Transport Of Some Glycopyrannosides Through A Liquid Organic Membrane Catalyzed By Ionic Liquids

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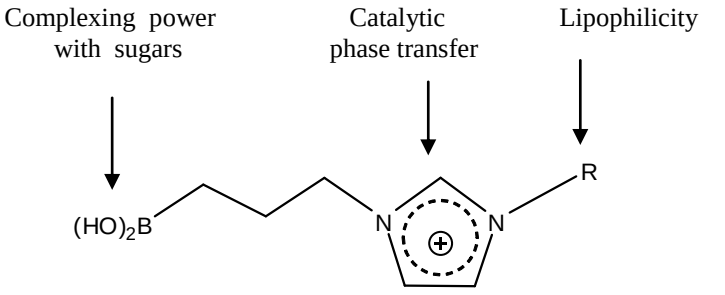
Abstract: *The synthesized ionic liquids 3 - (3-hexadecylimidazolium)-propylboronic acid and 3 - (3-decylimidazolium)-propylboronic acid can be used as catalyst to transfer some glycopyrannosides through a liquid organic membrane because they possess three properties: the complexing power with sugars, the role as phase transfer catalytist and the lipophilicity thanks respectively to their boronic acid function, their imidazolium nucleus and their long carbon chain.*

Key words: Ionic liquid, imidazolium, transfer, glycopyrannoside, lipophilicity, catalyst.

Introduction

Ionic liquids (ILs), made of relatively large organic cations and inorganic anions, could contribute as solvents and catalysts to green organic synthetic reactions.[1] These compounds are recognized as green solvents and can dissolve a wide varieties of organic compounds such as carbohydrates [2]. Recently it was discovered that solubility of carbohydrates and sugar alcohols can exceed even 75 wt% at an easily achievable temperature depending on the choice of the ionic liquid.[3,4] Furthermore, it was found that increasing the chain length of alkyl substituents on both cations and anions leads to greater lipophilicity of the ionic liquid.[5] Due to their unique properties, ionic liquids (ILs) have become increasingly popular over the last few years in the field of green organic synthesis and their importance has affected all areas of chemistry, but their potential action as phase transfer catalysts of sugars has not yet been studied. The transporters of monosaccharides proposed by literature are phenylboronic acid (PBA) or its derivates [6-12] but in presence of trioctylmethylammonium chloride (TOMA $^{+}$ Cl^{-}) denoted Q^{+} Cl^{-} as extracted agent. The purpose of this investigation was to examine the potential of our synthesized ionic liquids (Fig.1) to transport some sugars through organic liquid membrane. The advantages of our synthesized ILs are : the lipophilicity, the complexing power with sugars and the catalytic phase transfer propriety respectively provided by the presence of long chain of carbon, boronic function and imidazolium nucleus.



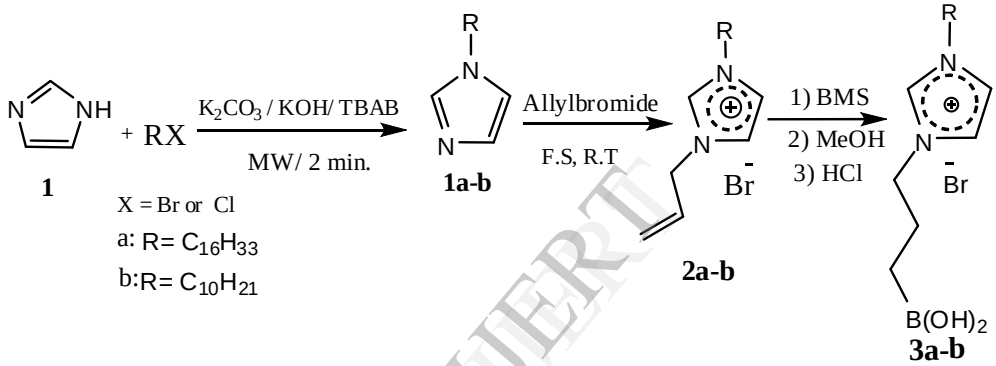
3a: R= $C_{16}H_{33;}$ **3b**:R=$C_{10}H_{21}$

FIGURE 1: Ionic liquids synthesized and their properties.

