ORIGINAL ARTICLE



Synthesis, Surface Activity, and Antimicrobial Efficacy of Hydrogenated Cardanol-Derived Positively Charged Asymmetric Gemini Surfactants

Mengen Huang¹ · Jingyi Ma¹ · Xunshen Wu¹ · Min Zhao² · Limin Wang^{1,3} · Fei Che⁴ · Hui Qian⁴

Received: 29 November 2018 / Accepted: 3 May 2019 © 2019 AOCS

Abstract Nine different hydrogenated cardanol-based quaternary ammonium compounds including one conventional single-tale single-head surfactant, one bicephalic single-tale double-head surfactant, and seven asymmetric Gemini surfactants were synthetized using a simple process with high yields. Their structures were characterized using ¹H NMR, ¹³C NMR, and high-resolution mass spectral studies. Their surface active properties were evaluated by the wilhelmy plate method at 25 °C and physical parameters like CMC, γ_{CMC} , π_{CMC} , C₂₀, τ_{CMC} , and A_{\min} were calculated. The Krafft temperature values of C-BP-1, C-BP-4, and C-BP-6 are lower than 0 °C, suggesting high-potential industrial application. All synthesized compounds but C-BP-F exhibit great antimicrobial ability against Gram-positive bacteria (S. aureus [ATCC 25923] and C. glutamicum [ATCC 13032]) while inadequate antimicrobial ability against Gram negative strains (E. coli [ATCC 25922] and P. aeruginosa [ATCC 27853]).

Keywords Cardanol · Quaternary ammonium compound · Gemini surfactant · Antimicrobial agent

Limin Wang wanglimin@ecust.edu.cn

- ¹ Key Laboratory for Advanced Materials, Institute of Fine Chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai, 200237, P. R. China
- ² School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai, 200237, P. R. China
- ³ Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, 345 Lingling Road, Shanghai, 200032, P. R. China
- ⁴ Shanghai Bronkow Chemical Co., Ltd., Chuangtong Road 88, Jinshan District, Shanghai, 201512, China

J Surfact Deterg (2019).

Introduction

Humankind has been utilizing fossil fuel resources in the fields of energy production and synthesis of petroleumoriginated products for centuries (Danner and Braun, 1999). Because the total amount of petroleum feedstock is limited and chemicals originated from fossil fuels cannot be degradable, many academic and industrial groups have begun to investigate renewable resources as potential alternatives. To date, research in the categories of plant-based resources and animal-based resources such as polysaccharides, lignin, tannins, vegetable oils, and proteins has generated a vast library of sustainable materials (Ragauskas et al., 2006).

Among the investigated biorenewable resources, cashew nut shell liquid (CNSL) has attracted the attention of many research groups owing to its straightforward isolation process promising high yields and versatile derivatization possibilities. CNSL is a by-product originating from the cashew nut (Anacardium occidentale L.) processing industry (Voirin et al., 2014). Its annual production has reached approximately 450,000 metric tons in 2011 and it was promised that it will reach 600,000 metric tons in the near future (Attanasi et al., 2006; Balachandran et al., 2013). CNSL locates in the brown-colored mesocarp of the unprocessed nut, accounts for 18-27% of the total unshelled nut weight, and can be extracted from the mesoscarp via diverse processes like mechanical extraction, solvent extraction, hot oil bath, etc. (Balachandran et al., 2013). The compositions of CNSL mainly depend on the extraction method adopted. And, it generally contains cardanol, cardol, anacardic acid, 2-methyl



Fig. 1 Chemical structure of CNSL compositions

cardol, and polymeric materials with their structures shown in Fig. 1. During the subsequent process of double vacuum distillation (at 3-4 mm torr), thermal decarboxylation occurs under heating and cardanol is collected at a boiling point of 220 ± 15 °C as a transparent yellowish liquid (Anilkumar, 2017). Cardanol is a mixture of four meta-alkyl phenols differing in the degree of unsaturation of the meta-alkyl chain. To be specific, it contains 3-(pentadecyl)-phenol (5%), 3-(8Zpentadecenvl)-phenol (49%), 3-(8Z,11Z-pentadecadienvl)phenol (17%), and 3-(8Z,11Z,14-pentadecatrienyl)-phenol (29%).

As shown in Fig. 2, in the structure of cardanol locates a reactive phenolic -OH group, meta-alkyl chain with different numbers of cis double bonds and an aromatic ring. Bearing these three active sites in one molecule, cardanol serves as a promising starting molecule allowing for chemical modification to obtain a vast library of functional chemicals. And, because it is relatively difficult to synthesize phenol with a side long alkyl chain at the meta position, cardanol could be adopted as a natural phenol-based monomer with a meta-substituted alkyl chain for further functionalization. Research focusing on the derivatization of cardanol has successfully converted this scaffold into various functional chemicals such as antioxidants (Amorati et al., 2011), fluorescent markers (Braga et al., 2017), thermosets (Nguyen et al., 2017), flame retardants (Amarnath et al., 2017), electrodes (Molji et al., 2017), etc. The metasubstituted long alkyl chain with odd-numbered carbon atoms has brought cardanol with intrinsic hydrophobicity and amphiphilicity. And, various types of derivatization on the phenolic -OH group or aromatic ring have contributed to a vast library of cardanol-based anionic surfactants (Ahire and Bhagwat, 2017; Bruce et al., 2009; Castro Dantas et al., 2008; Kattimuttathu et al., 2011; Peungjitton et al., 2008; Scorzza et al., 2009), nonionic surfactants



Fig. 2 Chemical structure of cardanol

(Atta et al., 2018; Tyman and Bruce, 2003, 2004), and cationic amphiphilic compounds (Bhadani et al., 2011; Ezzat et al., 2017; Wang et al., 2016).

Gemini surfactant is a special class of amphiphile having two polar heads as well as two hydrophobic chains together in one molecule. The linker or spacer connecting two surfactant monomers usually exists between two polar heads or at the location of alkyl chain, which is very near to the hydrophilic heads (Mondal et al., 2015; Sharma and Ilies, 2014). Presenting unique surface-active properties like lower critical micelle concentrations (CMC), Gemini surfactant has been an interest in the surfactant area for more than 30 years (Menger and Keiper, 2000; Monger and Littau, 1991). Meanwhile, quaternary ammonium compound (QAC) is an important class of antiseptics, exhibiting antibacterial ability via first being electrostatically attracted to the negatively charged cell membrane of bacteria and second leading to the disruption of cell membrane, leakage of cytoplasm, and death of the microorganism (Tischer et al., 2012).

