (*s*, *N*-$(CH_3)_2$), 8.46 (*d*, *J* = 9.0, H-3), 8.90 (*d*, *J* = 9.0, H-4), 8.35 (*d*, *J* = 7.8, H-5), 7.91 (*t*, *J* = 7.8, H-6), 8.12 (*t*, *J* = 7.8, H-7), 8.40 (*d*, *J* = 7.8, H-8), 7.70 (*d*, *J* = 15.3, H-1′), 8.09 (*d*, *J* = 15.3, H-2′), 7.88 (*d*, *J* = 8.7, H-2″, H-6″), 7.05 (*d*, *J* = 8.7, H-3″, H-5″), 7.30 (*d*, *J* = 8.1, H-2‴, H-6‴), 7.63 (*d*, *J* = 8.1, H-3‴, H-5‴). Anal. calcd. for $C_{26}H_{25}ClN_2O_3S$: C, 64.92; H, 5.24; N, 5.82; S, 6.67; O, 9.98. Found: C, 64.81; H, 5.44; N, 5.86; S, 6.65; O, 9.99.

2.2.3.5. (E)-2-(4-(dimethylamino)styryl)-1-methylquinolinium 4-aminobenzenesulfonate ***(15)***. M.p. 265–266 °C, 0.29 g (89%) yield. UV (CH_3OH) λ_{max} (nm): 203.0, 235.0, 252.0, 282.0, 327.0, 522.0; IR (KBr, cm^{-1}): νC=C; 1582 s, νC–N; 1334 s, νS = O; 1182 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.49 (*s*, 1-CH_3), 3.12 (*s*, *N*-$(CH_3)_2$), 8.40 (*d*, *J* = 8.2, H-3), 8.69 (*d*, *J* = 8.2, H-4), 8.30 (*d*, *J* = 8.2, H-5), 7.78 (*t*, *J* = 8.2, H-6), 8.08 (*t*, *J* = 7.8, H-7), 8.18 (*d*, *J* = 7.8, H-8), 7.47 (*d*, *J* = 15.9, H-1′), 7.90 (*d*, *J* = 15.9, H-2′), 7.75 (*d*, *J* = 8.4, H-2″, H-6″), 6.52 (*d*, *J* = 8.4, H-3″, H-5″), 7.89 (*d*, *J* = 8.1, H-2‴, H-6‴), 6.78 (*d*, *J* = 8.1, H-3‴, H-5‴), 4.65 (*br s*, 4‴-NH_2). Anal. calcd. for

$C_{26}H_{27}N_3O_3S$: C, 67.65; H, 5.90; N, 9.10; S, 6.95; O, 10.40. Found: C, 67.64; H, 5.89; N, 9.08; S, 6.96; O, 10.43.

2.2.4. (E)-2-(4-ethoxystyryl)-1-methylquinolinium iodide ***(QET)***

(*E*)-2-(4-ethoxystyryl)-1-methylquinolinium iodide was synthesized by mixing a solution (1:1:1 mole ratio) of 1,2-dimethylquinolinium iodide (2.00 g, 7.0 mmol) which was synthesized by the previous method [29], 4-ethoxybenzaldehyde (4.32 ml, 7.0 mmol) and piperidine (0.69 ml, 7.0 mmol) in hot methanol. The resulting red solution was refluxed for 6 h under nitrogen atmosphere. The resultant orange-brown solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 219–221 °C, 2.20 g (68%) yield. UV (CH_3OH) λ_{max} (nm): 217.5, 252.8, 314.1, 416.2; IR (KBr, cm^{-1}): νC=C; 1605 s, νC = O; 1233 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.60 (*s*, 1-CH_3), 1.42 (*t*, *J* = 7.2, CH_3), 4.15 (*q*, *J* = 7.2, OCH_2), 8.50 (*d*, *J* = 9.0, H-3), 8.93 (*d*, *J* = 9.0, H-4), 8.27 (*d*, *J* = 7.5, H-5), 7.90 (*t*, *J* = 7.5, H-6), 8.15 (*t*, *J* = 7.5, H-7), 8.45 (*d*, *J* = 7.5, H-8), 7.74 (*d*, *J* = 15.6, H-1′), 7.95 (*d*, *J* = 15.6, H-2′), 7.89 (*d*, *J* = 8.7, H-2″, H-6″), 7.02 (*d*, *J* = 8.7, H-3″, H-5″). Anal. calcd. for $C_{20}H_{20}INO$: C, 57.57; H, 4.83; N, 3.36; O, 3.83. Found: C, 57.45; H, 4.89; N, 3.37; O, 3.79.

2.2.4.1. (E)-2-(4-ethoxystyryl)-1-methylquinolinium 4-methylbenzenesulfonate ***(16)***. A 0.24 g (0.58 mmol) solution of **QET** in hot methanol (50 ml) was mixed with 0.20 g (0.58 mmol) of silver (I) 4-methylbenzenesulfonate in hot methanol (50 ml). The mixture turned to brown and cloudy immediately. After stirring for 30 min, the precipitate of silver iodide was filtered and the filtrate was evaporated to give a yellow solid. The resultant yellow solid was filtered off, washed with diethyl ether, dried in vacuo and purified by recrystallization. M.p. 219–221 °C, 0.14 g (54%) yield. UV (CH_3OH) λ_{max} (nm): 202.7, 217.6, 256.2, 413.9; IR (KBr) ν(cm^{-1}): νC=C; 1605 s, νC–O; 1233 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.52 (*s*, 1-CH_3), 1.39 (*t*, *J* = 7.2, CH_3), 4.09 (*q*, *J* = 7.2, OCH_2), 8.42 (*d*, *J* = 9.0, H-3), 8.85 (*d*, *J* = 9.0, H-4), 8.22 (*d*, *J* = 7.5, H-5), 7.83 (*t*, *J* = 7.5, H-6), 8.08 (*t*, *J* = 7.5, H-7), 8.05 (*d*, *J* = 7.5, H-8), 7.70 (*d*, *J* = 15.9, H-1′), 7.89 (*d*, *J* = 15.9, H-2′), 7.88 (*d*, *J* = 8.7, H-2″, H-6″), 6.95 (*d*, *J* = 8.7, H-3″, H-5″), 7.04 (*d*, *J* = 7.8, H-2‴, H-6‴), 7.58 (*d*, *J* = 7.8, H-3‴, H-5‴), 2.25 (*s*, 4‴-CH_3). Anal. calcd. for $C_{27}H_{27}NO_4S$: C, 70.25; H, 5.90; N, 3.03; S, 6.95; O, 13.87. Found: C, 70.20; H, 5.88; N, 3.01; S, 7.10; O, 13.81.

