New Quaternary Ammonium Salts Derived from Cardanol and their Use as Phase Transfer Catalyst

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Cardanol obtained from cashew nut shell liquid, a side product of the Brazilian industry, was the starting material for the synthesis of three new quaternary ammonium salts. High molecular weight quaternary nitrogen compounds generally possess high bactericidal activity. This report also presents the results of an investigation of the effectiveness of the new compounds as phase transfer catalysts in oxidation and alkylation reactions, whose yields were comparable to and some even greater than those obtained using the commercial catalyst Aliquat®.

Keywords: cashew nut shell liquid, cardanol, quaternary ammonium salt, phase transfer catalyst.

Introduction

Cashew nut shell liquid (CNSL) is obtained as a by-product in the production of cashew kernels. With an increasing production of raw cashew nuts, Brazil is also one of the leading world producers of CNSL¹. Commercial CNSL is chiefly cardanol (1)², a mixture of 3-alkylphenols (Figure 1) mainly produced by decarboxylation of anarcardic acid (2), the primary constituent of the original oil, after exposure to high temperatures of the industrial treatment of the raw nut. Anarcardic acid (2), a mixture of 2-carboxy-3-alkylphenols, is the main component of the cold pressed or solvent extracted CNSL.

Chemicals derived from CNSL find demand in coating, photographic, polymer and surfactant markets. Our group has been developing a continuing effort on the synthetic transformation of the CNSL constituents into new substances with potential applications³. High molecular weight quaternary nitrogen compounds are very stable, soluble in water, odourless and generally possess high bactericidal activity and act as surface active agents. These properties have made them particularly attractive as germicides, disinfectants and sanitizing agents, especially in food and dairy industries. The importance of long alkyl chain and quaternary nitrogen atom as fundamental units of structure for the activity of quaternary nitrogen compounds was established as early as 1930 by Domagk⁴. CNSL has been used previously to prepare quaternary ammonium salts, the aim of the investigation then was to prepare water soluble compounds to be tested as germicides⁵. We report an entirely different approach, in which the quaternary ammonium cation is placed at the end of the aliphatic chain, enhancing the lipophilic character of the resulting quaternary salts, which is a requirement for a substance to function as a phase transfer catalyst.

In this work, three new quaternary ammonium salts were synthesized from cardanol for use as phase transfer catalysts. Heterogeneous reactions were tested, such as oxidation with KMnO₄⁶, oxidation with NaClO⁷ and in Williamson ether synthesis⁸. The yields obtained are comparable to, and in some cases surpass, those obtained using the commercial product Aliquat®.
Results and Discussion

The starting material, commercial CNSL (1), was initially distilled under reduced pressure and then treated with dimethyl sulfate (Scheme 1). Distillation of the methylated material under reduced pressure and subsequent chromatography on neutral alumina gave methylcardanol (3) in 70% yield. Treating 4 with hydroxylamine hydrochloride and sodium acetate under reflux in ethanol gave oxime 5 in excellent yield (97%). Hydrogenation of oxime 5 over PtO2 in presence of small amounts of chloroform yielded the amine hydrochloride 6 (80% yield).

The primary amine hydrochloride 6 was treated with methyl iodide and sodium bicarbonate in refluxing methanol to give the quaternary ammonium salt 7 in 92% yield. Compound 8 was obtained in 83% yield, after quaternization of amine hydrochloride 6 with ethyl iodide and sodium bicarbonate. Under analogous conditions compound 9 was prepared in 93% yield from 6 and propyl iodide.

Obtained when using Aliquat® as catalyst in the same reactions. Interestingly, results achieved with the new catalysts in the Williamson ether synthesis (Scheme 4) were consistently better than the yield obtained with the commercial product.

