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ORIGINAL ARTICLE

Phase Transfer Catalysis with Quaternary Ammonium Type Gemini Surfactants: *O*-Alkylation of Isovanillin

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Abstract In this paper, *O*-alkylation of isovanillin with unusual phase transfer catalysts alkandiyl-α,ω-bis(dimethylalkylammonium bromide) dimeric surfactants (also known as gemini surfactants) is described. Some dimeric surfactants with simple hydrophobic alkyl chains and others with hydrophobic alkyl chains containing ester functionalities with different lengths were synthesized and characterized in our laboratory. The alkylation of isovanillin with alkyl halide was successively carried out in the presence of potassium carbonate and a phase transfer catalyst in tetrahydrofuran. The same reactions were also performed with both the traditional phase transfer catalyst tetrabutylammonium bromide and without any catalyst. The results were compared with those of dimeric surfactants. Consequently, it was expressed that alkandiyl-α,ω-bis(dimethylalkylammonium bromide) dimeric surfactants successively exhibit the character of phase transfer catalysts through environmentally friendly procedures under mild conditions. The most significant feature of this work is that dimeric surfactants have been determined to act as phase transfer agents.

Keywords Phase transfer catalysis · *O*-Alkylation · Gemini surfactants · Green methodology

Introduction

Organic synthesis is the principal way to produce various chemical products such as pharmaceuticals, dyes, monomers, etc. In the synthesis of desired final products from starting materials, a number of chemicals are usually used, such as additional reagents, solvents and catalysts. Many waste materials are produced in addition to the desired products of the organic synthesis reactions. The development of new synthetic methodologies holds the key to minimize these wastes which create a heavy burden on the environment [1]. Bringing together a water soluble nucleophile and an electrophilic organic water-insoluble reagent in the reaction media is difficult. This problem has been traditionally solved by addition of a solvent which has hydrophilic and lipophilic character together such as ethanol that is both water-like and organic-like. Even so, the rate of the reaction is not sufficiently fast due to excessive solvation of the nucleophile. Alternatively, dipolar aprotic solvents like dimethyl formamide (DMF) or dimethyl sulfoxide (DMSO) can be used, but they suffer from some drawbacks such as difficulty in the isolation and recovery of solvents [2].

Phase transfer catalysis (PTC) seems to be the most general, efficient and environmentally friendly methodology to perform reactions in which organic and inorganic anions react with organic substrates [3]. According to this methodology, reactions are performed in immiscible two-phase systems. Phase transfer catalysts are chemical agents that facilitate the transfer of a molecule or an ion from one phase to another and in doing so can greatly accelerate the rate of biphasic reaction processes. PTC can be used widely in the organic synthesis reactions of various organic chemicals in both liquid–liquid and solid–liquid systems. The simplest examples of these processes are normal biphasic phase transfer reactions in which the catalyst facilitates reactions by solubilizing a reagent or ion in the organic phase. One phase is a reservoir of reacting anions or a base for generation of organic anions, whereas the organic reactants and catalysts are located in the second,

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organic phase. In 1971, Starks introduced the term "phase transfer catalysis" to explain the critical role of tetraalkylammonium or phosphonium salts in the reaction between two substances located in different immiscible phases [4, 5]. This methodology was discovered and introduced into laboratory practice in the late 1960s by Makosza [1, 6–10]. The most commonly used PTCs in organic synthesis reactions are quaternary ammonium compounds (QACs). QACs are usually inexpensive and biodegradable [11–13]. Various organic solvents can be used and product isolation is effortless in the phase tranfer catalysis. Because of these advantages, phase transfer reactions have been recognized as "green" alternatives to many homogeneous reaction processes, and they have found widespread application in synthetic organic chemistry. Furthermore, increasing attention has focused on the development of asymmetric phase transfer processes in recent years [14–22].

Phase transfer-catalyzed reactions of organic anions are mechanistically more complicated. In these cases, the inorganic phase contains a base such as conc. aqueous or solid NaOH or KOH or solid K_2CO_3, whereas the organic phase contains the anion precursor, an electrophilic reactant and eventually a solvent [1]. In this state, the organic anions with metal ions ($-C^-Na^+$) are very unreactive, as they are able to react only with very strong electrophiles. In the presence of a catalyst (Q^+, Quaternary ammonium compound such as tetrabutylammonium cation), the ion exchange results in the formation of lipophilic ion pairs ($-C^-Q^+$) which are then transferred into the organic phase [3]. Further reactions, for instance, alkylations, occur in the organic phase (Fig. 1).