Compounds **17**–**20** were synthesized with identical procedure of **16** by replacing silver (I) 4-methylbenzenesulfonate with silver (I) 4-methoxybenzenesulfonate (for **17**), silver (I) 4-bromobenzenesulfonate (for **18**), silver (I) 4-chlorobenzenesulfonate (for **19**), and silver (I) 4-aminobenzenesulfonate (for **20**). All of the resulting solids were further purified by recrystallization.

2.2.4.2. (E)-2-(4-ethoxystyryl)-1-methylquinolinium 4-methoxybenzenesulfonate ***(17)***. M.p. 256–257 °C, 0.26 g (80%) yield. UV (CH_3OH) λ_{max} (nm): 330.3, 413.1; IR (KBr, cm^{-1}): νC=C; 1571 s, νC = O; 1219 s, νS = O; 1163 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.60 (*s*, 1-CH_3), 1.45 (*t*, *J* = 7.2, CH_3), 4.15 (*q*, *J* = 7.2, OCH_2), 8.47 (*d*, *J* = 9.0, H-3), 8.89 (*d*, *J* = 9.0, H-4), 8.25 (*d*, *J* = 7.5, H-5), 7.89 (*t*, *J* = 7.5, H-6), 8.18 (*t*, *J* = 7.5, H-7), 8.40 (*d*, *J* = 7.5, H-8), 7.70 (*d*, *J* = 15.6, H-1′), 8.09 (*d*, *J* = 15.6, H-2′), 7.85 (*d*, *J* = 8.7, H-2″, H-6″), 7.70 (*d*, *J* = 8.7, H-3″, H-5″), 7.01 (*d*, *J* = 7.8, H-2‴, H-6‴), 6.80 (*d*, *J* = 7.8, H-3‴, H-5‴), 3.78 (*s*, 4‴-OCH_3). Anal. calcd. for $C_{27}H_{27}NO_5S$: C, 67.90; H, 5.70; N, 2.93; S, 6.72; O, 16.75. Found: C, 67.92; H, 5.66; N, 2.90; S, 6.70; O, 16.82.

2.2.4.3. (E)-2-(4-ethoxystyryl)-1-methylquinolinium 4-bromobenzenesulfonate ***(18)***. M.p. 249–251 °C, 0.24 g (72%) yield. UV (CH_3OH) λ_{max} (nm): 221.0, 255.5, 413.9; IR (KBr, cm^{-1}): νC=C; 1591 s, νC = O; 1223 s, νS = O; 1168 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.60 (*s*, 1-CH_3), 1.43 (*t*, *J* = 7.1, CH_3), 4.15 (*q*, *J* = 7.1, OCH_2), 8.48 (*d*, *J* = 9.0, H-3), 8.89 (*d*, *J* = 9.0, H-4), 8.25 (*d*, *J* = 7.5, H-5), 7.87 (*t*, *J* = 7.5, H-6), 8.09 (*t*, *J* = 7.5, H-7), 8.44 (*d*, *J* = 7.5, H-8), 7.72 (*d*, *J* = 15.6, H-1′), 8.03 (*d*, *J* = 15.6, H-2′), 7.84 (*d*, *J* = 8.7, H-2″, H-6″), 6.98 (*d*, *J* = 8.7, H-3″, H-5″), 7.41 (*d*, *J* = 8.4, H-2‴, H-6‴), 7.60 (*d*, *J* = 8.4, H-3‴, H-5‴). Anal. calcd. for $C_{26}H_{24}BrNO_4S$: C, 59.32; H, 4.60; N, 2.66; S, 6.08; O, 12.16. Found: C, 59.29; H, 4.58; N, 2.60; S, 6.01; O, 12.32.

2.2.4.4. (E)-2-(4-ethoxystyryl)-1-methylquinolinium 4-chlorobenzenesulfonate ***(19)***. M.p. 254–256 °C, 0.26 g (84%) yield. UV (CH_3OH) λ_{max} (nm): 228.7, 268.4, 410.2; IR (KBr, cm^{-1}): νC=C; 1590 s, νC = O; 1224 s, νS = O; 1152 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.60 (*s*, 1-CH_3), 1.46 (*t*, *J* = 7.2, CH_3), 4.18 (*q*, *J* = 7.2, OCH_2), 8.45 (*d*, *J* = 9.0, H-3), 8.90 (*d*, *J* = 9.0, H-4), 8.28 (*d*, *J* = 7.8, H-5), 7.91 (*t*, *J* = 7.8, H-6), 8.12 (*t*, *J* = 7.8, H-7), 8.41 (*d*, *J* = 7.8, H-8), 7.72 (*d*, *J* = 15.9, H-1′), 8.10 (*d*, *J* = 15.9, H-2′), 7.88 (*d*, *J* = 8.7, H-2″, H-6″), 7.00 (*d*, *J* = 8.7, H-3″, H-5″), 7.30 (*d*, *J* = 8.7, H-2‴, H-6‴), 7.74 (*d*, *J* = 8.7, H-3‴, H-5‴). Anal. calcd. for $C_{26}H_{24}ClNO_4S$: C, 64.79; H, 5.02; N, 2.90; S, 6.65; O, 13.28. Found: C, 64.70; H, 5.17; N, 2.68; S, 6.60; O, 13.45.

