NUSANTARA BIOSCIENCE
Vol. 14, No. 1, pp. 25-33
May 2022

ISSN: 2087-3948
E-ISSN: 2087-3956
DOI: 10.13057/nusbiosci/n140103

Synthesis of novel polymer quaternary ammonium salt derived from glucose as a phase transfer catalyst

IHSAN ALRUBAIE[1], AHMED THAMER SALIM[2], MOHAUMAN MOHAMMAD MAJEED[3,♥], ALI JABBAR RADHI[4,5]
[1] College of Pharmacy, Islamic University. Najaf 54001, Iraq
[2] College of Pharmacy, Al-Nahrain University. Al Jadriyah Bridge, Baghdad 64074, Iraq
[3]Department of Chemistry, Faculty of Science, Kufa University. Kufa, Najaf 54001, Iraq. Tel. +964-726-521-7601,
♥email: muhaimin.alrufaie@uokufa.edu.iq
[4] College of Pharmacy, University of Al-Kafeel. Najaf 61001, Iraq
[5]Ministry of Education, General Directorate of Education in Najaf Al-Ashraf. Najaf, Iraq

Manuscript received: 19 December 2021. Revision accepted: 12 February 2022.

Abstract. *Alrubaie I, Salim AT, Majeed MM, Radhi AJ. 2022. Synthesis of novel polymer quaternary ammonium salt derived from glucose as a phase transfer catalyst. Nusantara Bioscience 14: 25-33.* Some new polymers containing quaternary ammonium salts based-carbohydrate starting from methyl-4,6-*O*-benzylidene-glucopyranoside have been prepared. The ammonium groups are connected to the glucose structure in various positions (2 and 3). Our synthesis used methyl-4,6-*O*-benzylidene-α-D-glucopyranoside through nucleophilic reagents to produce the main intermediates. The monomer glucose-quaternary ammonium salts are immobilized on the polyvinyl azide to give the final structure of the Polymer-Supported quaternary ammonium salts. In certain new kinds of phase transfer catalysts, the effectiveness of the polymer glucose-quaternary ammonium salts was tested in the Williamson etherification. Ether synthesis is a typical example of using a phase transfer catalyst. The reactions were performed in a liquid-liquid two-phase system, applying a mixture of toluene and a 50% solution of aqueous sodium hydroxide in the presence of a 20 mg/mmol catalyst (compound 9). Compared to other derivatives, the reaction of 4-nitrophenol with dibromoethylene gives the highest yields. On the other hand, compound 9 with the C16 chain gives high activity in the phase transfer catalyst.

Keywords: Carbohydrates, QAS, Quaternary ammonium salts, polymer, PTC

INTRODUCTION

Phase-transfer catalysis (PTC), a broadly utilized methodology in organic chemistry, has gained growing recognition in recent years for many reasons (Chokaouychai and Zhang 2020; Iribarren and Trujillo 2020; Pudi et al. 2020; Roagna et al. 2020; Weatherley 2020; Xu et al. 2021). For instance, phase transfer catalysis has been identified as an influential green chemistry method that decreases waste generation (Lucchese and Marzorati. 2000; Makosza, 2000; Ikunaka, 2008; Nelson and Benjamin. 2011). In the meantime, the advancement of the asymmetric variant of PTC has created considerable attention because of its possible applicability in the industrial asymmetric synthesis of pharmaceuticals (Haraguchi et al. 2010). The mechanism of PTC typically includes activation of anionic varieties by the carrier of the ion of an aqueous phase, where ions are extremely solvated and unreactive, to a nonpolar organic solvent, where more limited solvation of the ions can lead to enhanced reactivity towards a neutral substrate. Various types of PTC have been utilized, the most common ones being quaternary ammonium salts, with the tetraalkylammonium ion acting as the counter ion of the reactive anion. These quaternary ammonium salts are applied in liquid-liquid phase-transfer catalysis (Annunziata et al. 2000; Chinchílla et al. 2000; Denmark et al. 2011; Waser et al. 2012; Jia et al. 2015; Jin et al. 2018).

A general Figure 1 of the quaternary ammonium salt promoted SN2 reaction involving a (Q+X-) salt with an alkyl halide (RX) is also presented (Vander Zwan and Hartner 1978; Gianluca and Fish 2011). These versatile catalysts can catalyze many reactions, and an especially attractive application is the quaternary ammonium salts that promote nucleophilic Williamson etherification (Freedman and Bubois 1975; Vander Zwan and Hartner 1978; Annunziata et al. 2000; Chinchílla et al. 2000; Denmark et al. 2011; Gianluca and Fish 2011; Naik 2017). Most frequently, sugar-based quaternary ammonium salts are extensively utilized in various applications (Dmochowska et al. 2011; Dmochowska et al. 2016). Carbohydrate derivatives have a wide range of applications for stereochemical control as chiral auxiliaries (Kunz and Rück 1993; O'Doherty 2013), ligands (Lehnert et al. 2011; Henderson et al. 2016), organocatalysts (Phillips 2014; Sabah et al. 2020), and PTC (Bakó et al. 2012, 2015; Erfurt et al. 2020).

The building of the structure of the sugars into the chiral catalyst has many advantages: Carbohydrates utilized as starting materials are, in most states, inexpensive and readily available commercial products. In addition, carbohydrates contain functions that can create secondary connecting sites and catalytic sites (Rapi et al. 2014, 2016, 2017, 2018). Immobilizing the sugar-based quaternary ammonium salt onto polymers allows for many advantages, such as easy handling, recyclability, and adaptation to continuous processes for this important complexant set (Leelamma and Devaky 2009; Itsuno et al. 2010).

Polymers involving ammonium salt compounds are widely used in the chemistry of polymers and have been known for a long time (Jiang et al. 2005; Liao and Ye 2018; Popescu et al. 2019). Recently, these ammonium salt compounds containing polymers have been studied intensively due to their peculiarities and self-assemblies of QAS systems (You et al. 2021). Moreover, immobilizing the QAS onto polymers allows for many advantages, such as easy handling, recyclability, and adaptation to continuous processes for this important set of compounds (Chinchílla and Nájera 2009; Haraguchi et al. 2010; Zhang et al. 2012).

In this research, we prepared poly-quaternary ammonium salt derivatives and applied them as catalysts in PTC operation in Figure 1.

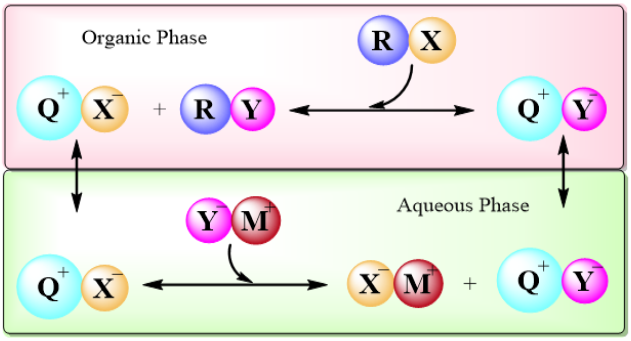


Figure 1. Mechanism of phase-transfer catalysis

MATERIALS AND METHODS

Instrumentation

FT-IR spectra were recorded using Fourier transform infrared Alpha-Broker (Germany) infrared spectrophotometer between 4000 and 600 cm^{-1}. In addition, ^{1}H and ^{13}C NMR spectra in DMSO-d_6 were obtained on Bruker spectrometer (300MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR, respectively). Mass spectra were recorded on the MS system, model 5975 quadrupole analyzer, performed at Tarbiat Modares University, Tehran, Iran. Transmittance Electron Microscopy (TEM) CM-130 microscope was installed in 2005; it is a 300 kV analytical TEM/STEM with a LaB6 source. Measurements are made at the Department of Electricity, Faculty of Engineering, Shahid Beheshti University, Iran. FESEM INSPECT S50 Measurements, Shahid Beheshti University, Iran.