RESULTS AND DISCUSSION

1) Synthesis

Recently, there has been growing interest in the application of microwave irradiation in chemical reaction. Microwave assisted reaction under dry conditions are especially appealing as they provide an opportunity to work with open vessels thus avoiding the risk of high pressure and with a possibility of up scaling the reaction on the preparative scale[13]. The ILs **3 a-b** were synthesized by a three-step sequence outlined in scheme1. Imidazole **1** with 50% excess alkyl bromide and a catalytic amount of tetrabutylammonium bromide (TBAB) was adsorbed on the mixture of potassium carbonate and potassium hydroxide ratio 1:1 and then irradiated in an open vessel in a domestic microwave oven for 3 min[14] till it changed to reddish orange color to give imidazole derivates **1 a-b**. In ^{1}H NMR we note a deshielding of methylene protons group of allylbromid (3 to 4 ppm). Allyl bromide reacts on **1 a-b** in free solvent condition [15] leads to **2a-b**. There in ^{1}H NMR a deshielding of methylene protons group of allylbromid (4 to 5 ppm). Hydroboration followed by methanolysis and acid hydrolysis affords to the desired products **3a** and **3b**. H. C. Brown [16] proposes acid hydrolysis of boranes in aqueous phase to achieve the corresponding boronic acids but in our case, we pass by methanolysis step because our intermediate boranes are immiscible in aqueous solution. The absence of peaks due to ethylene protons (between 5 and 6 ppm) proves the reduction of allylic bond.



SCHEME 1: Synthesis of ionic liquids in three steps.

2) Transfer of glycopyrannosides

To avoid balances that may occur between different conformations of sugars (linear forms, ring forms) our study are focused on phenyl-β-D-glucopyrannoside **I** and phenyl-β-D-galactopyrannoside **II** (Fig. 3) and moreover, the presence of a phenyl group allows us to detect compounds by UV.

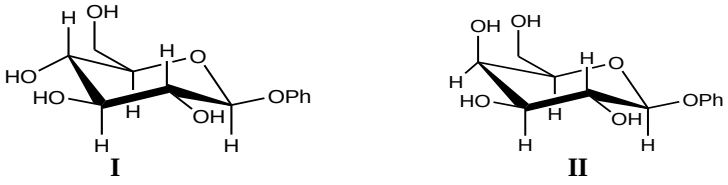
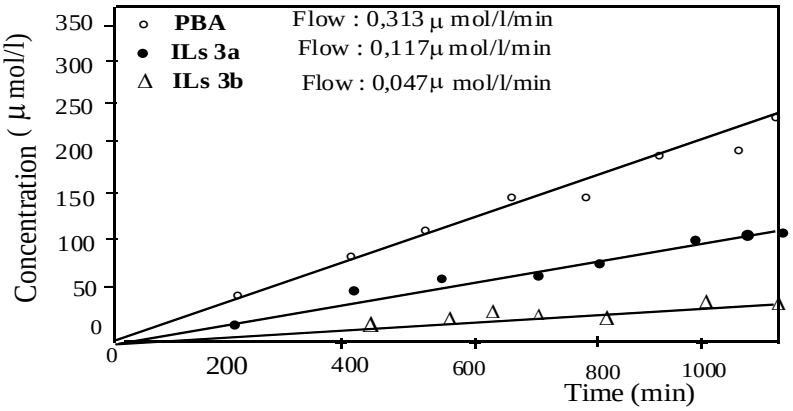