While many research studies in the field of cardanolderived surfactants have been published, cardanol-based asymmetric Gemini cationic surfactants with a rigid linker group and their use as antimicrobial agents have never been published before. In this work, hydrogenated cardanol has been successfully converted into a series of positively charged asymmetric Gemini surfactants with their structures confirmed using ¹H NMR, ¹³C NMR, and high-resolution mass spectral studies. The surface-active properties were evaluated with physical parameters like CMC, γ_{CMC} (surface tension at CMC), Π_{CMC} (surface pressure), C_{20} (adsorption efficiency), $\tau_{\rm CMC}$ (maximum surface excess concentration), and A_{\min} (minimum surface area per molecule) being calculated and compared with other published Gemini cationic surfactants. The Krafft temperature was measured. The antibacterial efficacy of this series of compounds was assessed on two strains of Gram-positive bacteria (S. aureus and C. glutamicum) and two strains of Gram-negative bacteria (E. coli and P. aeruginosa) with minimum inhibitory concentration (MIC) values measured. It was suggested that four water soluble QAC, C-BP, C-BP-1, C-BP-4, and C-BP-6, exhibited excellent surface-active ability with CMC values lower than 15 μ mol L⁻¹. Meanwhile, all QAC but C-BP-F exhibit great antimicrobial ability toward Gram-positive S. aureus and C. glutamicum with corresponding MIC values lower than 64 μ g mL⁻¹.

WILEY ACCS 🕷

Experimental Section

Materials and Characterization Methods

All reagents and solvents were of analytical grade and were purchased commercially. All solvents were used as received unless otherwise mentioned. The ¹H NMR (400 MHz, TMS) and ¹³C NMR (100 MHz, TMS) spectra were obtained using a Bruker AM-500 spectrometer with *J* values being listed in Hertz. Melting point values were measured using a SGW X-4 melting point apparatus supplied by Shanghai Precision & Scientific Instrument Co. Ltd. (Anting District, Shanghai, China) with all data uncorrected. The high-resolution mass spectra were measured on a Micromass GTC spectrometer.

Organic Synthesis

The synthetic route for target compounds is illustrated in Scheme 1. Nine hydrogenated cardanol-derived QAC were obtained with their chemical structures listed in Fig. 3.

Synthesis of Cardanol-Derived Conventional Cationic Surfactant (C-BP)

Two steps are required to obtain C-BP. First, into a 500 mL round-bottom flask, (*E*)-1,4-dibromobut-2-ene 12.83 g (60 mmol), anhydrous K_2CO_3 16.58 g (120 mmol), and 100 mL of acetone were added. Agitation was started to fully dissolve (*E*)-1,4-dibromobut-2-ene. Meanwhile, 6.09 g (20 mmol) of hydrogenated

cardanol was added into a 50 mL flask containing 20 mL of acetone and mixed to obtain a clear and brownish solution. The hydrogenated cardanol solution was slowly dripped into the 500 mL round-bottom flask containing (E)-1,4-dibromobut-2-ene dissolved in acetone and the mixture was then heated to 56 °C. After 24 h of reaction, the mixture was cooled to room temperature and filtrated to remove the solid K₂CO₃. Meanwhile, the obtained liquid was subjected to column chromatography on silica gel eluted with pure petroleum ether to yield the intermediate product C-Br. Second, into a reaction tube, C-Br 0.43 g (1 mmol), 4,4'-bipyridine 0.78 g (5 mmol), and DMF were added. The reaction mixture was heated to 80 °C for 22 h. After completion of the reaction, the mixture was cooled to room temperature followed by dropwise addition of diethyl ether. White solid (the targeting product C-BP) was noticed, filtrated, and finally recrystallized from MeOH/EA (1:10, by vol).

C-Br

Yield in 54%, as a yellow liquid, ¹H NMR (400 MHz, CDCl₃): δ 7.15–7.19 (m, 1H), 6.69–6.79 (m, 3H), 5.95–6.10 (m, 2H), 4.52–4.53 (d, J = 4.0 Hz, 2H), 3.97–3.98 (d, J = 4.0 Hz, 2H), 2.54–2.58 (t, J = 8.0 Hz, 2H), 1.58–1.61 (m, 2H), 1.25–1.30 (m, 24H), and 0.87–0.89 (t, J = 4.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 153.15, 139.48, 125.07, 123.95, 123.87, 116.04, 109.73, 106.33, 61.88, 30.81, 26.46, 26.17, 24.19, 24.33, 24.17, 17.5, and 8.93. HRMS (ESI-TOF) *m/z*: [M + H] + Calcd for C₂₅H₄₂BrO 437.2419; Found 437.2418.



Scheme 1 Synthetic routes for the target hydrogenated cardanol-based quaternary ammonium compounds

WILEY ACCS*



Fig. 3 Chemical structure of hydrogenated cardanol-based quaternary ammonium compounds

C-BP

Yield in 87%, as a pale white solid, m.p. 61.6–64.9 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.08–9.10 (d, J = 8.0 Hz, 2H), 8.83–8.84 (d, J = 4.0 Hz, 2H), 8.52–8.53 (d, J = 4.0 Hz, 2H), 7.98–8.00 (d, J = 8.0 Hz, 2H), 7.14–7.18 (m, 1H), 6.72–6.77 (m, 3H), 6.20–6.39 (m, 2H), 5.35–5.36 (d, J = 4.0 Hz, 2H), 4.65–4.66 (d, J = 4.0 Hz, 2H), 2.53–2.57 (t, J = 8.0 Hz, 2H), 1.55–1.59 (m, 2H), 1.27–1.30 (m, 24H), and 0.87–0.91 (t, J = 8.0 Hz, 3H); ¹³C NMR (101 MHz, CD₃OD): δ 159.75, 151.84, 150.96, 145.87, 143.62, 137.06, 130.34, 127.20, 124.78, 123.58, 122.43, 115.97, 112.79, 110.11, 67.77, 63.43, 36.94, 33.08, 32.65, 30.77, 30.48, 30.34, 23.74, and 14.44. HRMS (ESI-TOF) *m/z*: [M-Br]⁺ Calcd for C₃₅H₄₉N₂O 513.3839; Found 513.3837.