On the other hand, a new class of quaternary ammonium compounds, referred to as dimeric surfactants (also known as gemini surfactants), has attracted increasing attention in current studies due to their superior surface activity compared to that of the conventional (monomeric) surfactants. They tend towards a much lower critical micelle concentration (CMC), which can produce lower surface tension than conventional surfactants at the same molar concentration. Gemini surfactants have better solubilizing, wetting and foaming abilities, and stronger biological activity and lime soap dispersing properties compared to conventional surfactants. These surfactants are made up of two hydrophobic tails and two polar heads separated by a spacer group, which considerably changes the physical and chemical properties of the gemini surfactant. The quaternary ammonium dimeric surfactants [$C_mH_{2m+1}(CH_3)_2$–N^+–C_sH_{2s}–$N^+(CH_3)_2C_mH_{2m+1}$], $2X^-$ (X^- = counter-ion), are abbreviated as *m*–*s*–*m*, where *m* and *s* denote respectively, the number of carbon atoms in the alkyl chain and the spacer. Recently, many articles and books have been published about the synthesis and physicochemical properties of these surfactants [23–37].

In organic synthesis, the alkylation of various compounds such as imines and phenols with phase transfer catalysis has great importance and attraction in recent years. PTC is a significant methodology for alkylation of a large variety of organic anions derived from OH, NH, CH, SH, etc. Among these, *O*-alkylation of isovanillin has critical importance as 3-cyclopentyloxy-4-methoxybenzaldehyde is an intermediate in the synthesis of phosphodiesterase IV isoenzyme inhibitor PDA-641 used for the treatment of asthma, inflammatory disorders, and depression and can be prepared by *O*-alkylation of isovanillin with cyclopentyl bromide in a liquid–solid PTC system [38]. Although many types of phase transfer catalysts such as quaternary ammonium and phosphonium salts, crown ethers, cryptands, etc. can be used in organic synthesis, the examples of phase transfer catalysis with quaternary ammonium type-gemini surfactants in two-phase reactions are exiguous [39–41]. So, we aimed to investigate experimentally the behavior of cationic dimeric surfactants as phase transfer catalysts in the alkylation of isovanillin. For this purpose, we synthesized some quaternary ammonium dimeric surfactants with both simple and ester functional hydrophobic alkyl chains with different lengths. We

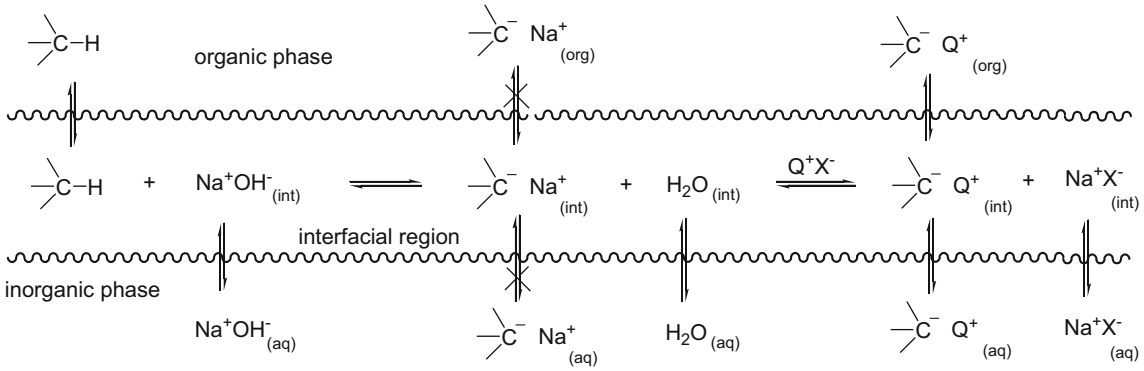


Fig. 1 Mechanism of the phase transition in two-phase systems

intended to use these dimeric surfactants as phase transfer agents and to determine the dimeric surfactants as phase transfer agents.

Experimental Section

Materials

Some dimeric quaternary ammonium compounds, e.g., alkanediyl-α-ω-bis(alkyl dimethylammonium bromide), were synthesized in our laboratory. For the synthesis of these dimeric quaternary ammonium compounds, 1-bromooctane, 1-bromodecane, 1-bromododecane, 1-bromohexadecane, bromocyclopentane, *N,N,N′,N′*-tetramethylethylenediamine, dimethylaminopyridine (DMAP) 1,6-dibromo hexane, 1,10-dibromodecane, α,α′-dibromo-*p*-xylene, *N,N*-dimethylhexadecylamine, isovanillin, potassium carbonate, tetrahydrofuran (THF) and acetone were commercially supplied and all the required fine chemicals were directly used without further purification. These dimeric surfactants were used in alkylation of isovanillin as phase transfer catalysts. Column chromatography was performed on silica gel (0.063–0.200 mm) with EtOAc–hexane (1:5). Thin layer chromatography (TLC) was performed on silica gel 60F-254 precoated sheets. Infrared (IR) spectra were recorded with Shimadzu IR 470 or ATI Unicam Mattson 1000 Fourier transform IR spectrophotometers and are reported in reciprocal centimeter (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded in deuteriochloroform solution with a Varian Mercury Plus 300 MHz spectrometer. ^{13}C spectra were recorded at 75 MHz. Mass spectra were recorded on an UPLC-UHR-Q/TOF ABSCIEX Triple TOF 4600 and Thermo Trace GC Ultra DSQ II instrument with electron impact at 70 eV. Only isolated yields were reported.