2.2.4.5. (E)-2-(4-ethoxystyryl)-1-methylquinolinium 4-aminobenzenesulfonate ***(20)***. M.p. (decompose) 242–244 °C, 0.21 g (64%) yield. UV (CH_3OH) λ_{max} (nm): 204.0, 248.0, 302.0, 412.0; IR (KBr, cm^{-1}): νC=C; 1588 s, νC = O; 1221 s, νS = O; 1150 s; ^1H NMR (d_6-DMSO mixed with $CDCl_3$): δ 4.65 (*s*, 1-CH_3), 8.83 (*d*, *J* = 8.3, H-3), 8.39 (*d*, *J* = 8.3, H-4), 7.90 (*t*, *J* = 8.3, H-5), 8.19 (*t*, *J* = 8.3, H-6), 8.23 (*t*, *J* = 8.3, H-7), 8.24 (*d*, *J* = 8.3, H-8), 7.66 (*d*, *J* = 15.6, H-1′), 8.01 (*d*, *J* = 15.6, H-2′), 7.89 (*d*, *J* = 8.7, H-2″, H-6″), 7.01 (*d*, *J* = 8.7, H-3″, H-5″), 7.01 (*d*, *J* = 7.8, H-2‴, H-6‴), 7.85 (*d*, *J* = 7.8, H-3‴, H-5‴), 4.34 (*br s*, 4‴-NH_2). Anal. calcd. for $C_{26}H_{26}N_2O_4S$: C, 67.50; H, 5.67; N, 6.06; S, 6.93; O, 13.84. Found: C, 67.44; H, 5.88; N, 6.01; S, 6.81; O, 13.86.

All ^1H NMR spectra were available as supplementary materials.

2.3. Crystal structure determination

In addition, single crystals of compound 5 were obtained by recrystallization from methanol and further determined by X-ray diffraction analysis. Crystallographic data were collected on a Bruker SMART APEXII CCD area-detector diffractometer with a graphite monochromated Mo-Kα radiation (λ = 0.71073 Å) at 100.0(1) K with the Oxford Cryosystem Cobra low-temperature attachment. The collected data were reduced using SAINT and the empirical absorption corrections were performed using SADABS program [30]. The structures were solved by direct methods and refined by least-squares using the *SHELXTL* [31] software package. The crystallographic data, selected bond lengths, bond angles and torsion angles for compound **5** were listed in Tables 1 and 2, respectively. The hydrogen bonding geometries were listed in Table 3. X-ray ORTEP diagram and packing diagram of compound **5** are shown in Figs. 6 and 7, respectively.

3. Antibacterial assay

All of the purified compounds were tested against both Gram-positive bacteria i.e. *B. subtilis, E. faecalis, S. aureus,* Methicillin-Resistant *S. aureus* and Vancomycin-Resistant *E. faecalis* and Gram-negative bacteria i.e. *Pseudomonas aeruginosa, Salmonella typhi* and *S. sonnei*. Bacteria *S. typhi*, *S. sonnei, B. subtilis* and *P. aeruginosa* were obtained from culture collection, Department of Industrial Biotechnology and Department of Pharmacognosy and Botany, Prince of Songkla University. Methicillin-Resistant *S. aureus* (MRSA) ATCC 43300, Vancomycin-Resistant *E. faecalis* (VRE) ATCC 51299, *S. aureus* TISTR517 and *E. faecalis* TISTR459 were obtained from Microbial Research Center (MIRCEN), Bangkok, Thailand. The antimicrobial assay employed was the colorimetric microdilution broth technique using RPMI1640 medium and Alamar Blue as an indicator. Microbial inoculation were prepared as suspension in RPMI1640 medium and mixed with 1% 100× Alamar Blue indicator. The cell suspension was

Table 1
Crystal data and structure refinement parameters for the compound **5.**

Chemical formula: $C_{16}H_{19}N_2^+.C_6H_6NO_3S^-.H_2O$
Formula weight: 429.53
Crystal system: monoclinic
Space group: $P2_1/c$ $Z = 2$
$a = 6.9229(6)$ Å
$b = 12.6106(10)$ Å
$c = 11.9705(10)$ Å
$\beta = 94.849(6)^\circ$
$V = 1041.31(15)$ Å^3
$D_{cal} = 1.370$ g cm^{-3}
μ(Mo–K$_\alpha$) = 0.190 mm^{-1}
$T = 100.0(1)$ K
$F(000) = 456$
Crystal size = 0.53 × 0.33 × 0.25 mm^3
θ range for data collection 2.35–35.00°
$R = 0.1151$
$R_w = 0.3534$
No. of unique data measured = 8910
No. of observed data with [I ≥ 2σ(I)] = 8910
No. of parameters = 275
Goodness-of-fit = 1.104
$(\Delta\rho)_{max} = 2.502$ e. Å^{-3}
$(\Delta\rho)_{min} = -2.551$ e. Å^{-3}
Measurements; Bruker APEX2 CCD diffractometer
Program system: Apex2
Structure determination; direct method (SHELXTL)[11]
Refinement: full-matrix least-squares
CCDC759537 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif.

then transferred into a 96-well microliter plate (100 μl/well except for first row which contained 190 μl/well). Sample (10 μl) dissolved in DMSO at a concentration of 25 mg/ml was added to each well of the first row and mixed well with a micropipette. Half of the mixtures of cell suspension and compounds in the first rows were then transferred to the next well in the second row to perform a half-fold dilution. The dilution process was repeated as a sequence until the compounds were diluted 128 times in the last row. The excess 100 μl of the mixture in the last row was discarded. The plates were incubated at 37 °C for 8–12 h. The antimicrobial activity was determined as the MIC value which was the least concentration of the compound that could inhibit the change of Alamar Blue indicator from blue to red. All assays were repeated at least three times [32].