Synthesis of Cardanol-Derived Bicephalic and Gemini Cationic Surfactants (C-BP-R)

Three subsequent steps are required to obtain a series of nine C-BP-R. First, C-Br was synthesized as mentioned above. Second, in accordance to work published by Kevin P. C. Minbiole's group, two efficient routes of synthesizing BP-1 and BP-R were adopted with minor modifications (Grenier et al., 2012). Briefly, to obtain BP-1, 4,4'bipyridine 3.12 g (20 mmol) and CH₃I (1.5 mL, 24 mmol) were, respectively, dissolved in dichlormethane (DCM). The DCM solution of CH₃I was added dropwise into 4,4'bipyridine, followed by heating to 40 °C and reacting for an hour. After cooling to room temperature, yellow precipitate was observed, filtrated, and recrystallized from MeOH to obtain the intermediate compound BP-1. To obtain BP-R, 4,4'-bipyridine 2.34 g (15 mmol), corresponding alkyl halide (3 mmol) and anhydrous acetonitrile were added into a reaction tube pretreated with water removal and argon filling. The mixture was maintained at 82 °C for 18 h. After cooling to room temperature, noticeable solid was precipitated out, filtrated and recrystallized from MeOH/EA (1:10, by vol) as intermediate compound BP-R. Finally, into a dry reaction tube pre-installed with an argon atmosphere, C-Br 0.525 g (1.2 mmol) and corresponding BP-1 or BP-R (1 mmol) were added. After reacting at 82 °C for 18 h, target compounds were precipitated, filtrated, and washed with anhydrous acetonitrile (15 mL \times 3).

WILEY ACCS*

C-BP-1

Yield in 82%, as a red solid, m.p. 194.8–197.7 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.25–9.27 (d, J = 8.0 Hz, 2H), 9.19–9.21 (d, J = 8.0 Hz, 2H), 8.66–8.70 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.77 (m, 3H), 6.23–6.45 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 4.54 (s, 3H), 2.54–2.57 (t, J = 6.0 Hz, 2H), 1.55–1.62 (m, 2H), 1.28–1.31 (m, 24H), and 0.88–0.91 (t, J = 6.0 Hz, 3H); ¹³C NMR (101 MHz, CD₃OD): δ 159.78, 150.97, 145.87, 137.51, 130.37, 128.39, 128.04, 124.46, 122.41, 116.01, 112.74, 67.82, 63.94, 36.97, 33.10, 32.69, 30.79, 30.50, 30.39, 23.77, and 14.49. HRMS (ESI-TOF) *m/z*: [M-Br-I]²⁺ Calcd for C₃₆H₅₂N₂O 264.2034; Found 264.2029.

C-BP-4

Yield in 91%, as a pale yellow solid, m.p. 201.3–203.7 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.29–9.30 (d, J = 4.0 Hz, 2H), 9.25–9.27 (d, J = 8.0 Hz, 2H), 8.69–8.71 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.78 (m, 3H), 6.23–6.44 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.74–4.78 (t, J = 8.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 2.54–2.58 (t, J = 8.0 Hz, 2H), 2.04–2.12 (m, 2H), 1.55–1.62 (m, 2H), 1.28–1.31 (m, 24H), 1.02–1.06 (t, J = 8.0 Hz, 3H), and 0.88–0.91 (t, J = 6.0 Hz, 3H); ¹³C NMR (101 MHz, CD₃OD): δ 159.77, 151.69, 145.88, 137.49, 130.35, 128.38, 124.44, 122.43, 121.36, 115.98, 112.71, 67.78, 63.96, 63.12, 36.95, 34.50, 32.67, 30.76, 30.48, 30.36, 23.75, 20.50, 14.46, and 13.79. HRMS (ESI-TOF) m/z: [M-2Br]²⁺ Calcd for C₃₉H₅₈N₂O 285.2269; Found 285.2271.

C-BP-6

Yield in 88%, as a pale yellow solid, m.p. 200.4–202.1 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.28–9.30 (d, J = 8.0 Hz, 2H), 9.25–9.27 (d, J = 8.0 Hz, 2H), 8.69–8.70 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.78 (m, 3H), 6.23–6.44 (m, 2H), 5.43–5.44 (d, J = 4.0 Hz, 2H), 4.74–4.77 (t, J = 6.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 2.54–2.58 (t, J = 8.0 Hz, 2H), 2.06–2.13 (m, 2H), 1.55–1.62 (m, 2H), 1.28–1.47 (m, 30H), 0.88–0.95 (m, 6H); ¹³C NMR (101 MHz, CD₃OD): δ 159.77, 151.69, 145.88, 137.49, 130.35, 128.37, 124.44, 122.43, 121.20, 115.98, 112.70, 67.77, 63.97, 63.34, 36.95, 33.09, 32.66, 32.56, 30.76, 30.48, 30.36, 26.93, 23.75, 23.52, 14.45, 14.28. HRMS (ESI-TOF) m/z: [M-2Br]²⁺ Calcd for C₄₁H₆₂N₂O 299.2426; Found 299.2419.

C-BP-8

Yield in 85%, as a pale yellow solid, m.p. 200.8–202.4 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.29–9.30 (d, J = 4.0 Hz, 2H), 9.25–9.27 (d, J = 8.0 Hz, 2H), 8.69–8.71 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.78 (m, 3H), 6.23–6.44 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.74–4.77 (t, J = 6.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 2.54–2.57 (t, J = 6.0 Hz, 2H), 2.06–2.13 (m, 2H), 1.55–1.62 (m, 2H), 1.28–1.44 (m, 34H), and 0.88–0.92 (m, 6H); ¹³C NMR (101 MHz, CD₃OD): δ 159.77, 151.69, 145.88, 137.49, 130.35, 128.38, 124.45, 122.43, 121.63, 115.99, 112.71, 67.78, 63.96, 63.36, 36.95, 33.09, 32.90, 32.66, 32.61, 30.76, 30.48, 30.36, 30.14, 27.26, 23.75, 23.68, 14.46, and 14.41. HRMS (ESI-TOF) m/z: [M-2Br]²⁺ Calcd for C₄₃H₆₆N₂O 313.2582; Found 313.2589.