Methods for Synthesis of Dimeric Quaternary Ammonium Compounds

There are two general methods, method I and method II, for the synthesis of the dimeric quaternary ammonium compounds [26].

Method I

A mixture of *N,N,N′,N′*-tetramethylethylenediamine and a corresponding alkyl bromide were refluxed in acetone for 24 h to synthesize 10-2-10, 12-2-12 and 16-2-16 type cationic gemini surfactants (Fig. 2). The white solid was filtered after cooling and then was recrystallized from acetone at least two times.

Method II

A mixture of *N,N*-dimethylhexadecylamine and a corresponding dihaloalkane were refluxed in acetone for 24 h to synthesize 16-6-16 and 16-10-16 type gemini cationic surfactants (Fig. 3). The white solid was filtered after

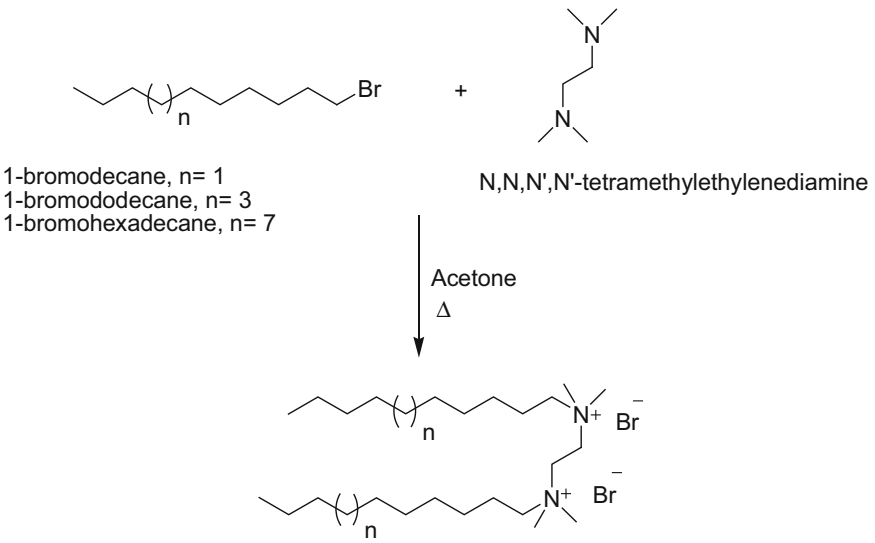


Fig. 2 Synthesis of R-2-R type dimeric quaternary ammonium compounds

N,N'-didecyl-N,N,N',N'-tetramethyl-N,N'-ethanediyl-diammonium dibromide(10-2-10), n= 1
N,N'-didodecyl-N,N,N',N'-tetramethyl-N,N'-ethanediyl-diammonium dibromide(12-2-12), n= 3
N,N'-dihexadecyl-N,N,N',N'-tetramethyl-N,N'-ethanediyl-diammonium dibromide(16-2-16), n= 7