Reagents and materials

1-Bromohexadecane (>99%), 1-Bromotetradecane (>99%), 1-Bromododecane (>99%), 1-Bromo decane (>99%) were purchased from Sigma Aldrich (Iran). The 3-Chloro-N, N-diethylpropan-1-amine (>99%), Methyl 4,6-O-benzylidene-α-D-glucopyranoside (>97%) were purchased from N.D.B. Co., Ltd. (China). Benzyl Alcohol (>96%), Cyclohexanol (>95%), Phenol (>95%) were purchased from GCC (India). Dibromoethylene (>98%) and Benzyl Chloride (>97%) were purchased from GCC (Malaysia). Dimethyl sulfoxide (>95%), Chloroform (>95%), Sodium ascorbate (>95%), Cuprous chloride (>95%), Hexane (>96%), Ethyl acetate (>95%), Ethanol (>97%), propargyl bromide (>93%), *N,N*- Dimethylformamid (>97%), were purchased from Sigma Aldrich (US). Acetone (>99%), Diethyl ether (>98%), Tetrahydrofurane (>98%), toluene (>97%), Nitric acid (>97%), were purchased from Fisher (US). Sodium hydroxide (>94%) was purchased from BDH (England).

Synthesis of methyl-4,6-*O*-benzylidene-2,3-di-*O*-propargyl-*α*-D- glucopyranoside 2

A solution of methyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (4g, 14.16 mmol) was dissolved in 150 mL of anhydrous THF, and sodium hydride (0.68 g, 28.32 mmol) was added and cooled with an ice-salt bath. The mixture reaction was stirred for 20 mins before 2.14 mL (3.36 g, 28.32 mmol) of propargyl bromide was added slowly over 1 h. The reaction mixture is stirred for 3 days at room temperature and continues stirring until the reaction is complete. The reaction course was followed by TLC ethyl acetate: Hexane (1:1) as an eluent to afford the product. MeOH is added to the destruction of excess sodium hydride. The solvent was removed under diminished pressure, and the residue was taken up in 250 mL of CH_2Cl_2 and 150 mL of water. The organic layer was dried using $MgSO_4$, filtered, and concentrated by evaporated solvent. The crude material was purified by column chromatography and concentrated under a rotary evaporator to give desired compound 2 (70%) yellowish-white solid, m.p 76-78. FT-IR cm^{-1}: 3284 (CH- acetylenic), 3066 (CH-aromatic), 2118 (-C≡C-). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 7.49-7.35 (m, 5H, Ph). 5.64 (s, 1H, PhCH-), 4.90 (d, J = 3.5 Hz, 1H, H-1), 4.26 (m, 1H; H-6ax), 4.16 (m, 1H; H-6eq), 4.15-4.10 (m, 4H, -OCH_2C≡C), 3.86-3.75 (m,1H, H-2), 3.72- 3.63 (m, 1H, H-4), 3.59-3.57 (m,1H, H-5), 3.57-3.52 (m,1H, H-3), 3.42 (s,3H,-OCH_3), 3.5 (s, 2H,-C≡CH). ^{13}C NMR (75 MHz, DMSO) δ 138.00, 129.31, 128.59, 126.54 (Ph), 100.83 (PhCH-),98.32 (C-1), 81.13, 80.83, 80.73 (C-2/C-4/C-3), 78.29 (-OCH_2C≡CH), 77.94 (-OCH_2.C≡CH), 67.43 (C-6), 62.47 (C-5), 59.35 (-OCH_2C≡C), 58.06 (-OCH_2C≡C), 55.08 (-OCH_3). MS: [M+] calcd. for $C_{20}H_{22}O_6$: 358.39; found: 358,2.

Synthesis of 3-azido-*N,N*-diethylpropan-1-amine(azido-tert-amine) 4

To a solution (3.26 mL, 3 g, 22.11 mmol) of 3-chloro-*N*, *N*-diethylpropan-1-amine in (15 mL) DMSO, (1.17 gm, 18 mmol) of sodium azide was added, and the mixture was stirred for 72 hrs. The reaction course was followed by TLC ethyl acetate: Hexane (1:1) as eluent to afford the product, 50 mL of DCM was added for extraction, the organic layer was separated, and the residue was washed with DCM, the product 4 yellow liquid 3.11 mL (95%). FT-IR cm^{-1}: 2090 (azide group).

Synthesis of methyl-4,6-*O*-benzylidene-2,3-bis-*O*-[2-(4-ethyl-1H-1,2,3-triazol-1-yl)-*N,N*-diethylpropan-1-amine]-*α*-D-glucopyranoside 5

To a solution (3.2 g, 8.92 mmol) of compound 1 in (30 mL) of DCM, (2.54 g, 17.84 mmol) of azido-tert-amine was added. After the mixture showed homogeneity, sodium ascorbate (0.35 g, 1.78 mmol) and cuprous chloride (0.17 g, 1.78 mmol) were added, and the mixture was stirred at room temperature for 72 hrs. The reaction course was followed by TLC ethyl acetate: Hexane (1:1) as eluent. The solvent was removed under diminished pressure, and the residue was taken up in 50 mL of CH_2Cl_2 and 150 mL of water. The crude material was purified by column chromatography-ethylacetate: Hexane (1:1) and concentrated under a rotary evaporator to give desired compound 5 (76%) as a yellow solid, m.p 104-106. FT-IR cm^{-1}: 3136 (CH-triazole rings), 3066 (CH-aromatic). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 8.14(s, 2H,-CH-triazole ring), 8.00 (s, 2H,-CH-triazole ring), 7.55-7.35 (m, 5H, Ph), 5.67 (s, 1H, PhCH-), 4.85-4.80 (m, 1H, H-1), 4.80-4.63(m,4H, $-OCH_2-$), 4.42-4.30 (m,4H, $-CH_2CH_2-CH_2N(CH_2CH_3)_2$), 4.29 (m, 1H; H-6ax), 4.15 (m, 1H; H-6eq), 3.82-3.67 (m, 1H, H-4), 3.87-3.82 (m,1H, H-2), 3.60-3.51 (m, 1H, H-3), 3.66-3.62 (m,1H, H-5), 3.47 (s, 3H,-OCH_3), 2.44-2.26 (m, 8H, $-N(CH_2CH_3)_2$), 1.97-1.78 (m, 8H, $-CH_2-CH_2N(CH_2CH_3)_2$), 0.96-0.83 (t,12H, -$N(CH_2CH_3)_2$). ^{13}C NMR (75 MHz, DMSO) δ 144.90, 144.45 (-C=CH-triazole ring), 138.10, 129.27, 128.57, 126.51(Ph), 124.42(-C=CH-triazole ring), 124.05 (-C=CH-triazole ring), 100.85 (PhCH-), 98.54 (C-1), 81.15, 80.77, 80.59 (C-2/C-4/C-3), 67.48 (C-6), 65.75 (C-5), 64.07, 62.59 ($-OCH_2-$), 55.08 ($-OCH_3$), 49.31 ($-CH_2-CH_2-CH_2N(CH_2CH_3)_2$), 48.09, 48.00 ($-CH_2N$ $(CH_2CH_3)_2$), 46.63, 46.59 ($-N(CH_2$ $CH_3)_2$), 27.95, 27.89 ($-CH_2-CH_2N(CH_2CH_3)_2$), 12.06, 12.04 (-N $(CH_2$ $CH_3)_2$). MS: [M+] calcd. for $C_{34}H_{54}N_8O_6$: 670.86; found: 670.5.