C-BP-10

Yield in 89%, as a pale yellow solid, m.p. 201.2–203.5 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.29–9.30 (d, J = 4.0 Hz, 2H), 9.25–9.27 (d, J = 8.0 Hz, 2H), 8.69–8.71 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.77 (m, 3H), 6.23–6.45 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.74–4.77 (t, J = 6.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 2.54–2.57 (t, J = 6.0 Hz, 2H), 2.06–2.13 (m, 2H), 1.53–1.61 (m, 2H), 1.27–1.44 (m, 38H), and 0.87–0.91 (t, J = 8.0 Hz, 6H); ¹³C NMR (101 MHz, CD₃OD): δ 159.77, 151.27, 145.87, 137.49, 130.35, 128.39, 124.46, 122.42, 121.42, 116.00, 112.71, 67.79, 63.95, 63.37, 36.96, 33.09, 33.05, 32.67, 32.61, 30.77, 30.62, 30.55, 30.42, 30.18, 27.27, 23.71, and 14.44. HRMS (ESI-TOF) m/z: [M-2Br]²⁺ Calcd for C₄₅H₇₀N₂O 327.2738; Found 327.2732.

C-BP-12

Yield in 79%, as a pale yellow solid, m.p. 200.3–203.1 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.28–9.30 (d, J = 8.0 Hz, 2H), 9.25–9.27 (d, J = 8.0 Hz, 2H), 8.68–8.71 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.78 (m, 3H), 6.24–6.43 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.73–4.77 (t, J = 8.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 2.54–2.57 (t, J = 6.0 Hz, 2H), 2.06–2.13 (m, 2H), 1.55–1.62 (m, 2H), 1.28–1.44 (m, 42H), and 0.87–0.91 (t, J = 8.0 Hz, 6H); ¹³C NMR (101 MHz, CD₃OD): δ 159.77, 151.29, 145.88, 137.49, 130.35, 129.85, 124.45, 122.43, 115.96, 112.70, 67.78, 63.96, 63.37, 36.95, 33.08, 32.67, 32.61, 30.76, 30.48, 30.36, 30.18, 27.27, 23.75, and 14.45. HRMS (ESI-TOF) m/z: [M-2Br]²⁺ Calcd for C₄₇H₇₄N₂O 341.2895; Found 341.2908.

C-BP-14

Yield in 83%, as a pale yellow solid, m.p. 201.1–203.5 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.28–9.30 (d, J = 8.0 Hz, 2H), 9.25–9.27 (d, J = 8.0 Hz, 2H), 8.69–8.71 (m, 4H), 7.14–7.18 (m, 1H), 6.73–6.77 (m, 3H), 6.23–6.44 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.74–4.77 (t, J = 6.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 2.53–2.57 (t, J = 8.0 Hz, 2H), 2.06–2.13 (m, 2H), 1.55–1.62 (m, 2H), 1.28–1.44 (m, 46H), and 0.87–0.91 (t, J = 8.0 Hz, 6H); ¹³C NMR (101 MHz, CD₃OD): δ 159.77, 151.27, 145.87, 137.48, 130.35, 128.39, 124.46, 122.42, 121.42, 116.00, 112.70, 67.78, 63.95, 63.36, 36.96, 33.09, 32.68, 32.62, 30.78, 30.37, 30.19, 27.27, 23.76, and 14.46. HRMS (ESI-TOF) m/z: [M-2Br]²⁺ Calcd for C₄₉H₇₈N₂O 355.3052; Found 355.3042.

C-BP-F

Yield in 81%, as a red solid, m.p. 247.6–249.7 °C, ¹H NMR (400 MHz, CD₃OD): δ 9.42–9.43 (d, J = 4.0 Hz, 2H), 9.26–9.28 (d, J = 8.0 Hz, 2H), 8.75–8.77 (d, J = 8.0 Hz, 2H), 7.14–7.18 (m, 1H), 6.73–6.78 (m, 3H), 6.24–6.45 (m, 2H), 5.43–5.45 (d, J = 8.0 Hz, 2H), 4.66–4.67 (d, J = 4.0 Hz, 2H), 3.18–3.27(m, 2H), 2.54–2.58 (t, J = 8.0 Hz, 2H), 1.55–1.62 (m, 2H), 1.28–1.31 (m, 24H), and 0.88–0.91 (t, J = 4.0 Hz, 3H); ¹³C NMR (101 MHz, CD₃OD): δ 159.76, 151.40, 145.58, 142.64, 130.35, 128.59, 126.55, 124.39, 122.43, 120.68, 118.70, 118.63, 115.98, 112.69, 111.53, 67.76, 63.96, 62.83, 36.96, 33.09, 32.68, 30.77, 30.49, 30.37, 24.55, 23.76, and 14.46. HRMS (ESI-TOF) *m*/*z*: [M-I-Br]²⁺ Calcd for C₄₁H₅₃F₉N₂O 380.2002; Found 380.1995.

Surface Tension Measurements

Tensiometry method was adopted to evaluate the surfaceactive properties of the synthesized compounds. The surface tension values were acquired on an automatic tensiometer (JK99B, Shanghai Zhongchen Digital Technic Apparatus Co., Ltd., Putuo District, Shanghai, China) at 298.15 K based on the Wilhelmy plate method (Ahire and Bhagwat, 2017). The testing solutions were aged overnight prior to measurement. Before each round of measurement, the platinum plate was scrubbed with absolute ethyl alcohol and distilled water, followed with heating on the alcohol lamp to remove potential residuals. The surface tension value at each concentration was measured three times with its mean value as well as SD being listed in Fig. 4.





Fig. 4 Surface tension isotherms of compounds C-BP, C-BP-1, C-BP-4, and C-BP-6 at 25 $^{\circ}\mathrm{C}$

Krafft Temperature

The Krafft temperature was determined in accordance with the method reported before (Scorzza et al., 2009). In brief, solutions of tested compound in the concentration of 1% (mass percent) were prepared and heated to 90 °C with agitation to obtain a transparent liquid. Upon cooling, the temperature at which turbidity first occurred was marked down as its Krafft temperature. Each sample was tested at least three times with the final results being listed in Table 1.