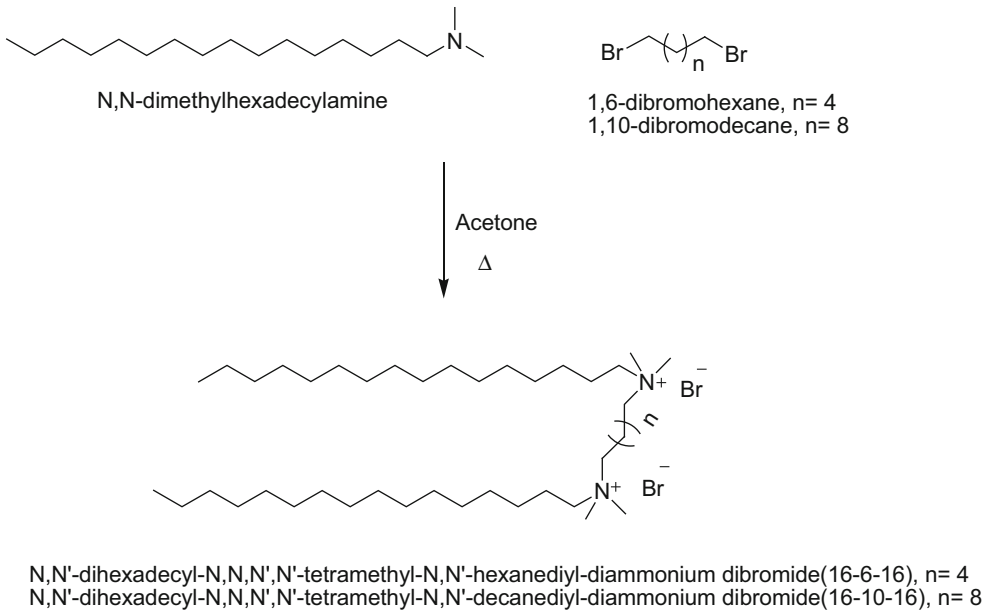
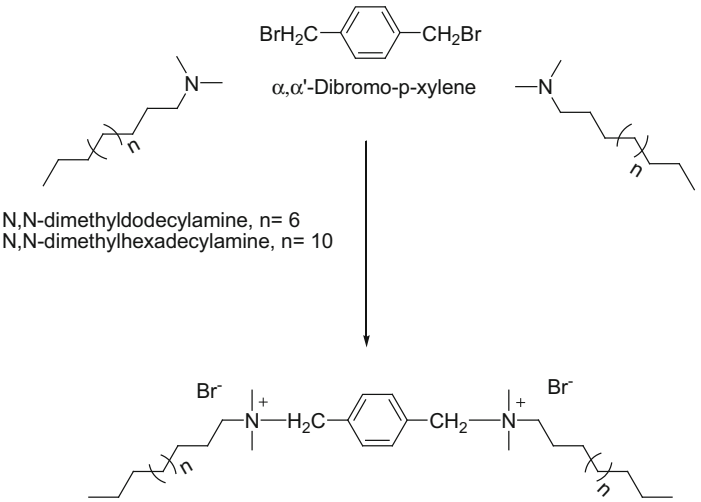


Fig. 3 Synthesis of 16-s-16 type dimeric quaternary ammonium compounds

Fig. 4 Synthesis of $R\text{-}CH_2ArCH_2\text{-}R$ type dimeric quaternary ammonium compounds



N,N'-didodecyl-N,N,N',N'-tetramethyl-N,N'-p-Xylenediyl-diammonium dibromide $12\text{-}CH_2\text{-}Ar\text{-}CH_2\text{-}12$ n= 6
N,N'-dihexadecyl-N,N,N',N'-tetramethyl-N,N'-p-Xylenediyl-diammonium dibromide $16\text{-}CH_2\text{-}Ar\text{-}CH_2\text{-}16$ n= 10

cooling and was then recrystallized from acetone at least two times.

Dimeric surfactants with simple hydrophobic alkyl chains were synthesized according to method I and II as shown on Figs. 2 and 3. On the other hand, dimeric quaternary ammonium compounds containing an aromatic spacer were synthesized according to method II as shown on Fig. 4.

Synthesis of dimeric quaternary ammonium compounds containing ester functional groups was carried out by treatment of *N,N,N′,N′*-tetramethylethylenediamine with alkyl α-bromo acetates derived from bromoacetyl bromide and corresponding alcohols as shown on Fig. 5 [42]. Products were recrystallized from acetone.

Method for *O*-Alkylation of Isovanillin Using Phase Transfer Catalysis

O-Alkylation of isovanillin was carried out in a THF-K_2CO_3 liquid–solid, two-phase system. Bromocyclopentane and 1-bromooctane were used as alkyl halide in