Synthesis of methyl-2,3-bis-*O*-[2-(4-ethyl-1H-1,2,3-triazol-1-yl)-*N, N*-diethylpropan-1-amine]-*α*-D-glucopyranoside 6

To a solution (4.4 g, 6.55 mmol) of compound 3 in methanol, 100 mg of Pd-C 5% was added, then the flask was flashed with hydrogen gas to remove the O_2 atmosphere. The H_2 was filled in a balloon, attached to the flask, and stirred at RT for 72 hrs at room temperature. The reaction course was followed by TLC methanol: Chloroform (1:3) as an eluent to afford the product. Filtrating the product was concentrated. The residue was purified by column chromatography on silica gel using methanol: Chloroform (1:3) as eluent to make the product 6 (83%) yellowish semisolid. FT-IR cm^{-1}: 3399 (-OH), 3143 (-CH-triazole rings). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 8.14(s, 2H, -CH-triazole ring),7.99 (s, 2H, -CH-triazole ring), 5.54 (s, 1H, 4-OH), 4.83-4.79 (m, 1H, H-1), 4.42-4.32 (m, 4H, $-CH_2CH_2-CH_2N$ $(CH_2CH_3)_2$), 4.31 (m, 1H; H-6ax), 4.16 (m, 1H; H-6eq), 3.88-3.83 (m, 1H, H-2), 3.82-3.69 (m, 1H, H-4), 3.67-3.62 (m, 1H, H-5), 3.61-3.52 (m, 1H, H-3), 3.30 (s,3H, $-OCH_3$), 2.48-2.30 (m, 8H, -$N(CH_2CH_3)_2$), 1.97-1.63 (m, 8H, $-CH_2-CH_2N$ $(CH_2CH_3)_2$), 0.98-0.84 (q, 12H, $-N(CH_2CH_3)_2$), ^{13}C NMR (75 MHz, DMSO) δ 144.91, 144.45 (-C=CH-triazole ring), 124.08, 124.45 (-C=CH-triazole ring), 98.53 (C-1), 81.13, 80.66, 80.58 (C-2/C-4/C-3), 68.47(C-6), 65.72 (C-5), 64.05, 62.58 ($-OCH_2-$), 55.07 ($-OCH_3$), 49.15, 49.10 ($-CH_2-CH_2-CH_2N(CH_2$ $CH_3)_2$), 47.94 ($-CH_2N$ $(CH_2CH_3)_2$), 46.53, 46.50 ($-N(CH_2CH_3)_2$), 27.53 ($-CH_2-CH_2N(CH_2CH_3)_2$), 11.72 (-N $(CH_2$ $CH_3)_2$). MS: [M+] calcd. for $C_{27}H_{50}N_8O_6$: 582.75; found: 582.4.

Synthesis of methy-4,6-*O*-dipropargyl-2,3-*O*-bis[2-(4-ethyl-1H-1,2,3-triazol-1-yl)-*N, N*-diethylpropan-1-amine]-*α*-D-glucopyranoside 7

A solution (2.8 g, 4.50 mmol) of compound 4 was dissolved in 70 mL anhydrous THF, and sodium hydride (0.21 g, 9 mmol) was added and cooled with an ice-salt bath. The mixture reaction was stirred for 20 mint before 0.68 mL (1.07 g, 9 mmol) of propargyl bromide was added slowly over 1 h. the reaction mixture is stirred for 3 days at room temperature and continues stirring until the reaction is complete. The reaction course was followed by TLC ethyl acetate: Hexane (1:1) as an eluent to afford the product. MeOH was added carefully until gas formation ceased (destruction of excess sodium hydride). The solvent was removed under diminished pressure, and the residue was taken up in 80 mL of CH_2Cl_2 and 150 mL of water. The organic layer was dried using $MgSO_4$, filtered, and concentrated by evaporated solvent. The crude material was purified by column chromatography to make the product 7 (72 %) yellowish-white solid, m.p 119-121 ℃. FT-IR cm^{-1}: 3285 ,(CH-acetylenic), 2117, (-C≡C-). ^{1}HNMR (300 MHz, DMSO-d_6) δ 8.50(s, 2H,-CH-triazole ring), -8.00 (s, 2H,-CH-triazole ring), 4.86-4.77 (m, 1H, H-1), 4.74-4.65 (m, 4H, $-OCH_2-$), 4.53-4.37 (m,4H, $-CH_2CH_2-CH_2N$ $(CH_2CH_3)_2$), 4.37-4.24 (m, 4H, $-OCH_2C{\equiv}C$), 4.23 (m, 1H; H-6ax), 4.16 (m, 1H; H-6eq), 3.86-3.73 (m, 1H, H-2), 3.72-3.63 (m, 1H, H-4), 3.62-3.58 (m, 1H, H-5), 3.58-3.54 (m, 1H, H-3), 2.71-2.51 (m, 1H), 2.68-2.57 (m, 8H, -$N(CH_2$ $CH_3)_2$), 3.50 (s, 2H,-C≡CH), 2.07-1.90 (m, 8H, -$CH_2-CH_2N(CH_2CH_3)_2$), 1.04-0.91 (t,12H, -N $(CH_2$ $CH_3)_2$). ^{13}CNMR (75 MHz, DMSO) δ 144.90, 144.80 (-C=CH-triazole ring), 124.05 (-C=CH-triazole ring), 124.95 (-C=CH-triazole ring), 98.26 (C-1), 81.29, 80.88, 80.34 (C-2/C-4/C-3), 67.07 (C-6), 65.43 (C-5), 64.90, 62.39($-OCH_2-$), 57.83, 55.57($-OCH_3$), 49.75 ($-CH_2-CH_2-CH_2N(CH_2CH_3)_2$), 47.71 ($-CH_2N$ $(CH_2$ $CH_3)_2$), 46.72 (-$N(CH_2CH_3)_2$), 25.70 ($-CH_2-CH_2N(CH_2CH_3)_2$), 11.20 (-N $(CH_2$ $CH_3)_2$). MS: [M+] calcd. for $C_{33}H_{54}N_8O_6$: 658.85; found: 658.5.