4. Result and discussion

4.1. Synthesis of all pyridinium and quinolinium stilbene derivatives

4.1.1. FT-IR and UV–vis spectroscopy

The (*E*)-2-(4-ethoxystyryl)-1-methylpyridinium iodide (**PET**) was conventionally prepared by refluxing the mixture of 1,2-dimethylpyridinium iodide, 4-ethoxybenzaldehyde and piperidine for 4 h in methanol. The product could be easily purified by recrystallization from methanol or ethanol [33]. All three stilbene iodide derivatives (**PAM**, **QAM** and **QET**) were achieved from the same synthesis method. The structures of all compounds were confirmed by UV–vis absorption spectra, IR, and ^{1}H NMR data.

Table 2
Selected bond lengths (Å), bond angles (o) and torsion angles (o) of compound **5.**

N2–C11	1.367(7)	O1W–H1W1	0.8501
N2–C15	1.471(8)	O1W–H2W1	0.8500
N1–C1	1.346(7)	S1–O1	1.446(4)
N1–C5	1.357(7)	S1–O2	1.459(5)
N1–C14	1.483(8)	S1–O3	1.474(4)
C6–C7	1.351(8)	S1–C17	1.773(5)
C11–N2–C16	120.5(5)	C15–N2–C16	119.9(5)
C5–N1–C1	121.9(5)	O1–S1–O2	112.9(3)
C5–N1–C14	120.6(5)	O1–S1–C17	106.6(3)
C4–C5–C6–C7	−4.7(9)	C16–N2–C11–C10	−174.5(5)
C5–C6–C7–C8	−179.3(6)	C15–N2–C11–C12	1.0(8)
C6–C7–C8–C13	−1.3(10)		

Table 3
Hydrogen bonding geometry (Å, o) of compound **5.**

D-H A	D-H	H…A	D…A	D–H…A
O1W–H1W1…O3	0.85	1.97	2.822(7)	180
O1W–H2W1…O1^{i}	0.85	2.04	2.849(7)	158
N3–H3B–O2^{ii}	0.86	2.44	3.193(8)	147
N3–H3C–O3^{iii}	0.86	2.21	3.041(7)	163
C1–H1A–O1W^{iv}	0.93	2.14	3.038(7)	162
C14–H14C–O3	0.96	2.58	3.398(8)	143
C19–H19A–O2^{ii}	0.93	2.48	3.286(7)	145
C21–H21A–O2^{iii}	0.93	2.59	3.495(7)	163
C22–H22A–O3	0.93	2.58	2.957(7)	105
C3–H3A…Cg_I^{v}	0.93	2.76	3.519(7)	140
C12–H12A…Cg_I	0.93	2.76	3.601(5)	150

Symmetry codes: (i) $1+x, y, z$; (ii) $-x, \frac{1}{2}+y, 1-z$; (iii) $1-x, \frac{1}{2}+y, 1-z$; (iv) $1-x, -\frac{1}{2}+y, -z$; (v) $x, y, -1+z$. Cg_I is the centroid of C17–C22 ring.

The UV–vis absorption spectra were made using methanol in the wavelength range of 200–800 nm. The UV–vis absorption spectrum of **5** was shown in Fig. 4. It should be mentioned that analysis of UV–vis spectra revealed *trans*-configuration for all obtained compounds since *trans*-stilbenes exhibit the values of λ_{max} in the range 290–360 nm [34,35]. The UV–vis spectra of quinolinium derivatives in methanol showed absorption bands between 200 and 415 nm. The position of the absorption maximum (ca. 415 nm) ascribed to the π–π^* transition of the quinolinium ring.

IR spectra of all compounds have been investigated in the frequency range 400–4000 cm^{-1} and shown typical aromatic absorption i.e. for compound **5** (Fig. 5), there were resonance conjugated unsaturated stretching modes in the chromophore (C=C at 1611 cm^{-1}) and C–N at 1297 cm^{-1}. The peak found at 1195 cm^{-1} wave number pertains to S=O bond of sulfonate.

4.1.2. Crystallographic study

The crystallographic-information file for the monohydrated of compound **5** has been deposited in the Cambridge Crystallographic Data Center as CCDC759537. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

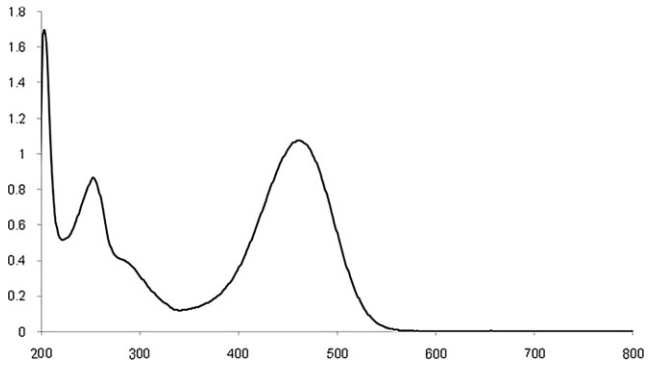


Fig. 4. UV–vis spectrum of compound **5** in CH_3OH.