Antimicrobial Activity

The antibacterial efficacy of the reported nine QAC was evaluated on two Gram positive strains (*S. aureus* ATCC 25923 and *C. glutamicum* ATCC 13032) as well as two Gram negative strains (*E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853). To measure MIC values, the broth microdilution method was performed according to the standard protocol (Matthew et al, 2009). In brief, overnight bacterial cultures of the four mentioned strains were grown in Mueller-Hinton Broth, followed by dilution to approximately 10^6 cfu mL⁻¹, which was comfirmed by optical density (OD) measurement at 600 nm. For water-

 Table 1
 Krafft temperature of hydrogenated cardanol-derived quaternary ammonium compounds

Compound	Krafft point (°C)
C-BP	3.5
C-BP-1	<0
C-BP-4	<0
C-BP-6	<0

Compound	$MIC (\mu g mL^{-1}) (\mu mol L^{-1})$						
	S. aureus ATCC 25923	C. glutamicum ATCC 13032	E. coli ATCC 25922	P. aeruginosa ATCC 27853			
C-BP	64 (108)	32 (54)	>128 (>216)	>128 (>216)			
C-BP-1	64 (87)	32 (44)	>128 (>174)	>128 (>174)			
C-BP-4	32 (44)	32 (44)	>128 (>176)	>128 (>176)			
C-BP-6	16 (21)	8 (11)	>128 (>169)	>128 (>169)			
C-BP-8	16 (20)	8 (10)	>128 (>163)	>128 (>163)			
C-BP-10	16 (20)	8 (9.8)	>128 (>158)	>128 (>158)			
C-BP-12	8 (9.5)	8 (9.5)	>128 (>152)	>128 (>152)			
C-BP-14	8 (9.2)	8 (9.2)	>128 (>147)	>128 (>147)			
C-BP-F	>128 (>132)	>128 (>132)	>128 (>132)	>128 (>132)			

Table 2 MIC values of hydrogenated cardanol-derived quaternary ammonium compounds toward four testing bacterial strains

soluble compounds (C-BP, C-BP-1, C-BP-4, and C-BP-6), each one was dissolved in 10 mL sterile water reaching a concentration of 1280 μ g mL⁻¹. For the other five slightly water-soluble compounds, each one was first dissolved in 1 mL absolute methanol and then diffused in 9 mL sterile water reaching 1280 μ g mL⁻¹ as well. Accordingly, absolute methanol controls were performed. Each stock solution was subjected to serial twofold dilution to obtain 11 testing solutions with concentration ranging from 1280 to 1.25 μ g mL⁻¹. In triplicate, 10 μ L of each testing solution and 90 µL of bacterial culture as mentioned above were pipetted into the corresponding well of a 96-well microtiter tray. Meanwhile, a growth control group containing no antimicrobial agent was added. The 96-well trays were kept at 37 °C in an ambient air incubator for 24 h. The MIC value was the lowest concentration at which the growth of bacteria within the well was completely inhibited, indicated by the phenomena that no turbidity within the well was observed visually. The MIC data are listed in Table 2.

Results and Discussion

Surfactant Synthesis and Characterization

The synthetic route to obtain C-BP and C-BP-R is clearly illustrated in Scheme 1. The structural elucidation was conducted using ¹H NMR, ¹³C NMR, and high-resolution mass spectroscopic studies and all data of spectral characteristics were presented in the Experimental Section. The formation of C-BP was confirmed by the doublet occurring at 5.35–5.36 ppm in ¹H NMR and characteristic peaks at 63.43 ppm in ¹³C NMR, indicating the quaternarization reaction that occurred between one nitrogen atom of the bipyridine ring and the carbon atom of C-Br that was substituted with Br before the reaction. Similarly, the formation of C-BP-R was confirmed by the doublet appearing

at 5.43–5.45 ppm in ¹H NMR and peaks at 63.90 ppm in ¹³C NMR. Meanwhile, high-resolution mass spectrum results suggested a minor difference lower than 0.001 between molecular ion peaks shown in the spectra and molecular ion weight calculated using ChemDraw, further confirming the validity of the synthesized structures (Ning, 2011).

Tensiometric Property

The tensiometric property of the synthesized amphiphiles was evaluated *via* the surface tension measurements adopting the Wilhelmy plate method. Among the reported surfactants, four of them (C-BP, C-BP-1, C-BP-4, and C-BP-6) exhibited great water solubility. With an increase in the hydrophobic chain length or the introduction of the fluorine-substituted side chain, the water solubility of the corresponding surfactants (C-BP-8, C-BP-10, C-BP-12, C-BP-14, and C-BP-F) decreased greatly. Thus, only the surface tension isotherms of four water-soluble surfactants (C-BP, C-BP-1, C-BP-4, and C-BP-6) are depicted in Fig. 4.

To obtain surface tension isotherm, firstly, the surface tension value of distilled water was measured as γ_0 . Following surface tension data, γ_i was individually determined after subsequent addition of specific volume of the prepared testing solutions. It was noticed during the measuring process that γ_i gradually decreased until reaching a plateau where further increase of concentration resulted in a minor γ_i decrease, resulting in two curve regions in the final surface tension plots. CMC was determined at the cross point of the two curve regions (Rosen and Kunjappu, 2012). As shown in Table 3, the CMC values of C-BP, C-BP-1, C-BP-4, and C-BP-6 are 0.011, 0.013, 0.010, and 0.005 mmol L^{-1} , respectively, much lower than commercially available hexadecyl trimethyl ammonium chloride (16 mmol L^{-1}) and other categories of the cationic surfactant (Jurij Lah and Vesnaver, 2000; Ray et al., 2005; Venable & Nauman,

Compound	CMC (mmol L^{-1})	$\gamma_{\rm CMC} ({\rm mN} \;{\rm m}^{-1})$	$\pi_{\rm CMC} ({\rm mN \ m}^{-1})$	$C_{20} (10^{-4} \text{ mol } L^{-1})$	$\frac{CMC}{C_{20}}$	$\tau_{\rm max}~(\mu { m mol}~{ m m}^{-2})$	$A_{\min} (\mathrm{nm}^2)$
C-BP	0.011	15.64	56.36	0.021	5.24	1.63	1.02
C-BP-1	0.013	30.53	41.47	0.030	4.33	1.03	1.61
C-BP-4	0.010	32.85	39.15	0.029	3.45	0.98	1.69
C-BP-6	0.005	33.28	38.72	0.015	3.21	0.99	1.67
C-BP-8	/	33.21	38.79	/	/	/	/
C-BP-10	/	34.21	37.79	/	/	/	/
C-BP-12	/	35.25	36.75	/	/	/	/
C-BP-14	/	36.46	35.54	/	/	/	/
C-BP-F	/	24.75	47.25	/	/	/	/

Table 3 Physical parameters of hydrogenated cardanol-derived asymmetric Gemini cationic surfactants