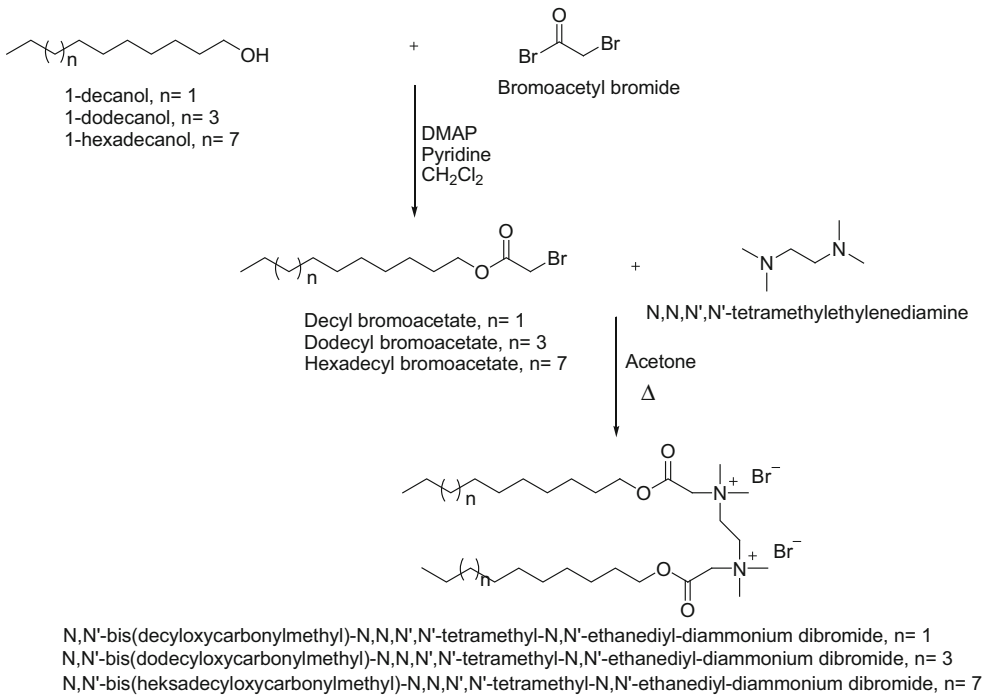


Fig. 5 Synthesis of dimeric quaternary ammonium compounds with ester functionality

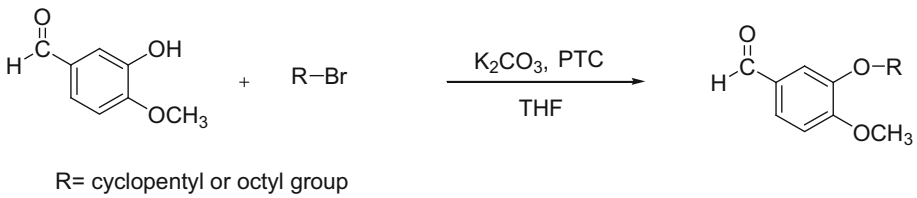


Fig. 6 *O*-Alkylation of isovanillin with phase transfer catalysis

alkylation reactions. Tetrabutylammonium bromide and dimeric quaternary ammonium compounds were added to the reaction mixture as phase transfer agents (Fig. 6). For the purpose of confirming the results, the same reaction was performed without any catalyst. Products were purified with column chromatography. Yields of the reactions were calculated after column chromatography.

Synthesis of Simple Dimeric Quaternary Ammonium Compounds

General Procedure

N,N′-Didecyl-N,N,N′,N′-Tetramethyl-N,N′-Ethanediyl-Diammonium Dibromide (10-2-10)

A magnetically stirred solution of *N,N,N′,N′*-tetramethylethylenediamine (4.64 g, 40 mmol) and 1-bromodecane (17.68 g, 80 mmol) in 200 mL of acetone was refluxed for 12 h. Then the mixture was cooled and was left for 12 h in cold conditions. The crude product was precipitated in the form of white crystals. It was recrystallized two times from acetone then filtered and dried in air, yielding 10.4 g of white crystals (47 %).

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.87$ (t, 6H), 1.22–1.41 (m, 28H), 1.80 (m, 4H), 3.48 (s, 12H), 3.70 (m, 4H), 4.72 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4, 22.9, 23.3, 26.5, 29.5, 29.7, 32.1, 51.3, 57.0, 66.1$.

N,N′-Didodecyl-N,N,N′,N′-Tetramethyl-N,N′-Ethanediyl-Diammonium Dibromide (12-2-12) Yield: 82 %

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (t, 6H), 1.17–1.30 (m, 36H), 1.81 (m, 4H), 3.47 (s, 12H), 3.70 (m, 4H), 4.70 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4, 22.9, 23.3, 26.5, 29.4, 29.6, 29.77, 29.80, 29.88, 32.2, 51.3, 57.0, 66.1$.

N,N′-Dihexadecyl-N,N,N′,N′-Tetramethyl-N,N′-Ethanediyl-Diammonium Dibromide (16-2-16) Yield: 90 %

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (t, 6H), 1.23–1.34 (m, 52H), 1.82 (m, 4H), 3.46 (s, 12H), 3.70 (m, 4H), 4.69 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4$, 22.9, 23.3, 26.5, 28.4, 29.0, 29.4, 29.60, 29.62, 29.67, 29.79, 29.83, 29.92, 29.98, 32.2, 51.3, 57.1, 66.0.