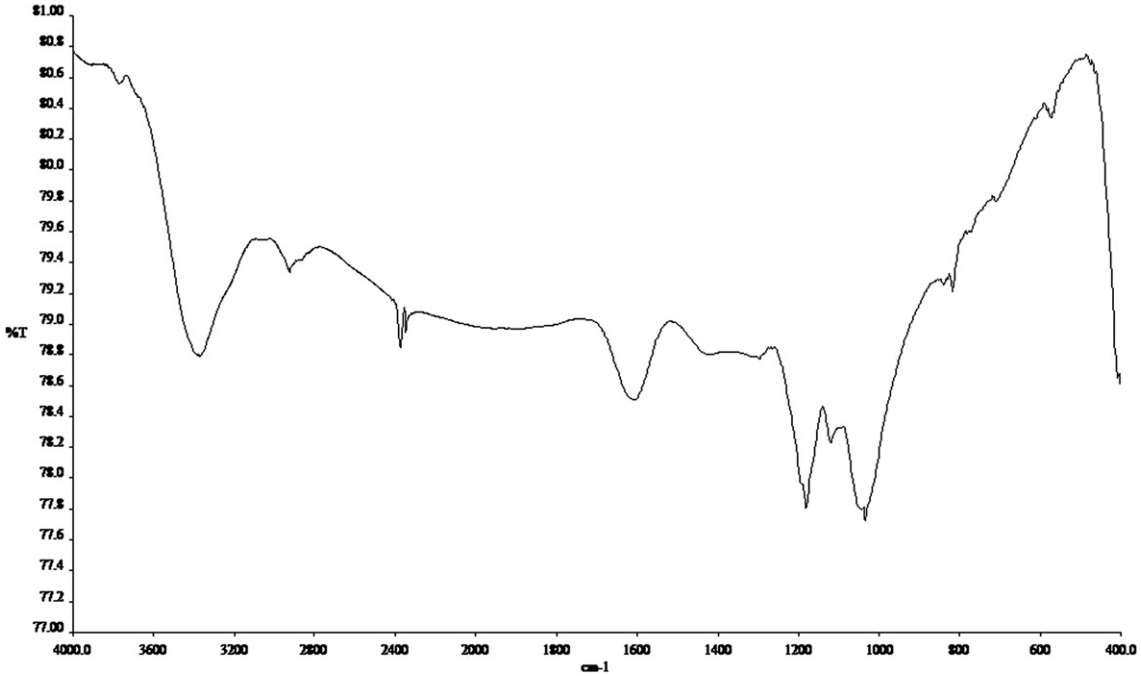


Fig. 5. FT-IR spectrum of compound **5**.

The crystallographic and experimental parameters used for data collection and determination of the structure are given in Table 1. All non-hydrogen atoms were refined anisotropically. All H atoms were positioned geometrically and allowed to ride on their parent atoms, with N–H = 0.86 Å, O–H = 0.85 Å, C–H = 0.93 Å for aromatic and CH and 0.96 Å for CH_3 atoms. The U_{iso} values were constrained to be $1.5U_{eq}$ of the carrier atom for methyl H atoms and $1.2U_{eq}$ for the remaining H atoms. The molecular structure and atom numbering of compound **5** are shown in Fig. 6, and the crystal packing is presented in Fig. 7. The selected bond lengths, bond angles and selected torsion angles were listed in Table 2. Compound **5** crystallizes in the $P2_1/c$ space group with $Z = 2$. The asymmetric unit of the title compound consists of a $C_{16}H_{19}N_2^+$ cation, a $C_6H_6NO_3S^-$ anion and one H_2O molecule (Fig. 6). This crystal is a twin with the ratio for the two twin components obtained by least-squares structure refinement being 0.639(6):0.361(6). The molecule exists in *trans*-configuration as indicated by the torsion angle C5–C6–C7–C8 = −179.3(6)° and slightly twisted with the dihedral angle between the pyridinium and the phenyl ring (C8–C13) being 7.3(3)°. It can be found that the carbon–carbon bond lengths of **5** are basically intermediate between typical C–C single (1.45 Å) and C=C double (1.35 Å) bonds. The dimethylamino is co-planar with the attached phenyl ring in which one methyl group is slightly deviated as indicated by torsion angles C15–N2–C11–C10 = 1.0(8)° and C16–N2–C11–C12 = 5.1(8)°. The anion is inclined to the cation with the dihedral angles between the benzene ring of the anion and pyridinium and benzene rings of the cation being 88.0(3) and 81.7(3)°, respectively.

In the crystal packing as shown in Fig. 7, the cations are linked with water molecules by weak C1–H1A…O1W interaction (symmetry code; $1 - x, -\frac{1}{2} + y, -z$) whereas the anions are linked with water molecules by O1W–H1W1…O3 (symmetry code; x, y, z) and O1W–H2W1…O1 (symmetry code; $1 + x, y, z$) hydrogen bonds (Table 3). The molecules are linked into two-dimensional network parallel to the *ab* plane by C–H…O and N–H…O hydrogen bonds and C–H…π interactions (Table 3). The crystal structure is further stabilized by C–H···π interactions involving pyridinium and anionic benzene rings with the C3–H3A…Cg_1 and C12–H12A…Cg_1 (Table 3, symmetry code; $x, y, -1 + z$ and x, y, z respectively); Cg_1 is the centroid of C17–C22 ring.

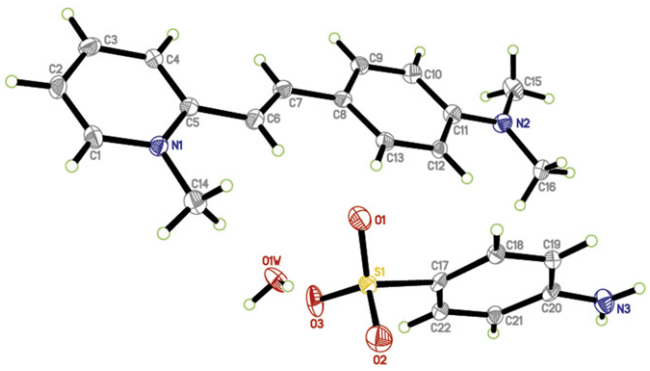


Fig. 6. The ORTEP plot of compound **5** showing the atom numbering scheme. Thermal ellipsoids of non-H atoms are drawn at the 50% probability level.