1964), and comparable to other cardanol-derived cationic amphiphiles (Bhadani et al., 2011; Wang et al., 2016). It was noticed that the bicephalic surfactant C-BP-1 shows a higher CMC value than the conventional surfactant C-BP. This was attributed to the increased hydrophilicity induced by the introduction of a second head group, which is in alignment with the finding of Kevin L. Caran's group's work of biscationic bicephalic (double-headed) amphiphiles exhibiting higher CMC values owing to increased water solubility (Roszak et al., 2009). Both Gemini surfactants C-BP-4 (0.010 mM) and C-BP-6 (0.005 mM) have lower CMC values compared with the conventional surfactant C-BP (0.011 mM), because in the structure of Gemini surfactant C-BP-R locates a rigid bipyridine spacer to covalently connect the head groups of two surfactant monomers, functioning against the electrostatic repulsion between head groups of two surfactant monomers when forming micelles, thus helping two hydrophobic chains within a Gemini surfactant to pack tightly, facilitating the formation of micelle and leading to a lower CMC value (Menger and Keiper, 2000; Sharma and Ilies, 2014). After elongation of the side alkyl chain, surfactant exhibits larger intermolecular hydrophobic interaction, leading to tight packing and decreased CMC values (Shukla and Tyagi, 2006). The surface tension at CMC was designated as γ_{CMC} . And the surface pressure $\pi_{\rm CMC}$ indicating the effectiveness of surface tension reduction was calculated by the following equation (Rosen and Kunjappu, 2012).

$$\pi_{\rm CMC} = \gamma_0 - \gamma_{\rm CMC} \tag{1}$$

Meanwhile, C_{20} indicating the concentration of the test amphiphile needed to reduce the surface tension of pure water by 20 mN m⁻¹ was also determined, standing for the adsorption efficiency of the test surfactant. The values of π_{CMC} were 56.36, 41.47, 39.15, and 38.72 mN m⁻¹ for C-BP, C-BP-1, C-BP-4, and C-BP-6, respectively. The decrease of π_{CMC} could be well explained by CMC/C₂₀ analysis. CMC/C₂₀ is a comparison parameter showing the preference of the test surfactant to form micelle or adsorb

WILEY ACCS*

into the air-water interface. The higher the parameter, the more the test surfactant prefers to lower the surface tension of its aqueous solution (Desnoyers, 1992). It was noted in Table 3 that the CMC/C₂₀ value decreases from C-BP to C-BP-4, which is in alignment with the fact that C-BP is the most efficacious one to reduce the surface tension of water. Furthermore, the maximum surface excess concentration τ_{max} (µmol m⁻²) as well as the minimum surface area per molecule A_{min} (nm²) were calculated *via* the Gibb's adsorption isotherm equation (Rosen and Kunjappu, 2012):

$$\tau_{\max} = \frac{10^{23}}{N_{\rm A} \times A_{\rm min}} = \frac{-1}{\rm nRT} \left(\frac{\partial \gamma}{\partial \ln C}\right)_T \tag{2}$$

where N_A denotes Avogadro's number, R means universal gas constant, T is the absolute temperature, C indicates the surfactant concentration, and $(\partial \gamma / \partial \ln C)_T$ is the premicellar slope in the surface tension isotherm (Chauhan et al., 2015). n was set as 2 for C-BP and 3 for the rest of the compounds based on the number of species formed after the dissolution of the test surfactant (Ahire and Bhagwat, 2017). CMC, γ_{CMC} , π_{CMC} , C_{20} , CMC/ C_{20} , τ_{max} , and A_{min} values are listed in Table 3.

Antimicrobial Activity

MIC value signifies the smallest concentration of the test compound above which the visible growth of a bacterium is inhibited (Matthew et al, 2009). The lower the MIC value, the better the antimicrobial efficacy. In this study, the MIC values of nine synthesized quaternary ammonium salts against two Gram positive strains (*S. aureus* and *C. glutamicum*) as well as two Gram negative strains (*E. coli* and *P. aeruginosa*) were measured. And the results are listed in Table 2. During measurement, for slightly water-soluble C-BP-8, C-BP-10, C-BP-12, C-BP-14, and C-BP-F, each one was firstly dissolved in 1 mL absolute methanol and then diffused in 9 mL sterile water to get testing solutions. Therefore, absolute methanol controls were

conducted. It was found that four bacterial strains could grow pretty well under the highest absolute methanol testing concentration of $128 \ \mu g \ mL^{-1}$, suggesting that methanol would not interfere with the MIC testing results. It was found that this series of compounds have great antimicrobial activity toward Gram-positive S. aureus and C. glutamicum while inadequate antimicrobial activity against two test Gram-negative strains. After the introduction of fluorinesubstituted side chain, C-BP-F exhibits poor antimicrobial ability toward all four testing stains. When comparing the conventional surfactant C-BP with the bicephalic surfactant C-BP-1, it was found that the introduction of a second head group decreased the MIC value against S. aureus from 108 μ mol L⁻¹ (C-BP) to 87 μ mol L⁻¹ (C-BP-1) and the MIC value against C. glutamicum from 54 μ mol L⁻¹ (C-BP) to 44 μ mol L⁻¹ (C-BP-1). The introduction of a second cationic head group helps to strengthen the electrostatic interaction between the cationic amphiphile and the anionic bacterial cell surface, leading to a better antimicrobial efficacy and a lower MIC value (Forman et al., 2016; Jayanta Haldar and Bhattachary, 2005). With the elongation of the long carbon chain R group on C-BP-R, the corresponding MIC value against two Gram-positive strains both gradually decreases. It was caused by the enhanced interaction between the prolonged lipophilic chain of the test surfactant and the hydrophobic sector of the membrane bilayer, which contributes to disrupt the integrity of the cell envelope and consequently leads to the breakage of the cell membrane, leakage of cytoplasm, and finally death of the bacterial cell (Tischer et al., 2012).

Conclusion

A set of seven hydrogenated cardanol-based asymmetric Gemini cationic surfactants with a rigid linker group 4,4'bipyridine, one bicephalic cationic surfactant as well as one conventional single-tale single-head cationic surfactant was synthesized with easy operation and high yields. Their tensiometric properties were measured via surface tension method and physical parameters like CMC, γ_{CMC} , Π_{CMC} , C_{20} , τ_{CMC} , and A_{min} were calculated. Bicephalic surfactant in this work has higher CMC values compared with the conventional one owing to the increased water solubility caused by the introduction of a second cationic head group. And, Gemini surfactants in this work presented lower CMC compared with the conventional one. CMC/C₂₀ proved to be a useful parameter in showing the preference of the test surfactant to form micelle or adsorb into the air-water interface and predicting effectiveness of surface tension reduction. These cationic surfactants have lower CMC values compared with other categories of cationic surfactants (Jurij Lah and Vesnaver, 2000; Ray et al., 2005; Venable & Nauman, 1964). The Krafft temperature of C-BP-1, C-BP-4, and C-BP-6 was lower than 0 °C, suggesting high-potential industrial applications. All synthesized compounds but C-BP-F exhibit great antimicrobial ability against Gram-positive bacteria (*S. aureus* and *C. glutamicum*) while inadequate antimicrobial ability against Gram negative strains (*E. coli* and *P. aeruginosa*).