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Experimental

1H-NMR (90 MHz) were recorded on a Varian Associates T-90 spectrometer, 1H-NMR (200 MHz) and 13C-NMR (50.3 MHz) were recorded on a Bruker spectrometer and the internal references were (CH3)4Si (d 0.00) and CDCl3 (d 77.00), respectively. Infrared (IR) spectra were recorded on either a Perkin-Elmer 283-B or a Nicolet 2DX-FT spectrometers. Ozonolysis was performed on a Welsbach apparatus. Hydrogenations were carried out on a 3910-Parr instrument. High resolution mass spectrometry data were obtained from a matrix-assisted laser desorption ionization time of flight (MALDI-TOF) Voyager-DE STR Bioworkstation spectrometer (PerSeptive Biosystems) using ferulic acid matrix. Melting points were determined on a Kofler apparatus and are uncorrected. Reactions requiring anhydrous conditions were carried out under nitrogen or argon atmosphere, using oven dried glassware. Solvents were purified by standard methodology. Light petroleum refers to the fraction with b.p. 40-60°C.
Cardanol (1)

Commercial CNSL, 50 g, was distilled under reduced pressure (1 mmHg). The pale yellow fraction collected at 206-208°C corresponds to cardanol 1 (33.1 g), displaying identical spectral data with those in the literature.14

Methylcardanol (3)

Cardanol 1 (18.7 g, ~ 62 mmol) was added to a stirred solution of KOH (5.3 g) in methanol (22 mL). To the cold solution, 9.0 mL of dimethyl sulfate was slowly added. When the addition was completed, the ice-bath was removed and the mixture was heated to 60°C for 1 h, then allowed to cool to room temperature and stirred for further 2 h. The reaction mixture was filtered and the inorganic residue washed with light petroleum. The combined washings and filtrate were then concentrated under reduced pressure, the crude methylcardanol was distilled at 180-185°C (1 mmHg) to give 16.8 g of a pale yellow oil. Further purification by chromatography on neutral alumina (elution with hexane) afforded 13.6 g (~ 44 mmol, 70%) of methylcardanol 3 as an oil: IR (film) υ (cm−1) : 1630, 1604, 1588, 1498, 1261; 1 H NMR (CDCl3, 50.3 MHz) δ: 0.9 (t, 1.1 H, CH3), 1.4 (br, 7.5 H, CH2), 2.1 (br, 2.6 H, CH2-C=), 2.6 (2 H, CH2-Ar), 2.8 (br, 2.5 H, =C-CH2-C=), 3.8 (s, 3 H, CH3O), 5.4 (m, 4.5 H, CH=), 6.7-7.2 (m, 4 H, HAr).

8-(3-Methoxy)-phenyl-1-(n)-octanaldehyde (4)

Methylcardanol 3 (2.37 g, ~ 7.6 mmol) was submitted to ozonolysis in two portions: the first portion (1.21 g, ~ 3.9 mmol) received identical treatment. The organic extracts of the two ozonolyses were then combined, filtered, and concentrated under reduced pressure. The residue was submitted to chromatography on 60 g of neutral alumina with 300 mL of hexane, and 350 mL of 5% ethyl acetate in hexane to afford 0.89 g (50%) of aldehyde 4 as a colorless oil: IR (film) υ (cm−1) : 2719, 1724, 1603, 1587, 1489, 1261; 1 H NMR (CDCl3, 90 MHz) δ: 1.3-1.6 (m, 10 H, CH2), 2.3 (t, 2 H, CH2CO), 2.5 (t, 2 H, CH2Ar), 3.7 (s, 3 H, CH3O), 6.6-7.1 (m, 4 H, HAr), 9.7 (t, 1 H, HCO).

8-(3-Methoxy)-phenyl-1-(n)-octylamine hydrochloride (6)