4.2. Biological results

The antibacterial activity results showed that these synthesized hybrid disinfectants exhibited interesting antibacterial activity in which all compounds were active against at least one of the tested strains and none of the compounds was totally inactive. The results suggested that this combination concept could lead to the potent antibacterial agents which can be easily modified by the variation of stilbene-QAC moiety or benzenesulfonate parts. The MIC values have proved that all compounds were active against MRSA and the main reason for the antibacterial activity in these hybrid compounds were related to the types of QAC-head groups.

Our antibacterial study (Table 4) showed that these compounds were more effective against Gram-positive than Gram-negative bacteria as generally found which may be due to the "intrinsic resistance" of Gram-negative bacteria [36,37]. In general,

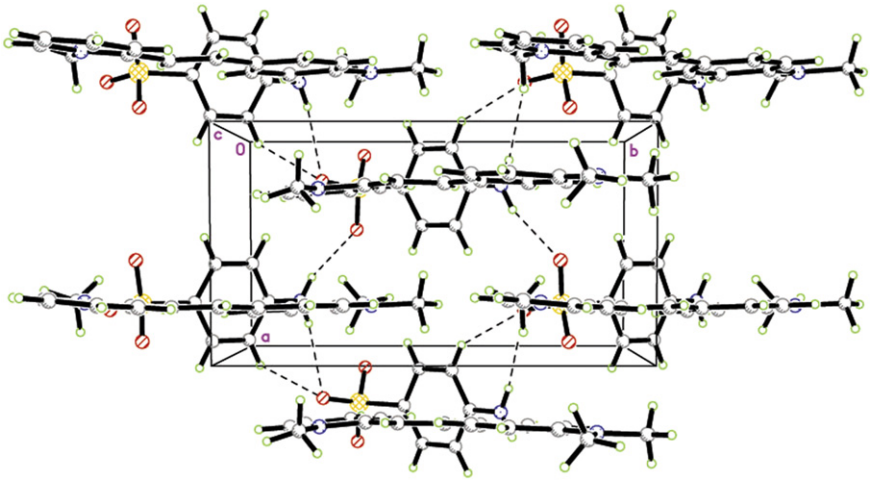


Fig. 7. The crystal packing of compound 5, viewed down the *c*-axis. Hydrogen bonds are shown as dashed lines.

quaternary ammonium halides such as 1-alkylpyridinium halides exhibit strong bacteriostatic activity against Gram-positive bacteria rather than those against Gram-negative bacteria [38]. In this study, the QAC-headgroups which are pyridinium and quinolinium, seem to be the key factor to the activity. The quinolinium headgroup-containing compounds exhibited more potent activity, especially against MRSA, than that of the pyridinium headgroup-containing compounds (see Table 4). Fig. 8 clearly showed the higher activity against MRSA ($1/\log MIC_{MRSA}$) of quinolinium (**11**–**20**) compared with pyridinium (**1**–**10**) derivatives.

The quinolinium derivatives (**11**–**20**) showed the better activity against Gram-positive than Gram-negative bacteria. Compounds **11**, **13** and **14** showed similar activity and were the most active compounds with the MICs value = 2.34 μg/ml against all tested Gram-positive bacteria and were better than that of the standard references BZK and vancomycin. For the tested results against

Table 4
Antibacterial activity of the synthesized compounds **PAM**, **PET**, **QAM**, **QET** and **1**–**20**.

Compound	MIC (μg/ml)							
	Gram-positive bacteria				Gram-negative bacteria			
	MRSA*	*S. aureus*	*B. subtilis*	VRE**	*E. faecalis*	*P. aeruginosa*	*S. typhi*	*S. sonnei*
PAM[a]	37.5	300	300	300	300	300	300	300
1	37.5	300	150	300	300	150	300	300
2	75	150	150	150	150	150	150	150
3	75	–	–	–	–	–	–	–
4	37.5	–	300	150	–	300	300	–
5	37.5	–	–	300	–	–	–	–
PET[b]	37.5	–	–	–	–	–	–	300
6	37.5	150	300	300	150	37.5	150	150
7	150	–	–	–	–	–	–	–
8	18.75	–	–	–	–	–	300	300
9	75	–	–	–	–	–	–	–
10	75	–	–	–	–	–	–	–
QAM[c]	9.37	18.75	9.37	4.68	18.75	300	300	4.68
11	2.34	2.34	2.34	2.34	2.34	300	300	2.34
12	2.34	–	75	150	150	–	–	150
13	2.34	2.34	2.34	2.34	2.34	300	300	2.34
14	2.34	2.34	2.34	2.34	2.34	300	300	2.34
15	2.34	75	18.75	18.75	75	150	75	75
QET[d]	2.34	–	37.5	37.5	75	–	–	150
16	2.34	–	9.37	37.5	37.5	–	–	150
17	2.34	–	18.75	18.75	75	–	–	150
18	2.34	300	18.75	18.75	37.5	–	–	75
19	2.34	–	75	150	75	–	–	300
20	4.68	37.5	37.5	75	37.5	–	75	75
BZK	9.37	<2.34	150	9.37	9.37	300	9.37	–
Vancomycin	<2.34	9.37	2.34	2.34	9.375	2.34	2.34	2.34

– No activity was observed up to 300 μg/mL.
* Methicillin-Resistant *S. aureus* ATCC 43300.
** Vancomycin-Resistant *E. faecalis* ATCC 51299.
[a] (*E*)-2-(4-(dimethylamino)styryl)-1-methylpyridinium iodide.
[b] (*E*)-2-(4-ethoxystyryl)-1-methylpyridinium iodide.
[c] (*E*)-2-(4-(dimethylamino)styryl)-1-methylquinolinium iodide.
[d] (*E*)-2-(4-ethoxystyryl)-1-methylquinolinium iodide.