Acknowledgements This research was financially supported by the National Nature Science Foundation of China (21772039, 21272069), the Fundamental Research Funds for the Central Universities, and Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

Conflict of Interest The authors declare that they have no conflict of interest.

References

- Ahire, M. B., & Bhagwat, S. S. (2017) Novel ester-linked anionic gemini surfactant: Synthesis, surface-active properties and antimicrobial study. *Journal of Surfactants and Detergents*, 20:789–797. https://doi.org/10.1007/s11743-017-1977-1
- Amarnath, N., Appavoo, D., & Lochab, B. (2017) Eco-friendly halogen-free flame retardant cardanol polyphosphazene polybenzoxazine networks. ACS Sustainable Chemistry & Engineering, 6:389–402. https://doi.org/10.1021/acssuschemeng.7b02657
- Amorati, R., Attanasi, O. A., Favi, G., Menichetti, S., Pedulli, G. F., & Viglianisi, C. (2011) Amphiphilic antioxidants from "cashew nut shell liquid" (CNSL) waste. Organic & Biomolecular Chemistry., 9:1352–1355. https://doi.org/10.1039/ c0ob01040e
- Anilkumar, P. (Ed.). (2017) Cashew nut shell liquid: A goldfield for functional materials. In *Cashew Nut Shell Liquid: A Goldfield for Functional Materials* (pp. 7–8). Switzerland: Springer International Publishing AG.
- Atta, A. M., Abdullah, M. M. S., Al-Lohedan, H. A., & Ezzat, A. O. (2018) Demulsification of heavy crude oil using new nonionic cardanol surfactants. *Journal of Molecular Liquids*, 252:311–320. https://doi.org/10.1016/j.molliq.2017.12.154
- Attanasi, O. A., Berretta, S., Fiani, C., Filippone, P., Mele, G., & Saladino, R. (2006) Synthesis and reactions of nitro derivatives of hydrogenated cardanol. *Tetrahedron*, **62**:6113–6120. https://doi. org/10.1016/j.tet.2006.03.105
- Balachandran, V. S., Jadhav, S. R., Vemula, P. K., & John, G. (2013) Recent advances in cardanol chemistry in a nutshell: From a nut to nanomaterials. *Chemical Society Reviews*, 42:427–438. https://doi. org/10.1039/c2cs35344j
- Bhadani, A., Kataria, H., & Singh, S. (2011) Synthesis, characterization and comparative evaluation of phenoxy ring containing long chain gemini imidazolium and pyridinium amphiphiles. *Journal of Colloid and Interface Science*, **361**:33–41. https://doi.org/10.1016/ j.jcis.2011.05.023
- Braga, F. C., Prasad, A. N., da Silva Gomes, R., do Nascimento, V. A., Oliveira, S. L., Caires, A. R. L., ... Beatriz, A. (2017) Design, synthesis and fluorescence analysis of potential fluorescent markers based on cardanol and glycerol. *Dyes and Pigments*, 141:235–244. https://doi.org/10.1016/j.dyepig.2017.02.032
- Bruce, I. E., Mehta, L., Porter, M. J., Stein, B. K., & Tyman, J. H. P. (2009) Anionic surfactants synthesised from replenishable phenolic

lipids. Journal of Surfactants and Detergents, 12:337-344. https://doi.org/10.1007/s11743-009-1116-8

- Castro Dantas, T. N., Vale, T. Y. F., Dantas Neto, A. A., Scatena Jr, H., & Moura, M. C. P. A. (2008) Micellization study and adsorption properties of an ionic surfactant synthesized from hydrogenated cardanol in air–water and in air–brine interfaces. *Colloid and Polymer Science*, 287:81–87. https://doi.org/10.1007/s00396-008-1956-1
- Chauhan, V., Singh, S., Kaur, T., & Kaur, G. (2015) Self-assembly and biophysical properties of gemini 3-alkyloxypyridinium amphiphiles with a hydroxyl-substituted spacer. *Langmuir : The ACS Journal of Surfaces and Colloids*, **31**:2956–2966. https://doi.org/ 10.1021/la5045267
- Danner, H., & Braun, R. (1999) Biotechnology for the production of commodity chemicals from biomass. *Chemical Society Reviews*, 28:395–405.
- Desnoyers, J. E. (1992) Surfactants and interfacial phenomena 2nd edition. By Milton J. Rosen, John Wiley and Sons, New York, 1989. 431 pp. *Journal of Colloid & Interface Science*, 149:299–300.
- Ezzat, A. O., Atta, A. M., Al-Lohedan, H. A., Abdullah, M. M. S., & Hashem, A. I. (2017) Synthesis and application of poly(ionic liquid) based on cardanol as demulsifier for heavy crude oil water emulsions. *Energy & Fuels*, **32**:214–225. https://doi.org/10.1021/ acs.energyfuels.7b02955
- Forman, M. E., MCJ, W. M. W., & Minbiole, K. P. C. (2016) Building a better quaternary ammonium compound (QAC): Branched Tetracationic antiseptic Amphiphiles. *ChemMedChem*, 11: 1401–1405. https://doi.org/10.1002/cmdc.201600176
- Grenier, M. C., Davis, R. W., Wilson-Henjum, K. L., LaDow, J. E., Black, J. W., Caran, K. L., et al. (2012) The antibacterial activity of 4,4'-bipyridinium amphiphiles with conventional, bicephalic and gemini architectures. *Bioorganic & Medicinal Chemistry Letters*, 22:4055–4058. https://doi.org/10.1016/j.bmcl.2012.04.079
- Jayanta Haldar, P. K., & Bhattachary, S. (2005) Synthesis and antibacterial properties of novel hydrolyzable cationic amphiphiles. incorporation of multiple head groups leads to impressive antibacterial activity. *Journal of Medicinal Chemistry*, 48: 3823–3831. https://doi.org/10.1021/jm0491061
- Jurij Lah, C. P., & Vesnaver, G. (2000) Calorimetric study of the micellization of alkylpyridinium and alkyltrimethylammonium bromides in water. *The Journal of Physical Chemistry*. B, 104: 2522–2526. https://doi.org/10.1021/jp9928614
- Kattimuttathu, I. S., Foerst, G., Schubert, R., & Bartsch, E. (2011) Synthesis and micellization properties of new anionic reactive surfactants based on hydrogenated cardanol. *Journal of Surfactants and Detergents*, 15:207–215. https://doi.org/10.1007/s11743-011-1294-z
- Menger, F. M., & Keiper, J. S. (2000) Gemini surfactants. Angewandte Chemie—International Edition, **39**:1906–1920. https://doi.org/10. 1002/1521-3773(20000602)39:11<1906::AID-ANIE1906>3.0.CO; 2-Q
- Matthew A. W., Janet F. H., Cockerill III F. R., Jean B. P., Karen B., Mair P., ... Jana M. S. (2009) *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard* (8th ed.). Wayne, PA: Clinical and Laboratory Standards Institute.
- Molji, C., Aashish, A., Neethu, K. S., & Devaki, S. J. (2017) Selfassembled polyaniline nanowires stippled graphene-3-pentadecylphenyl phosphate hybrid nanocomposite based green sustainable electrodes for supercapacitors. *Journal of Materials Chemistry A*, 5:16636–16645. https://doi.org/10.1039/c7ta05215d
- Mondal, M. H., Roy, A., Malik, S., Ghosh, A., & Saha, B. (2015) Review on chemically bonded geminis with cationic heads: Second-generation interfactants. *Research on Chemical Intermediates*, 42:1913–1928. https://doi.org/10.1007/s11164-015-2125-z
- Monger, F. M., & Littau, C. A. (1991) Gemini surfactants: Synthesis and properties. *Journal of the American Chemical Society*, **113**: 1451–1452. https://doi.org/10.1021/ja00004a077