General procedure for the quaternization of amino sugars 8

Compound 7 (1.5 mmol) was dissolved in DMF. Alkyl halide: 2 equivalents were added. The reaction mixture was refluxed for 5 hrs. After the reactions were complete, followed by TLC, the mixture was filtered, and the solvent was removed under reduced pressure. The purification processes of the different ammonium salts were done by recrystallization (using petroleum ether/hexane) of the product 8 (78 %) as a brown solid, m.p 165-167ºC. FT-IR cm^{-1}: 2931, 2771, 2441, 1428, 1465, 874, 758, ^{1}H NMR

(300 MHz, DMSO-d_6) δ 8.07 (s, 2H,-CH-triazole ring), 5.95-4.86 (m, 1H, H-1), 4.78-4.56 (m, 4H, $-OCH_2-$), 4.39-4.33 (m,4H, $-CH_2CH_2-CH_2N^+(CH_2CH_3)_2$), 4.23 (m, 1H; H-6ax), 4.14 (m, 1H; H-6eq), 4.14-4.08 (m, 4H, $-CH_2-CH_2N^+(CH_2CH_3)_2$), 4.07-4.02 (m, 4H, $-OCH_2C{\equiv}C$), 3.87 - 3.76 (m, 1H, H-2), 3.76-3.67 (m, 1H, H-4), 3.64-3.57 (m, 1H, H-5), 3.56-3.52 (m, 1H, H-3), 3.49 (s, 2H,-C≡CH), 3.43 (s,3H,$-OCH_3$), 3.29-3.18 (m, 8H, $-N^+(CH_2CH_3)_2$), 2.41-2.24 (m, 4H,$-CH_2-CH_2N^+(CH_2CH_3)_2$), 1.89-1.78 (m, 4H,$-CH_2-CH_2N^+(CH_2CH_3)_2$), 1.53-1.25 (m, 28H, $-(CH_2)_{14}-$), 1.06-0.92 (m, 18H, $-CH_3$). ^{13}C NMR (75 MHz, DMSO) δ 144.92, 144.85 (-C=CH-triazole ring), 124.62(-C=CH-triazole ring), 124.30 (-C=CH-triazole ring), 98.46 (C-1), 81.47, 80.77, 80.15 (C-2/C-4/C-3),78.36,78.26 (C≡CH), 76.51, 74.28 (C≡CH), 67.23 (C-6), 58.62 (C-5), 57.86 ($-OCH_2-$), 57.63, 57.39, 57.14, 56.89, 55.87 ($-OCH_3$), 55.71, 54.65 ($-CH_2-CH_2-CH_2N^+(CH_2CH_3)_2$), 52.66 ($-CH_2N^+(CH_2CH_3)_2$), 50.49 ($-N^+(CH_2CH_3)_2$), 31.49-28.07 ($-CH_2$), 27.53, 27.02 ($-CH_2-CH_2N^+(CH_2CH_3)_2$), 25.87, 23.46, 23.34 ($-CH_2$), 14.76, 14.76 ($-N^+(CH_2CH_3)_2$), 9.24($-CH_3$), MS: [M+] calcd. For $C_{53}H_{96}N_8O_6^{2+}$: 941.40; found: 941.3.

Synthesis of PVN_3

Polyvinyl chloride (PVC) (10 g) was dissolved in (30 mL) of DMSO, and then (3.5 g, 53 mmol) of sodium azide was added, and the mixture was stirred for 72 hrs. Finally, the mixture was washed extensively with water, and the product was dried to form a light-yellow solid (yield: 9.8 g).

Synthesis of polymeric QAS 9

Polyvinyl azide (PVN3) (2.4 g), compound 8 (0.00063 mol) was dissolved in (25 mL) of DCM and stirred for 15 minutes. After the mixture showed homogeneity, sodium ascorbate (0.6 g, 3 mmol) and cuprous chloride (0.3 g, 3 mmol) were added and stirred at room temperature for 72 hrs. The mixture was washed extensively with water and Ethanol. The solid product 9 was dried to form brown.

General procedure for Williamson reaction compound 10-15

A solution of alcohol (10 mmol), alkyl halides (mono-substation: 1eq, di-substation: 2 eq), and the polymeric catalyst (20 mg/mmol) was dissolved in a mixture of toluene and 50% aq. NaOH 3:2 ratio (10 mL). The mixture was stirred at a temperature of 65°C for 8 hrs. The end of the reaction was monitored by TLC (petroleum ether-ethylacetate 3:1). After filtration to recover the catalyst, 5 mL of toluene was added. The organic layer was separated by a separating funnel, washed two times with (10 mL) of water, dried over anhydrous magnesium sulfate, and filtered. The solvent was removed in a vacuum. The crude materials were purified by column chromatography.

RESULTS AND DISCUSSION

To synthesize carbohydrate derivatives with QASs, we introduced the quaternary ammonium group via a reaction between tert-amine with 1-bromo hexadecane, 1-bromotetradecane, 1-bromodecane, and 1-bromododecane. Methyl 4,6-O-benzylidene-2,3-O-bis[prop-2-yn-1-yl]-glucopyranoside (comp.2) was chosen as the beginning material, which was synthesized in our lab in one step starting with methyl 4,6-O-benzylidene-α-D-glucopyranoside (comp.1) in high yields according to literature procedure (Tankam et al. 2007). The copper-catalyzed click reaction between azides and terminal alkynes is ideal for many applications, with the balance of stability and reactivity, allowing new sugar development with a linking moiety. Furthermore, click chemistry allows the connection between alkynyl-carbohydrates (comp.2) and the azido-tert-amine (comp.4) through a heterocyclic triazole. This way, taking into account Figure 2, through 1,3-dipolar cycloaddition between a 1,3 dipole (azido-tert-amine) and a dipolarophile (alkynyl-glucose), we can obtain triazole di-substituted compound. The final step is converting compound 7 to quaternary ammonium salt compound 8.

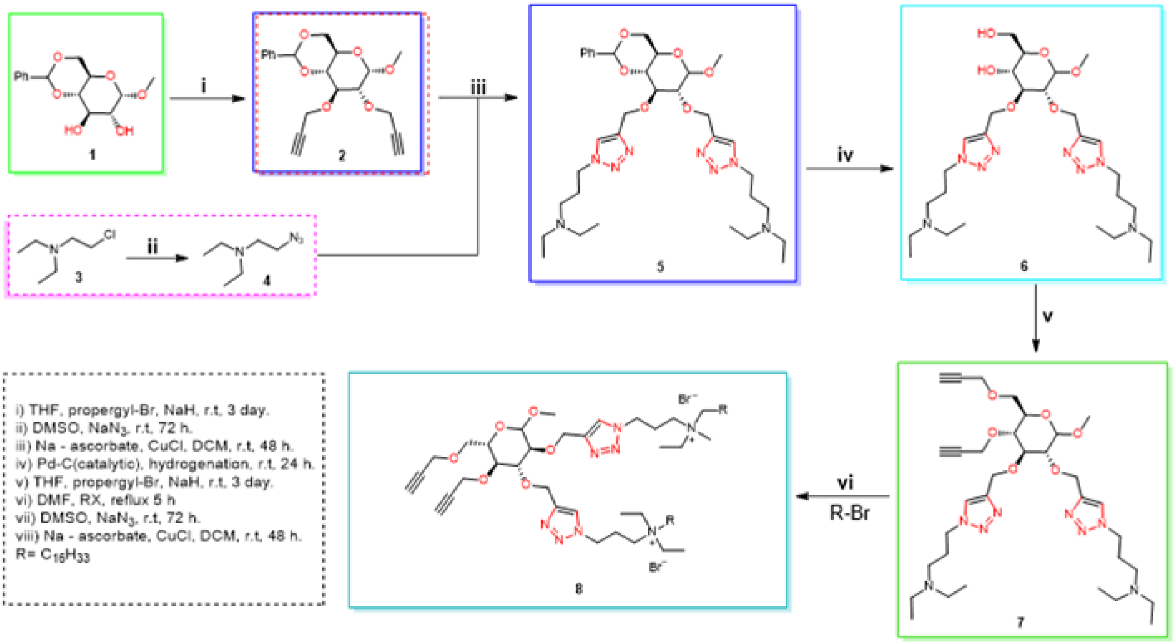
Structures of compounds 8

The intermediate compound 7 was further converted to quaternize with 1-bromohexadecane Figure 3. In most states, reactions were terminated in 5 h. These two products were isolated from the starting materials.