Oxime 5 (0.50 g, 2.0 mmol) was dissolved in dry ethanol (50 mL) and chloroform (3 mL) was added to the solution. The resulting solution was hydrogenated (60 psi) over PtO2 (0.05 g) for 2 h. The catalyst was then filtered off and the filtrate concentrated. The remaining white solid was washed twice with dry ether to give 0.44 g (80%) of compound 6 as a white solid: m.p. 79-81ºC; IR (KBr) υ (cm−1) : 3406, 1610, 1582, 1492; MS (70 eV) m/z: 149 (7.8%), 135 (8.9%), 122 (100%), 91 (14.9%), 77 (10.1%), 72 (25.2%), 55 (15.3%); 1 H NMR (CDCl3, 200 MHz) δ: 1.2-2.6 (m, 10 H, CH2), 2.2 (anti) and 2.38 (syn) (q, 2 H, CH2-CH3NOH), 2.58 (t, 2 H, CH2Ar), 3.79 (s, 3 H, CH3O), 6.7-6.8 (m, 3 H, HAr), 6.7-6.8 (syn and 7.42 (anti) (1 H, CHNOH), 7.19 (dt, 1 H, HAr); 13 C NMR (CDCl3, 50.3 MHz) δ: 25.91, 26.50, 27.53, 28.90, 29.16, 31.24, 35.89, 55.02, 110.70, 114.07, 120.77, 129.09, 144.37, 152.76 (syn) and 152.17 (anti), 152.41.

8-(3-Methoxy)-phenyl-1-(n)-octylammonium iodide (7)

A mixture of amine hydrochloride 6 (0.27 g, 1.0 mmol), methyl iodide (0.5 mL, 8.0 mmol), sodium bicarbonate (0.38 g,
4.0 mmol) and dry methanol (15 mL) was heated under reflux with stirring for 55 h. Additional methyl iodide (0.2 mL, 3.2 mmol each addition) was added after 24 and 48 h. The reaction mixture was then evaporated under reduced pressure and the residual solid was extracted three times with boiling chloroform. The combined extracts were cooled, filtered, and evaporated to dryness. The residue, a colorless soft solid weighing 0.37 g (92%), was identified as the quaternary ammonium salt 7: m.p. 101–102°C; IR (KBr) ν (cm⁻¹): 3464, 1602, 1589, 1486; MS (70 eV) m/z: 347 (3.1%), 277! (4.3%), 262 (21.7%), 142 (28.4%), 122 (62.1%), 91 (10.8%), 77 (4.2%), 72 (72.2%), 58 (100%); 1H NMR (CDCl₃, 200 MHz) δ: 1.26 (br, 8 H, CH₂), 1.50 (t, 2 H, CH₂), 1.64 (br, 2 H, CH₂), 2.47 (t, 2 H, CH₂Ar), 3.32 (s, 9 H, CH₃ N+), 3.50 (m, 2 H, CH₂ N+), 3.69 (s, 3 H, CH₃ O), 6.63–6.68 (m, 3 H, HAr), 7.04–7.25 (m, 1 H, HAr); 13C NMR (CDCl₃, 50.3 MHz): 23.03, 25.64, 28.96, 31.13, 35.77, 53.61 (3C, C₃N+), 55.10, 66.88, 110.76, 113.98, 120.72, 129.07, 144.28, 159.36. HRMS (M+ - I) calculated for C₁₈H₃₂NO+ 320.2953, found 320.3990.

8-(3-Methoxy)-phenyl-N,N,N-tripropyl-1-(n)-octylammonium iodide (8)

A mixture of the amine hydrochloride 6 (0.27 g, 1.0 mmol), ethyl iodide (0.6 mL, 8.0 mmol), sodium bicarbonate (0.38 g, 4.5 mmol) and dry methanol (15 mL) was heated under reflux with stirring for 22 h. Additional ethyl iodide (0.6 mL each) was added after 6 and 14 h. The reaction mixture was then evaporated under reduced pressure and the residual solid extracted three times with boiling chloroform. The combined extracts were cooled, filtered, and evaporated to dryness. Recrystallization of the residue from ethyl acetate gave 0.37 g (83%) identified as the quaternary ammonium salt 8: m.p. 101–102°C; IR (KBr) ν (cm⁻¹): 3464, 1602, 1589, 1486; MS (70 eV) m/z: 347 (3.1%), 277! (4.3%), 262 (21.7%), 142 (28.4%), 122 (62.1%), 91 (10.8%), 77 (4.2%), 72 (72.2%), 58 (100%); 1H NMR (CDCl₃, 200 MHz) δ: 1.26 (br, 8 H, CH₂), 1.50 (t, 2 H, CH₂), 1.64 (br, 2 H, CH₂), 2.47 (t, 2 H, CH₂Ar), 3.32 (s, 9 H, CH₃ N+), 3.50 (m, 2 H, CH₂ N+), 3.69 (s, 3 H, CH₃ O), 6.63–6.68 (m, 3 H, HAr), 7.04–7.25 (m, 1 H, HAr); 13C NMR (CDCl₃, 50.3 MHz): 23.03, 25.64, 28.96, 31.13, 35.77, 53.61 (3C, C₃N+), 55.10, 66.88, 110.76, 113.98, 120.72, 129.07, 144.28, 159.36. HRMS (M+ - I) calculated for C₂₁H₃₈NO+ 362.2484, found 362.2730.