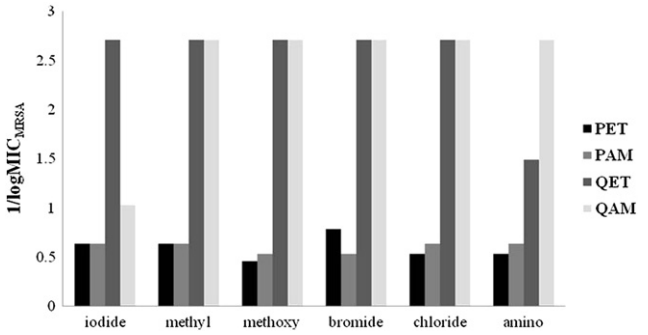


Fig. 8. The comparison of antimicrobial activities between pyridinium and quinolinium stilbenes salts against Methicillin-Resistant *S. aureus* ATCC 43300.

Gram-negative bacteria, compounds **11**, **13** and **14** were very active only against *S. sonnei* (MICs = 2.34 μg/ml) while all quinolinium derivatives were inactive against the rest Gram-negative bacteria (*P. aeruginosa* and *S. typhi*).

While comparing between two quinolinium derivatives series i.e. compounds **11**–**15** (dimethylamino-containing compounds) and compounds **16**–**20** (ethoxy-containing compounds), the results showed that both series showed the desirable activity with a bit different characteristic in which compounds **11**–**15** showed broad band spectrum against the tested Gram-positive and one Gram-negative (*S. sonnei*) whereas compounds **16**–**20** showed the very specific activity against only MRSA.

The pyridinium derivatives (**1**–**5** and **6**–**10** series) showed moderate to low activity against MRSA and low activity against the rest Gram-positive bacteria (*S. aureus, B. subtilis, E. faecalis* and Vancomycin-Resistant *E. faecalis*). These compounds were inactive against all tested Gram-negative bacteria (MICs > 150 μg/ml). While comparing between the two pyridinium derivatives series i.e. **1**–**5** and **6**–**10** series, it was found that the activity of **1**–**5** series was better than that of **6**–**10** which might be due to the presence of the dimethylamino group which was able to enhance the activity compared to the effect of the methoxy group in the **6**–**10** series.

All pyridinium derivatives (**1**–**10**) were less potent than the standard BZK and vancomycin so it might be concluded that the pyridinium-QAC-headgroup was not the promising molecular parameter for this hybrid antibacterial agents. However, compounds **1**, **2** and **6** were the most active compounds among the pyridinium derivatives with MIC values ranging from 37.5 to 300 μg/ml for the Gram-positive antibacterial activity.

From the antibacterial activity results (Table 4) it was seen that when the benzenesulfonate moiety was introduced (in **1**–**20**) in place of I^- (in **PAM**, **PET**, **QAM**, **QET**) the activity were clearly changed with the MIC values changing from 9.37 μg/ml in **QAM** to 2.34 μg/ml in compound **11**. The introduction of 4-substituted-benzenesulfonate part seems to promote the activity by 2–4 times only in quinolinium derivatives (**11**–**20**), especially in compounds **11**, **13** and **14**. However, the introduction of 4-substituted-benzenesulfonate moiety did not significantly enhance the antibacterial activity for the pyridinium derivatives as displayed by the comparison the antibacterial activity between iodide-containing and 4-substituted-benzenesulfonate-containing compounds for example, by changing from iodide (in **PET**) to 4-methylbenzenesulfonate (in compound **6**). The comparative antibacterial activity against MRSA can also be found in compounds **PAM** and compound **1** (see Table 4).

5. Conclusion

The new class of hybrid disinfectants were synthesized and reported in this study. The structural characterizations of the synthesized compounds were made by the spectroscopic methods. The structure of compound **5** was also confirmed by single crystal X-ray diffraction studies. All compounds showed the antibacterial activities as expected and the quinolinium derivatives displayed more potent activity than that of the pyridinium derivatives against the bacteria tested, whereas the dimethylamino-containing series exhibited better activity than ethoxy-containing series. The hybrid between quinolinium-QAC and sulfonamide-like structures showed good antibacterial activity. Among all compounds, **11**–**15** are wide-spectrum antibacterial substances while compounds **16**–**20** showed very specific activity against MRSA. For the wide-spectrum antibacterial substances, compounds **11**, **13** and **14** are the most active compounds which indicated the dominant antibacterial effect of quinolinium-QAC-headgroup and dimethylamino group.

Acknowledgements

KC thanks the Development and Promotion of Science and Technology Talents Project (DPST) and the Center of Excellence for Innovation in Chemistry (PERCH-CIC) for financial support. She also thanks Mr. Nawong Boonnak for his useful suggestions and Miss Thawanrat Kobkeatthawin for providing some starting materials for this work. The authors also thank the Prince of Songkla University, the Malaysian Government and Universiti Sains Malaysia for the Research University Golden Goose grant No. 1001/PFIZIK/811012.

Appendix. Supplementary data

Crystallographic data of compound **5** has been deposited at the CCDC as supplementary data, CCDC No. 759537. Copies of the data were available at CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. E-mail: deposit@ccdc.-cam.ac.uk. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ejmech.2010.06.014.