The ^1H-NMR spectrum of compound 8a-d showed there is a new signal at the range of 1.2-1.5 ppm for the protons of the alkyl chain due to ($-CH_2-$) groups of the aliphatic chain; the ^{13}C-NMR spectrum of compound 6a-d showed that there was a new signal at the range of 23-32 ppm for the carbons of alkyl chains due to ($-CH_2-$) groups of aliphatic chain and The characteristic bands of the FT-IR measures appeared about 2826-2994 cm^{-1} (C-H of CH_2 stretch), 2400-2700 cm^{-1} (ammonium ion), 1428-1467 cm^{-1} (C-N), and 757-781 cm^{-1} (skeletal "out of plane" vibration). Furthermore, for each series of compounds, the intensity of the aliphatic C-H absorption bands within the 2826-2994 cm^{-1} region was observed to increase with the length of the *N*-alkyl chain.

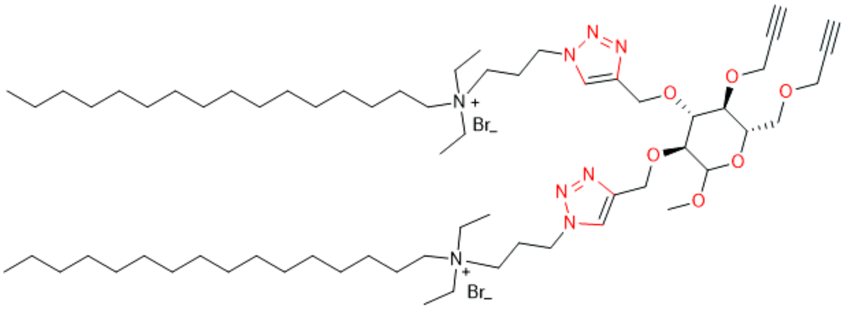
Synthesis polymeric (glucose-based triazole)-supported quarternary ammonium salts (QAS_S) 9

The polymerization method usually needs some criteria to achieve it in a good and economic system. However, the sugar involves QAS in a protecting group approach which increases the cost of synthesis. So, the polymerization of such materials will enhance the cost, and as a result, the process will shift to a different conformation of the resulting structure. Instead, our viewpoint in synthesizing such polymeric catalysis is included in crafting this material on commercially available polymers. Among them, PVC is becoming a starting polymer to be crafted with QAS derivative 9a-d, where price, availability, and stability are crucial factors for choice. The PVC was converted to another reactive precursor, polyvinyl azide (PVN_3), by an easily achieved nucleophilic replacement reaction, in which the chloride nucleophile could replace it with the more reactive azide (Figure 4).



i) THF, propergyl-Br, NaH, r.t, 3 day.
ii) DMSO, NaN_3, r.t, 72 h.
iii) Na - ascorbate, CuCl, DCM, r.t, 48 h.
iv) Pd-C(catalytic), hydrogenation, r.t, 24 h.
v) THF, propergyl-Br, NaH, r.t, 3 day.
vi) DMF, RX, reflux 5 h
vii) DMSO, NaN_3, r.t, 72 h.
viii) Na - ascorbate, CuCl, DCM, r.t, 48 h.
R= $C_{16}H_{33}$

Figure 2. A synthetic strategy, generally aqueous extraction, gives ammonium salts compound 8 in reasonable yield (75%).



8

Quatrnary ammoinum
salt with C_{16}
(Q-C_{16})

Figure 3. Quaternary ammonium salt 8

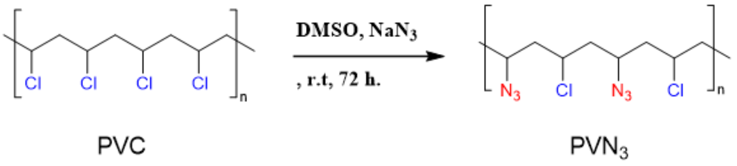


Figure 4. prepare of polyvinyl azide (PVN_3)

The FT-IR spectrum of PVN_3 showed a very strong band at 2110 cm^{-1} resulting from the starching vibration of the azide (N_3) group. Due to a review of the IR spectra of both PVC and the resulting PVN_3, the azide group was confirmed. The above reacted with propargylic glucose-QAS ether compounds 6a-d through a 1,3-dipolar Huisgen (click) cycloaddition reaction in Ethanol as the solvent, catalyzed by copper chloride and sodium ascorbate (Figure

5). The FT-IR range of the resulting polymer 9a-d revealed no alkyne CH signals at 3300 cm^{-1}. Furthermore, the peak between 2112-2118 cm^{-1} remained, indicating that there were unreacted azide groups in 9a-d due to the large volume of azide in the polymeric chain.

Field emission Scanning Electron Microscope (FESEM) analysis

The FESEM technique analyzes the materials' morphology to understand better some of the qualities that originate from the surfaces, leading to appropriate recommendations for using these materials in various applications. For example, the surface of linear polymer 9 was somewhat rougher, and some of the aggregations were seen in the morphological study of the FESEM image of linear polymer (9) (Figure 6).

Transmittance Electron Microscopy (TEM) analysis

The morphology of isolated polymer 9 (Q-C_{16}) was investigated by TEM. As was already apparent using the NTA in TEM images, a heterogeneous population of QAS groups on PVN3 was detected in Figure 7.

Application of the sugar-based quaternary salts in phase transfer catalyst Williamson ether synthesis

The catalytic activity of the new carbohydrate-based ammonium salts was tested to synthesize the ether compound. Various groups have broadly studied this type of reaction. The reactions were completed in a liquid-liquid two-phase system, applying a mixture of toluene and 50% aqueous NaOH solution in the presence of a 200 mg catalyst. The crude products were purified using preparative TLC in all cases. The results are summarized in Table 1. The ether synthesis is a typical example of using a phase transfer catalyst for the ether that is sensitive to other methods, like hydrides and alkoxides, when other side products may occur.