N,N′-Dihexadecyl-N,N,N′,N′-Tetramethyl-N,N′-Hexanediyl-Diammonium Dibromide (16-6-16) Yield: 49 %

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (t, 6H), 1.23–1.33 (m, 52H), 1.57 (m, 4H), 1.70 (m, 4H), 2.0 (m, 4H), 3.37 (s, 12H), 3.40–3.47 (m, 4H), 3.69–3.72 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4$, 21.8, 22.9, 23.1, 24.4, 26.5, 27.7, 27.9, 29.50, 29.59, 29.62, 29.70, 29.83, 29.85, 29.88, 29.91, 32.2, 51.3, 64.4, 65.1.

N,N′-Dihexadecyl-N,N,N′,N′-Tetramethyl-N,N′-Decanediyl-Diammonium Dibromide (16-10-16) Yield: 30 %

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$ (t, 6H), 1.23-1.32 (m, 48H), 1.35 (m, 8H), 1.44 (m, 8H), 1.74 (m, 8H), 3.35 (s, 12H), 3.43–3.49 (m, 4H), 3.75–3.80 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4$, 22.7, 22.9, 23.1, 26.1, 26.5, 28.4, 28.7, 29.49, 29.58, 29.64, 29.71, 29.83, 29.87, 29.91, 32.1, 51.2, 64.4, 64.5.

N,N′-Didodecyl-N,N,N′,N′-Tetramethyl-N,N′-(p-xylenediyl)-Diamonyum Dibromide (12-Ar(8)-12) Yield: 99 %

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 6H), 1.22-1.38 (m, 36H), 1.82 (m, 4H), 3.20 (s, 12H), 3.50 (m, 4H), 5.10 (s, 4H), 7.75 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 22.9, 23.2, 26.7, 29.6, 29.8, 29.9, 32.1, 49.8, 64.9, 66.6, 130.1, 134.2.

N,N′-Dihexadecyl-N,N,N′,N′-Tetramethyl-N,N′-(p-xylenediyl)-Diamonyum Dibromide (16-Ar(8)-16) Yield: 96 %

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.85 (t, 6H), 1.14-1.34 (m, 52H), 1.85 (m, 4H), 3.19 (s, 12H), 3.50 (m, 4H), 5.23 (s, 4H), 7.75 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 22.9, 23.2, 26.7, 29.6, 29.8, 29.9, 30.0, 32.2, 50.0, 65.0, 66.5, 130.2, 134.3.

Synthesis of the Alkyl α-Bromoacetates

General Procedure: Decyl α-Bromoacetate

To a magnetically stirred solution of 1-decanol (4.75 g, 30 mmol), DMAP (0.366 g, 3 mmol), and pyridine (2.38 g, 30 mmol) in dichloromethane (100 mL) was added bromoacetylbromide (12.12 g, 60 mmol) under nitrogen atmosphere at 0 °C. The reaction mixture was warmed after 2 h of cooling and stirred for 12 h at room temperature. The mixture was extracted with water, a saturated solution of $NaHCO_3$ and brine, respectively. The organic extracts were dried over anhydrous calcium chloride. Then dichloromethane was evaporated giving 7.6 g of crude product as brown oil. It was pure enough to use in the synthesis of quaternary ammonium compounds (98 %).

IR (KBr, cm^{-1}): 2953, 2876, 1753, 1472, 1293, 1165, 1114.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H), 1.25–1.30 (m, 14H), 1.61–1.68 (quin, 2H), 3.84 (s, 2H), 4.17 (t, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 22.9, 25.9, 26.2, 28.6, 29.4, 29.5, 29.8, 32.1, 66.7, 167.6.

MS (EI): $m/z = 278$–280 (M^+).

Dodecyl α-Bromoacetate Yield: 96 %

IR (KBr, cm^{-1}): 2953, 2876, 1752, 1471, 1295, 1163, 1112.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (t, 3H), 1.24–1.30 (m, 18H), 1.59–1.67 (quin, 2H), 3.82 (s, 2H), 4.15 (t, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 22.9, 26.0, 26.2, 28.6, 29.4, 29.6, 29.75, 29.85, 29.9, 32.2, 66.7, 167.6.

MS (EI): $m/z = 306$–308 (M^+).

Hexadecyl α-Bromoacetate Yield: 93 %

IR (KBr, cm^{-1}): 2953, 2876, 1752, 1472, 1294, 1164, 1114.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, 3H), 1.23–1.29 (m, 26H), 1.60–1.67 (quin, 2H), 3.81 (s, 2H), 4.15 (t, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 22.9, 26.0, 26.2, 28.6, 29.4, 29.6, 29.7, 29.8, 29.9, 32.2, 66.7, 167.6.

MS (EI): $m/z = 362$–364 (M^+).