- Nguyen, T. K. L., Livi, S., Soares, B. G., Barra, G. M. O., Gérard, J.-F., & Duchet-Rumeau, J. (2017) Development of sustainable thermosets from cardanol-based epoxy prepolymer and ionic liquids. ACS Sustainable Chemistry & Engineering, 5:8429–8438. https:// doi.org/10.1021/acssuschemeng.7b02292
- Ning, Y. C. (2011) Interpretation of organic spectra (pp. 123–126). Singapore: John Wiley & Sons (Asia) Pte Ltd.
- Peungjitton, P., Sangvanich, P., Pornpakakul, S., Petsom, A., & Roengsumran, S. (2008) Sodium cardanol sulfonate surfactant from cashew nut shell liquid. *Journal of Surfactants and Detergents*, **12**: 85–89. https://doi.org/10.1007/s11743-008-1082-6
- Ragauskas, A. J. W. C., Davison, B. H., Britovsek, G., Cairney, J., Eckert, C. A., Frederick Jr., W. J., ... Tschaplinski, T. (2006) The path forward for biofuels and biomaterials. *Science*, **311**:484–489. https://doi.org/10.1126/science.1114736
- Ray, G. B., Chakraborty, I., Ghosh, S., Moulik, S. P., & Palepu, R. (2005) Self-aggregation of alkyltrimethylammonium bromides (C₁₀⁻, C₁₂⁻, C₁₄⁻, and C₁₆TAB) and their binary mixtures in aqueous medium: A critical and comprehensive assessment of interfacial behavior and bulk properties with reference to two types of micelle formation. *Langmuir: The ACS Journal of Surfaces and Colloids*, 21:10958–10967. https://doi.org/10.1021/la051509g
- Venable, R. L., & Nauman, R. V. (1964) Micellar weights of and solubilization of benzene by a series of tetradecylammonium bromides. The effect of the size of the charged head. *The Journal of Physical Chemistry*, 68:3498–3503. https://doi.org/10.1021/j100794a010
- Rosen, M. J., & Kunjappu, J. T. (2012) Surfactants and interfacial phenomena (4th ed.) (pp. 99–113 & 242–256). Hoboken, New Jersey: John Wiley & Sons, Inc.
- Roszak, K. Z., Torcivia, S. L., Hamill, K. M., Hill, A. R., Radloff, K. R., Crizer, D. M., ... Caran, K. L. (2009) Biscationic bicephalic (double-headed) amphiphiles with an aromatic spacer and a single hydrophobic tail. *Journal of Colloid and Interface Science*, 331:560–564. https://doi.org/10.1016/j.jcis.2008.12.014
- Scorzza, C., Nieves, J., Vejar, F., & Bullón, J. (2009) Synthesis and physicochemical characterization of anionic surfactants derived from cashew nut shell oil. *Journal of Surfactants and Detergents*, 13:27–31. https://doi.org/10.1007/s11743-009-1143-5
- Sharma, V. D., & Ilies, M. A. (2014) Heterocyclic cationic gemini surfactants: A comparative overview of their synthesis, self-assembling, physicochemical, and biological properties. *Medicinal research reviews*, 34:1–44. https://doi.org/10.1002/med.21272
- Shukla, D., & Tyagi, V. K. (2006) Cationic Gemini surfactants: A review. Journal of Oleo Science, 55:381–390. https://doi.org/10. 5650/jos.55.381
- Tischer, M., Pradel, G., Ohlsen, K., & Holzgrabe, U. (2012) Quaternary ammonium salts and their antimicrobial potential: Targets or nonspecific interactions? *ChemMedChem*, 7:22–31. https://doi.org/ 10.1002/cmdc.201100404
- Tyman, J. H. P., & Bruce, I. E. (2003) Synthesis and characterization of polyethoxylate surfactants derived from phenolic lipids. *Journal of Surfactants and Detergents*, **6**:291–297.
- Tyman, J. H. P., & Bruce, I. E. (2004) Surfactant properties and biodegradation of polyethoxylates from phenolic lipids. *Journal of Surfactants and Detergents*, 7:169–173.
- Voirin, C., Caillol, S., Sadavarte, N. V., Tawade, B. V., Boutevin, B., & Wadgaonkar, P. P. (2014) Functionalization of cardanol: Towards biobased polymers and additives. *Polymer Chemistry*, 5:3142–3162. https://doi.org/10.1039/c3py01194a
- Wang, R., Luo, Y., Cheng, C.-J., Huang, Q.-H., Huang, H.-S., Qin, S.-L., & Tu, Y. M. (2016) Syntheses of cardanol-based cationic surfactants and their use in emulsion polymerisation. *Chemical Papers*, **70**:1218–1227. https://doi.org/10.1515/chempap-2016-0052

WILEY ACCS*