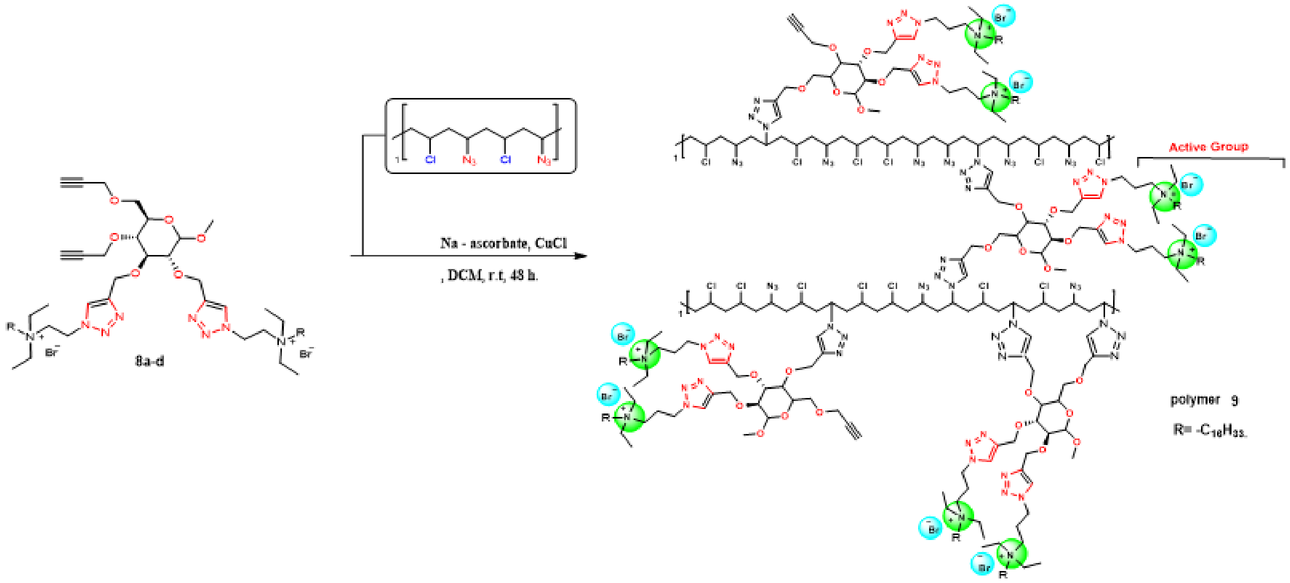


Figure 5. The steps of preparing compound 9

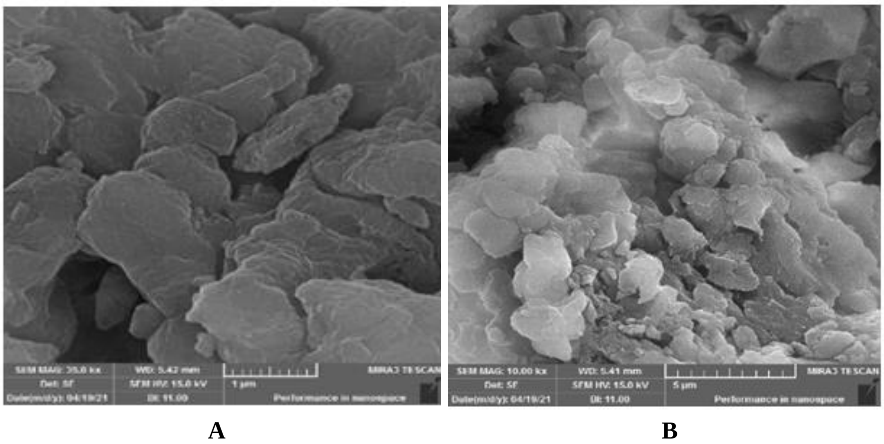

A
B

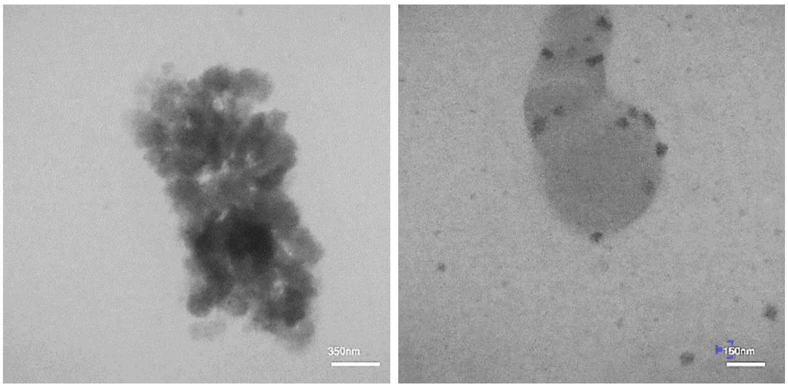
Figure 6. SEM analysis of polymer 9d: A. 5 µm, B. 1 µm

However, the prevention of elimination reaction that competitive the substitution required mild conditions available under phase transfer catalytic methodology. The various starting materials, including alkyl halides, alcohols, and phenols, were investigated to use quaternary salts and effectively study the limitations. In all cases, excellent to moderated yields were obtained using the optimum condition investigated with the less reactive alkyl halides and alcohols available to this study (Figure 8). Where other side products such as hydrides and alkoxides are present, ether synthesis is a common example of utilizing a phase transfer catalyst for ethers vulnerable to other methods such as hydrides and alkoxides. However, mild conditions were needed to avoid the removal reaction during competitive substitution, which are available in phase transfer catalytic methodology.

Several starting materials, including various alkyl halides, alcohols, and phenols, were examined to determine the effectiveness of utilizing quaternary salts as well as the limitations. In all instances, excellent-to-reasonable yields were obtained under optimal conditions, which were examined using the less reactive alkyl halides and alcohols available for this analysis.

The activity of the synthesized compound 9 is studied through the interaction of Williamson with different derivatives of alkyl halides and phenols, and it is found that compound 9 gave a good yield, noting that the difference in the yield is not clear or close to some extent. As compared to Phenol, 4-nitrophenol has the highest yields of nearly all alcohols, as seen in Table 1, while hexanol has the lower yields of nearly all alcohols used in the test.

Among all alkyl halides, the benzyl chloride shows high yields with almost all alcohols compared to the ethylene dibromide, as shown in Table 1. The synthesized compounds (10-15) were identified by 1HNMR and FT-IR spectroscopy. Similarly, the hydroxyl compound structures were investigated with the same alkyl halide. The benzyl alcohol and phenols showed a high yield compared to others. The Phenol with a strongly electron-withdrawing nitro group (compounds 13) exhibited an excellent yield (95%) due to the resonance effect, which is to withdraw the electron density from the oxygen of the hydroxyl group and, as a result, weakens the oxygen-hydrogen bond. In other words, the base could easily abstract that hydrogen and form a strong phenoxy anion, which attacks the halide to produce ether. Conversely, the cyclohexanol with donating aliphatic group (compound 11) gave a lower yield (75%). With a PTC process, one can accomplish quicker reactions, greater conversions or yields, fewer byproducts, remove the requirement for expensive or hazardous solvents that dissolve all the reactants in one phase, eliminate the need for expensive raw materials, and/or reduce waste. Phase-transfer catalysts are particularly beneficial in green chemistry because they allow water to be used.