Synthesis of the Dimeric Quaternary Ammonium Compounds with Ester Tails

All dimeric quaternary ammonium compounds containing ester functionality were synthesized similarly to those simple dimeric quaternary ammonium compounds from corresponding alkyl α-bromo acetate.

N,N′-Bis(decyloxycarbonylmethyl)-N,N,N′,N′-Tetramethyl-N,N′-Ethanediyl-diammonium Dibromide (10E-2-10E), Yield: 57 %

IR (KBr, cm^{-1}): 2927, 2876, 1753, 1472, 1191.

^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 6H), 1.22–1.35 (m, 28H), 1.62–1.75 (quin, 4H), 3.78 (s, 12H), 4.20–4.25 (t, 4H), 4.90 (s, 4H), 5.08 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 22.9, 25.9, 28.5, 29.4, 29.5, 29.7, 29.8, 32.1, 52.6, 57.2, 62.3, 67.8, 164.4.

N,N′-Bis(dodecyloxycarbonylmethyl)-N,N,N′,N′-Tetramethyl-N,N′-Ethanediyl-diammonium Dibromide (12E-2-12E), Yield: 53 %

IR (KBr, cm^{-1}): 2928, 2876, 1752, 1472, 1190.

^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 6H), 1.22–1.37 (m, 36H), 1.61–1.74 (quin, 4H), 3.77 (s, 12H), 4.19–4.25 (t, 4H), 4.91 (s, 4H), 5.08 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 22.9, 25.8, 28.4, 29.4, 29.6, 29.7, 29.8, 32.1, 52.5, 57.2, 62.2, 67.8, 164.5.

N,N′-Bis(hexadecyloxycarbonylmethyl)-N,N,N′,N′-Tetramethyl-N,N′-Ethanediyl-Diammonium Dibromide (12E-2-12E), Yield: 59 %

IR (KBr, cm^{-1}): 2927, 2876, 1753, 1472, 1190.

^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 6H), 1.20–1.37 (m, 52H), 1.62–1.75 (quin, 4H), 3.77 (s, 12H), 4.20–4.25 (t, 4H), 4.88 (s, 4H), 5.17 (s, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 22.9, 25.9, 28.5, 29.4, 29.6, 29.7, 29.9, 32.2, 52.5, 57.2, 62.2, 67.8, 164.4.

Phase Transfer Catalysis with Dimeric Quaternary Ammonium Compounds: *O*-Alkylation of Isovanillin

General Procedure

A magnetically stirred boiling solution of isovanillin (0.76 g, 5 mmol), K_2CO_3 (1.04 g, 7.5 mmol) and PTC (0.1 equivalent dimeric quaternary ammonium compounds) in THF (25 mL) was cooled to 40 °C after 1.5 h of refluxing. The mixture was refluxed for 12 h after a solution of alkyl halide (7.5 mmol) in 10 mL THF was added to the mixture. It was poured into 20 mL of water after cooling of the reaction mixture, and then the mixture was extracted with 20 mL of diethylether two times. The organic extracts were combined, washed with 30 mL of brine and dried over anhydrous calcium chloride. Then, organic solvents were evaporated giving crude products which were then chromatographed on silica gel packed in ethyl acetate:hexane (1:3), yielding a yellowish liquid.

3-(Cyclopentyloxy)-4-Methoxy Benzaldehyde

IR (KBr, cm^{-1}): 3080, 2978, 2876, 2748, 1702, 1600, 1446, 1268, 1140.

^1H NMR (300 MHz, $CDCl_3$): δ 1.5–2.1 (m, 8H), 3.96 (s, 3H), 4.8–4.9 (quin, 1H), 6.97–7.42 (m, 3H), 9.83 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 24.3, 32.9, 56.4, 80.6, 110.9, 112.2, 126.5, 130.2, 148.5, 155.6, 191.2.

HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{16}O_3$ $(M + H)^+$ 221.1177, found 221.1233.

3-(Octyloxy)-4-Methoxy Benzaldehyde

IR (KBr, cm^{-1}): 3080, 2927, 2876, 1702, 1600, 1472, 1293, 1165, 1140.

^1H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, 3H), 1.25–1.46 (m, 10H), 1.85 (quin, 2H), 3.94 (s, 3H), 4.06 (t, 2H), 6.99–7.41 (m, 3H), 9.85 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 22.9, 26.1, 29.2, 29.4, 29.5, 32.0, 56.4, 69.2, 110.3, 110.7, 126.9, 130.2, 149.3, 155.0, 191.2.

HRMS (ESI) *m*/*z* calcd. for $C_{16}H_{24}O_3$ $(M + H)^+$ 265.1804, found 265.1869.