References

[1] D. Demberelnyamba, K.-S. Kim, S. Choi, S.-Y. Park, H. Lee, C.-J. Kim, I.-D. Yoo, Bioorg. Med. Chem. 12 (2004) 853–857.
[2] S.S. Block, Disinfection, Sterilization, and Preservation, fifth ed. Lippincott Williams & Wilkins, Philadelphia, U.S.A, 2001.
[3] J. Pernak, J. Kalewska, H. Ksycifiska, J. Cybulski, Eur. J. Med. Chem. 36 (2001) 899–907.
[4] E. Fisicaro, M. Barbieri, E. Pelizzetti, P.J. Savarino, Chem. Soc. Faraday Trans. 87 (1991) 2983–2987.
[5] A.O. de Souza, C. Fabio, S. Galetti, L. Célio Silva, B. Bicalho, M.M. Parma, S. F. Fonseca, A.J. Marsaioli, Angela C.L.B. Trindade, R.P.F. Gil, F.S. Bezerra, M. Andrade-Neto, C. Maria, F. de Oliveira, Quim. Nova 30 (2007) 1563–1566.
[6] T. Maeda, Y. Manabe, M. Yamamoto, M. Yoshida, K. Okazaki, H. Nagamune, H. Kourai, Chem. Pharm. Bull. 47 (1999) 1020–1023.
[7] J. Reuda, J.A. Lázaro, J. Ducha, Rev. Sci. Tech. 22 (2003) 1097–1104.
[8] D.A. Basketter, M. Marriott, N.J. Gilmour, I.R. White, Contact Derm. 50 (2004) 213–217.
[9] B.H. Lee, S.-H. Kim, Korean J. Int. Med. 22 (2007) 244–248.
[10] M. Braoudaki, A.C. Hilton, Int. J. Antimicrob. Agents 25 (2005) 31–37.
[11] Y. Sakagami, H. Yokoyama, H. Nishimura, Y. Ose, T. Tashima, Appl. Environ. Microbiol. 55 (1989) 2036–2040.
[12] H. Nikaido, Biochim. Biophys. Acta 433 (1976) 118–132.
[13] H. Nikaido, T. Nakae, Adv. Microb. Physiol. 20 (1979) 163–250.
[14] E. Bore, M. Hébraud, I. Chafsey, C. Chambon, C. Skjæret, B. Moen, T. Møretrø, Ø. Langsrud, K. Rudi1, S. Langsrud, Microbiology 153 (2007) 935–946.
[15] E. Wyrzykiewicza, M. Wendzonka, B. Kędzia, Eur. J. Med. Chem. 41 (2006) 519–525.
[16] A. Skrzypczak, B. Brycki, I. Mirska, J. Pernak, Eur. J. Med. Chem. 32 (1997) 661–668.
[17] M. Diz, A. Manresa, A. Pinazo, P. Erra, M.R. Infante, J. Chem. Soc. Perkin Trans. 2 (1994) 1871–1876.
[18] M. Pavlikova, Y. Lacko, F. Devinsky, D. Mlynarcik, Coll. Czech. Chem. Comm. 60 (1995) 1213–1227.
[19] J. Pernak, I. Mirska, R. Kmiecik, Eur. J. Med. Chem. 34 (1999) 765–771.
[20] M. Wainwright, J. Antimicrob. Chemother. 47 (2001) 1–13.

[21] M. Spasova, N. Manolova, D. Paneva, R. Mincheva, P. Dubois, I. Rashkov, V. Maximova, D. Danchev, Biomacromolecules 11 (2010) 151–159.
[22] A.R. Martin, F.L. Rose, Biochem. J. 39 (1945) 91–95.
[23] P.M. Sivakumar, G. Sheshayan, M. Doble, Chem. Biol. Drug Des. 72 (2008) 303–313.
[24] G. Domagk, Klin. Wschr 16 (1937) 1412–1418.
[25] O.W. Barlow, Proc. Soc. Exp. Biol. Med. 37 (1937) 315.
[26] S. Chantrapromma, T. Suwanwong, H.-K. Fun, Acta. Crystallogr. E63 (2007) o821–o823.
[27] S. Chantrapromma, K. Chanawanno, H.-K. Fun, Acta. Crystallogr. E65 (2009) o1884–o1885.
[28] S. Chantrapromma, P. Ruanwas, H.-K. Fun, C. Karalai, Acta. Crystallogr. E64 (2008) o2072–o2073.
[29] S. Chantrapromma, P. Rodwatcharapiban, H.-K. Fun, Acta. Crystallogr. E62 (2006) o5689–o5691.
[30] Bruker, APEX2 (Version 2.1-4), SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, USA, 2005.
[31] G.M. Sheldrick, Acta. Crystallogr. A64 (2008) 112–122.
[32] A. Kanjana-Opas, Ph.D. Thesis, University of California, San Diego, 2002.
[33] C. Laksana, P. Ruanwas, S. Chantrapromma, H.-K. Fun, Acta. Crystallogr. E64 (2008) o145–o146.
[34] H.W. Thompson, P. Torkington, J. Chem. Soc. 184 (1945) 640–645.
[35] M. Oki, H. Kunimoto, Spectrochim. Acta 19 (1963) 1463–1471.
[36] A.R.M. Cutheon, S.M. Ellis, R.E.W. Hancock, G.H.N. Towers, J. Ethnopharmacol. 37 (1992) 213–223.
[37] N.V. Loginova, T.V. Kovalchuk, R.A. Zheldakova, N.P. Osipovich, V.L. Sorokin, G. I. Polozov, G.A. Ksedzova, G.K. Glushonak, A.A. Chernyavskaya, O.I. Shadyro, Bioorg. Med. Chem. Lett. 16 (2006) 5403–5407.
[38] H. Kourai, H. Takechi, M. Kume, K. Takeichi, I. Shibasaki, J. Antibact. Antifung. Agents 14 (1986) 55–63.