A B

Figure 7. TEM analysis of polymer 9: A. 350 nm, B. 150 nm

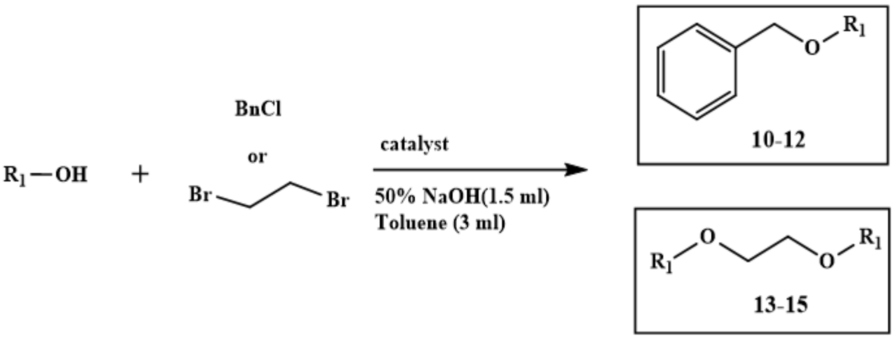
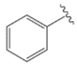
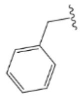
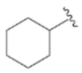
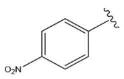
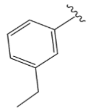
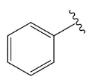


Figure 8. preparation of ether compounds

Table 1. Results of Williamson's reaction

Comp.	R$_1$	Temp. (C°)	Time (h)	Yield (%) 20 mg/mmol of catalyst (Compound 9)
Mono-substituted ethers				
10		65	8	91
11		65	8	80
12		65	8	75
Di-substituted ethers				
13		65	8	95
14		65	8	84
15		65	8	89

In conclusion, this paper describes the synthesis of a novel polymeric quaternary ammonium salt, PQAS, which carries a monosaccharide and is applied as a catalyst in PTC; the ammonium functionalities were put in various places on the glucose scaffold to investigate the structure-efficiency relationship of the new catalysts. When using long alkyl chains in QAS, the resultant polymer has a high enough molecular weight to be insoluble in most organic solvents. This characteristic gives stability to the polymer in various phases. In addition, they help us recover the polymer easily. The click reaction using CuCl in dichloromethane was effective enough to attach the quaternary sugar ammonium to PVN$_3$. The prepared cross polymer with active units of quaternary ammonium salts likely has a high affinity for PTC. By testing poly quaternary ammonium salts (9) in the Williamson reaction (as phase transfer catalysts), which includes the reaction of alkyl halide derivatives with alcohol or phenol derivatives. The reactions were performed in a liquid-liquid two-phase system. The length of the alkyl chain had a significant impact on the activity of the study phase transfer catalyst. During the reaction, Williamson: The reaction products of halides, alkyls, and alcohols differed depending on their structure; 4-nitrophenol had the highest yields of nearly all alcohols, while hexanol had the lowest yields of nearly all alcohols that were used in the test. In addition, the increase of the main units on the polymer leads to an increase in the activity of the polymer as the catalyst. Also, the chain length has an important role in the effectiveness of the quaternary salts, as we noticed during the presentation of the results.

ACKNOWLEDGEMENTS

The author gratefully acknowledges the financial support of the Tertiary Educational Fund of Kufa University, Iraq.

REFERENCES

Annunziata R, Benaglia M, Cinquini M, Cozzi F, Tocco GA. 2000. Poly (ethylene glycol)-supported quaternary ammonium salt: An efficient, recoverable, and recyclable phase-transfer catalyst. Org Lett 2: 1737-1739. DOI: 10.1021/ol005901r.

Bakó P, Keglevich G, Rapi Z, Toke L. 2012. The enantiomeric differentiation ability of chiral crown ethers based on carbohydrates. Curr Org Chem 16: 297-304. DOI: 10.2174/138527212799499877.

Bakó P, Rapi Z, Keglevich G. 2015 Sugar-based crown ethers in enantioselective syntheses. Periodica Polytechnica Chemical Engineering 59: 51-58. DOI: 10.3311/PPch.7308.

Chinchílla R, Nájera C. 2009. Asymmetric synthesis of α-amino acids using polymer-supported cinchona ammonium salts as phase-transfer catalysts. ACS Symp Ser Am Chem Soc 1009: 251-264.

Chinchílla R, Mazón P, Nájera C. 2000. Asymmetric synthesis of α-amino acids using polymer-supported Cinchona alkaloid-derived ammonium salts as chiral phase-transfer catalysts. Tetrahedron Asymmetry 11: 3277-3281. DOI: 10.1016/S0957-4166(00)00317-7.

Chokaouychai S, Zhang Q. 2020. Understanding phase-transfer catalytic synthesis of fullerenol and its interference from carbon dioxide and ozone. Res Chem Intermed 46: 5391-5415. DOI: 10.1007/s11164-020-04269-7.

Denmark SE, Gould ND, Wolf LMA. 2011. Systematic investigation of quaternary ammonium ions as asymmetric phase-transfer catalysts. Application of quantitative structure activity/selectivity relationships. J Org Chem 76: 4337-4357. DOI: 10.1021/jo2005457.

Dmochowska B, Piosik J, Woziwodzka A, Sikora K, Wiśniewski A, Sikora K, Wisniewski A, Wegrzyn G. 2011. Mutagenicity of quaternary ammonium salts containing carbohydrate moieties. J Hazard Mater 193: 272-278. DOI: 10.1016/j.jhazmat.2011.07.064.

Dmochowska B, Sikora K, Woziwodzka A, Piosik J, Podgórska B. 2016. Mutagenic activity of quaternary ammonium salt derivatives of carbohydrates. Beilstein J Org Chem 12: 1434-1439. DOI: 10.3762/bjoc.12.138.

Erfurt K, Markiewicz M, Siewniak A, Lisicki D, Zalewski M, Stolte S, Chobok A. 2020. Biodegradable surface active d-glucose based quaternary ammonium ionic liquids in the solventless synthesis of chloroprene. ACS Sustain Chem Eng 8: 10911-10919. DOI: 10.1021/acssuschemeng.0c03239.

Freedman HH, Bubois RA. 1975. An improved Williamson ether synthesis using phase transfer catalysis. Tetrahedron Letters 38: 5251-3254. DOI: 10.1016/S0040-4039(00)91417-5.

Gianluca P, Fish R. 2011. Synthesis of polypeptides by ROP of NCAs. Peptide-Based Mater 310: 1-26.

Haraguchi N, Takemura Y, Itsuno S. 2010 Novel polymer-supported organocatalyst via ion exchange reaction: Facile immobilization of chiral imidazolidin-4-one and its application to Diels-Alder reaction. Tetrahedron Lett 51: 1205-1208. DOI: 10.1016/j.tetlet.2009.12.088.

Henderson AS, Bower JF, Galan MC. 2016 Carbohydrates as enantioinduction components in stereoselective catalysis. Org Biomol Chem 14: 4008-4017. DOI: 10.1039/C6OB00368K.

Ikunaka M. 2008. PTC in OPRD: An illustrative overview. Org Process Res Dev 12: 698-709. DOI: 10.1021/op700262h.

Iribarren I, Trujillo C. 2020. Improving phase-transfer catalysis by enhancing non-covalent interactions. Phys Chem Chem Phys 22: 21015-21021. DOI: 10.1039/D0CP02012E.

Itsuno S, Paul DK, Salam MA, Haraguchi N. 2010. Main-chain ionic chiral polymers: Synthesis of optically active quaternary ammonium sulfonate polymers and their application in asymmetric catalysis. J Am Chem Soc 132: 2864-2865. DOI: 10.1021/ja909972d.

Jia X, Fan X, Liu Y, Li W, Tian L, Fan L, Zhang B, Zhanga H, Zhang Q. 2015. Quaternary ammonium functionalized Fe_3O_4@P(GMA-EGDMA) composite particles as highly efficient and dispersible catalysts for phase transfer reactions. RSC Adv 5: 60691-60697. DOI: 10.1039/C5RA09088A.