Results and Discussion

Some dimeric surfactants with simple hydrophobic alkyl chains and others with hydrophobic alkyl chains containing ester functionalities with different lengths were synthesized and characterized in our laboratory. Then, they were used in *O*-octylation and *O*-cyclopentylation of isovanillin as phase transfer catalysts. The alkylation of isovanillin with alkyl halide was successively carried out in tetrahydrofuran in the presence of potassium carbonate and a phase transfer catalyst. The same reactions were also performed with both the traditional phase transfer catalyst tetrabutylammonium bromide and without any catalyst. When carbonate was used in the absence of PTC, the result was a low conversion of isovanillin. When carbonate was used in the presence of PTC, lipophilic ion pairs (Q^+ ArO^-) are likely to form because the deprotonation of the phenol occurs at the surface of the carbonate. Wilk et al. found that successful completion of the alkylation of isovanillin depends on the particle size of potassium carbonate under PTC conditions. According to Wilk's results, the carbonates with particle size 30–50 μm give quantitative conversion of isovanillin, whereas those with larger particle size (520–570 μm) result in incomplete conversion [38]. We did not change the

Table 1 *O*-Alkylation of isovanillin with phase transfer catalysis

Octylation reaction		Cyclopentylation reaction	
Catalysts	Yields (%)	Catalyst	Yields (%)
Without catalyst	2	Without catalyst	1
TBAB	76	TBAB	65
10-2-10	44	10-2-10	27
12-2-12	47	12-2-12	22
16-2-16	77	16-2-16	45
16-6-16	29	16-6-16	33
16-10-16	75	16-10-16	46
16-Ar(8)-16	60	16-Ar(8)-16	42
12-Ar(8)-12	79	12-Ar(8)-12	41
E10-2-10E	57	E10-2-10E	28
E12-2-12E	36	E12-2-12E	25
E16-2-16E	37	E16-2-16E	17

original partical size of potassium carbonate in the present study. The results are compared in Table 1. Table 1 shows that especially 16-2-16, 16-10-16, 16-Ar(8)-16, 12-Ar(8)-12 and its ester derivative E10-2-10E from geminis synthesized have remarkably exhibited the character of a phase transfer catalyst in the alkylation of isovanillin. The results denoted that the phase transfer character of dimeric quaternary ammonium compounds with long hydrophobic alkyl chains (16-s-16) was sometimes as strong as tetrabutylammonium bromide. On the other hand, geminis with an ester functional tail did not produce a good catalytic effect as much as simple geminis. Johnstone and Rose reported that alkylation of phenols with primary alkyl halides is more effective than that of secondary alkyl halides [43]. Because of the S_N2 rules, yields of the reactions with the secondary alkyl halide, 1-bromocyclopentane, were lower than those of the primary alkyl halide, 1-bromooctane, in accordance with Johnstone and Rose's study.

The alkylation reaction is an important transformation in organic synthesis whereas generally involving a rigorous condition such as the strong base and high temperature. Most of the commonly used methods involve alkylation of phenol or phenoxide ion; the phenoxide ion is generated by treatment of the phenol with a base such as sodium, sodium hydride or sodium amide in a appropriate solvent; alkylation is then normally carried out in the same solvent. 1,4-diazabicyclo [2] octane as an organic base could be used concurrently with K_2CO_3 for the *O*-alkylation of phenolic compounds under solvent-free conditions as reported by Jing et al. [44]. In other work, a phase transfer agent tetrabutylammonium bromide was also used under microwave irradiation in dry media for *O*-alkylation of phenols and alcohols [45]. Low reaction time, low environmental contamination and high yield were aimed for in all studies. In our work, a catalytic amount of a gemini as a phase transfer agent and a relatively harmless base K_2CO_3 was used in all alkylation reactions and, additionally, the solvent THF was recycled. Consequently, we used dimeric quaternary ammonium compounds in phase transfer catalysis and determined the value of the dimeric surfactants as phase transfer agents. We established a facile and environmentally friendly synthesis of 3-(cyclopenthyloxy)-4-methoxy benzaldehyde and 3-(octyloxy)-4-methoxy benzaldehyde with phase transfer catalysis.

In summary, we have demonstrated that dimeric quaternary ammonium compounds can be used in organic synthesis as phase transfer catalysts. Due to the low cost of dimeric quaternary ammonium compounds, this method provides a simplified way to synthesize various organic compounds with *O*-alkylation, *N*-alkylation, condensation reactions, etc. The presented methodology delivers an attractive alternative to classical procedures, and environmental problems can be circumvented. Additionally, an environmental advantage can be provided through the hydrolysable and biodegradable properties of dimeric quaternary ammonium compounds having biological motifs like amides, amino acids and esters. Our study will smooth the path for steadily increasing usage of geminis in phase transfer catalysis.

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