Oxidation of cis-cyclooctene (10) with KMnO₄

To a stirred mixture of potassium permanganate (2.52 g, 16.0 mmol) and phase transfer catalyst 7 (0.08 g, 0.2 mmol) in water (3.0 mL), a solution of cis-cyclooctene 10 (0.44 g, 4.0 mmol) in benzene (1.0 mL) was added after 0.5 h period. The reaction mixture was stirred overnight at room temperature and then the excess permanganate was destroyed with 10% sodium metabisulfite solution. The product was basified with NaOH and the benzene solution extracted with ethyl acetate. The aqueous phase was acidified and extracted with ethyl acetate. The combined ethyl acetate extracts were dried over Na₂SO₄, filtered and the solvent evaporated to give a white solid residue (0.65 g). After dry flash chromatography (30 g of silica gel, elution with 20% of ethyl acetate in hexane), 0.53 g (76%) of 1,8-octanodioic acid (11) were recovered. The IR and 1H-NMR spectra of the isolated product were consistent with the assigned structure.

Analogous procedures were carried out using compound 8 (0.09 g), 9 (0.10 g) and Aliquat® (0.068 g) as phase transfer catalysts, affording 1,8-octanodioic acid (11) in 74% (0.52 g), 60% (0.42 g) and 64% (0.44 g) yields respectively.

Oxidation of benzyl alcohol (12) with NaClO

To a solution of 12 (0.432 g, 4.0 mmol) and phase transfer catalyst 7 (0.08 g, 0.2 mmol) in dichloromethane (10 mL), a 4% sodium hypochlorite solution (25 mL) was added. The mixture was stirred at room temperature for 6 h, then extracted with dichloromethane, dried over Na₂SO₄, and filtered. The solvent was evaporated to yield 0.28 g (67%) of a yellow viscous liquid was identified as benzaldehyde (13), by comparison of the IR and 1H-NMR spectra with those of an authentic sample.

Identical procedures, performed with phase transfer catalysts 8 (0.08 g), 9 (0.10 g) and Aliquat® (0.08 g), gave aldehyde 13 in 27% (0.12 g), 26% (0.11 g) and 49% (0.21 g) yields, respectively.
Williamson synthesis of benzyl ether (15)

To a mixture of benzyl alcohol 12 (0.54 g, 5.0 mmol) and compound 7 (0.10 g, 0.3 mmol), benzyl chloride 14 (1.2 mL, 10 mmol) and a 50% sodium hydroxide solution (5.4 mL) were added. The reaction mixture was stirred at room temperature overnight. The reaction products were then extracted with ethyl acetate and the organic extracts were dried (Na₂SO₄), filtered and evaporated. The residue, a yellow liquid, was distilled under reduced pressure (1 mmHg) affording 0.75 g (76%) of compound 15, which was identified by IR and ¹H-NMR spectroscopy.

Same procedure was repeated three times, using compounds 8 (0.10 g), 9 (0.12 g) and Aliquat® (0.10 g) as phase transfer catalysts. Yields of 15 were 98% (0.97 g), 84% (0.83 g) and 60% (0.59 g) respectively.

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