Jiang S, Wang L, Yu H, Chen Y. 2005. Preparation of crosslinked polystyrenes with quaternary ammonium and their antibacterial behavior. React Funct Polym 62 (2): 209-213. DOI: 10.1016/j.reactfunctpolym.2004.11.002.

Jin L, Zhao S, Chen X. 2018. Synthesis of both enantiomers of chiral phenylalanine derivatives catalyzed by cinchona alkaloid quaternary ammonium salts as asymmetric phase transfer catalysts. Molecules 23: 1-16. DOI: 10.3390/molecules23061421.

Kunz H, Rück K. 1993. Carbohydrates as Chiral Auxiliaries in Stereoselective Synthesis. New Synthetic Methods (90). Angewandte Chemie International Edition in English 32: 336-358. DOI: 10.1002/anie.199303361.

Leelamma PN, Devaky KS. 2009. Synthesis of polymer-supported quaternary ammonium salts and their phase-transfer catalytic activity in halogen-exchange reactions. J Appl Polym Sci 112: 2750-2756. DOI: 10.1002/app.28522.

Lehnert T, Özüduru G, Grugel H, Albrecht F, Telligmann S, Boysen M. 2011. More than just sweet - Sugar-derived stereodifferentiating agents for asymmetric synthesis. Synthesis 17: 2685-2708. DOI: 10.1055/s-0030-1260143.

Liao J, Ye Z. 2018. Quaternary ammonium cationic polymer as a superior bifunctional binder for lithium-sulfur batteries and effects of counter anion. Electrochimica Acta 259: 626-636. DOI: 10.1016/j.electacta.2017.10.194.

Lucchese AM, Marzorati L. 2000 Catálise de transferência de fase. Química Nova 23: 641-652. DOI: 10.1590/S0100-40422000000500014.

Makosza M. 2000 Phase-transfer catalysis. A general green methodology in organic synthesis. Pure Appl Chem 72: 1399-1403. DOI: 10.1351/pac200072071399.

Naik SD. 2017 Engineering analysis and mathematical modeling of solid-liquid phase transfer catalysis. Chem Eng Sci 52 (24): 4533-4546. DOI: 10.1016/S0009-2509(97)00297-2.

Nelson KV, Benjamin I. 2011. Effect of a phase transfer catalyst on the dynamics of an SN2 reaction. A molecular dynamics study. J Phys Chem C 115: 2290-2296. DOI: 10.1021/jp110796n.

O'Doherty GA. 2013. Carbohydrates-tools for stereoselective synthesis. In: Boysen MMK (eds). Angewandte Chemie International Edition 52: 10156-10156. DOI: 10.1002/anie.201305971.

Phillips AMF. 2014 Applications of carbohydrate-based organocatalysts in enantioselective synthesis. Eur J Org Chem 2014: 7291-7303. DOI: 10.1002/ejoc.201402689.

Popescu I, Pelin IM, Ailiesei GL, Ichim DL, Suflet DM. 2019. Amphiphilic polysaccharide based on curdlan: Synthesis and behaviour in aqueous solution. Carbohydr Polym 224: 115157. DOI: 10.1016/j.carbpol.2019.115157.

Pudi A, Karcz AP, Shadravan V, Andersson MP, Mansouri SS. 2020. Modeling of liquid-liquid phase transfer catalysis: Process intensification via integration of process systems engineering and computational chemistry. Comput Aided Chem Eng 48: 43-48. DOI: 10.1016/B978-0-12-823377-1.50008-2.

Rapi Z, Démuth B, Keglevich G, Grun A, Drahos L, Sóti P, Bakó P. 2014. Enantioselective Michael addition of malonates to aromatic nitroalkenes catalyzed by monosaccharide-based chiral crown ethers. Tetrahedron Asymmetry 25: 141-147. DOI: 10.1016/j.tetasy.2013.12.007.

Rapi Z, Grün A, Keglevich G, Stirling A, Bakó P. 2016. Synthesis of α-d-galactose-based azacrown ethers and their application as enantioselective catalysts in Michael reactions. New J Chem 40: 7856-7865. DOI: 10.1039/C6NJ02030E.

Rapi Z, Nemcsok T, Grün A, Pálvölgyi A, Samu G, Hessz D, Kubinyi M, Kallay M, Keglevich G, Bako P. 2018. Asymmetric cyclopropanation reactions catalyzed by carbohydrate-based crown ethers. Tetrahedron 74: 3512-3526. DOI: 10.1016/j.tet.2018.04.087.

Rapi Z, Nemcsok T, Pálvölgyi Á, Keglevich G, Grün A. 2017. Synthesis of L - threitol - based crown ethers and their application as enantioselective phase transfer catalyst in Michael additions. Chirality 29 (6): 257-272. DOI: 10.1002/chir.22678.

Roagna G, Ascough DMH, Ibba F, Vicini AC, Fontana A, Christensen KE, Peschiulli A, Oehlrich D, Misale A, Trabanco AA, Paton RS, Pupo G, Gouverneur V. 2020. Hydrogen bonding phase-transfer catalysis with ionic reactants: Enantioselective synthesis of γ-fluoroamines. J Am Chem Soc 142: 14045-14051. DOI: 10.1021/jacs.0c05131.

Sabah KJ, Sead FF, Mohammed HJ, Abedul-Hussien I. 2020 H. Novel polymer crafted sugar thiacrown ether and its applications in recovery of metal ions. Carbohydr Polym 495: 108057. DOI: 10.1016/j.carres.2020.108057.

Tankam PF, Mischnick P, Hopf H, Jones PG. 2007. Modification of methyl O -propargyl- D -glucosides: Model studies for the synthesis of alkynyl based functional polysaccharides. Carbohyd Res 342: 2031-2048. DOI: 10.1016/j.carres.2007.05.007.

Vander Zwan MC, Hartner FW. 1978. Solid-liquid phase-transfer catalysis by a quaternary ammonium salt. A comparison with crown ethers and polyalkylamines. J Org Chem 43: 2655-2657. DOI: 10.1021/jo00407a020.

Waser M, Gratzer K, Herchl R, Mueller N. 2012. Design, synthesis, and application of tartaric acid derived n-spiro quaternary ammonium salts as chiral phase-transfer catalysts. Org Biomol Chem 43: 23-24. DOI: 10.1002/chin.201223024.

Weatherley LR. 2020. Liquid-Liquid Phase-Transfer Catalysis. Intensification of Liquid-Liquid Processes. Cambridge University Press, Cambridge. DOI: 10.1017/9781108355865.001.

Xu L, Li BG, Jie S, Li Z, Bu Z. 2021. 110th anniversary: The epoxidation of polybutadiene via reaction-controlled phase-transfer catalysis. Ind Eng Chem Res 58: 13085-13092. DOI: 10.1021/acs.iecr.9b02371.

You X, Qiao C, Peng D, Liu W. 2021. Preparation of alkaline polyelectrolyte membrane based on quaternary ammonium salt-modified cellulose and its application in Zn-Air flexible battery. Polymers 13 (1): 9. DOI: 10.3390/polym13010009.

Zhang YY, Chen L, Yin SF, Luo SL, Au C. 2012. T. Low-cost polymer-supported quaternary ammonium salts as high-efficiency catalysts for cycloaddition of CO_2 to epoxides. Catal Lett 142: 1376-1381. DOI: 10.1007/s10562-012-0909-y.