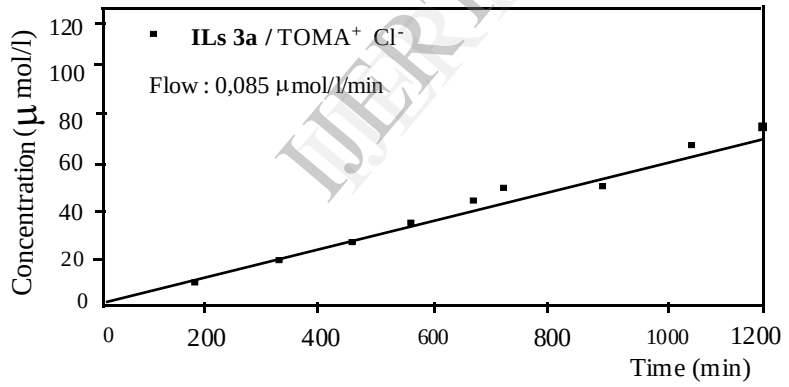
FIGURE 2: Sugars with two different configurations used in our study.

On the graph 1 is represented transport of phenyl-β-D-glucopyrannoside by respectively **PBA**, IL**3a** and IL**3b**. Our results show that IL **3a** had power to transfer phenyl-β-D-glucopyrannoside better than **3b** but less than reference PBA. The lack of transport observed with **3b** seems to be due to its lower lipophilicity.



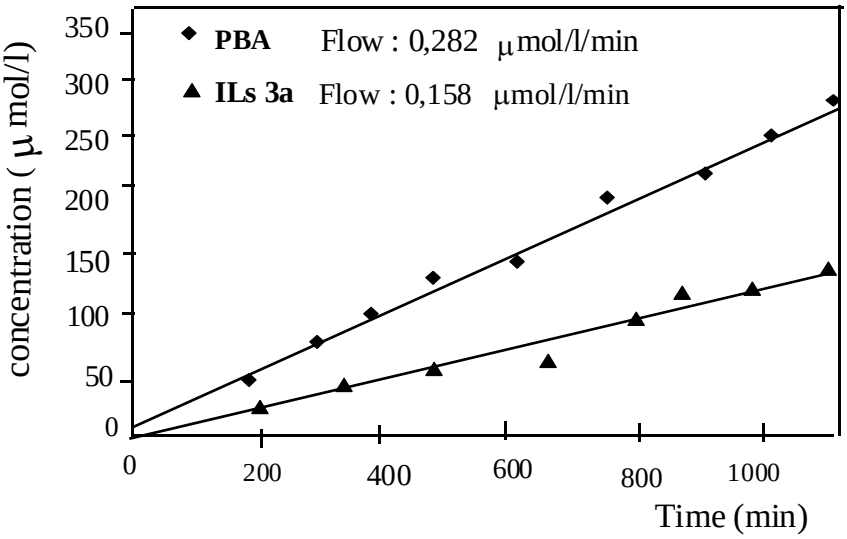
GRAPH 1: Transport of phenyl-β-D-glucopyrannoside by IL 3a, IL3b and reference PBA. Chromatographic conditions: HPLC equipped with a column Hypersil ODS C_{18} reversed phase coupled with UV detection (214 nm). Eluent: water/ acetonitrile 85/15. Flow rate: 1.5 mL / min.

In order to see the effect of catalytist $TOMA^+Cl^-$ we conducted an experience involving IL**3a** and phenyl-β-D-glucopyrannoside in presence of $TOMA^+Cl^-$ at the same chromatographic conditions. The results (Graph 2) show that the presence of the catalyst $TOMA^+Cl^-$ does not affect significantly the flow of transportation (0.085 micromol / L / min instead of 0.117 micromol / L / min) and we can say that IL**3a** plays its double role of transporter agent and catalyst transfer



GRAPH 2: Transport of phenyl-β-D-glucopyrannoside by ILs **3a** in presence of $TOMA^+ Cl^-$.

Another experience has been conducted using phenyl-β-D-galactopyrannoside and IL**3a** in order to see the effect induced by changing configuration of sugar. The results (Graph 3) show that IL **3a** is able to transfer phenyl-β-D-galactopyrannoside where the flow (0.158 micromol/l/min) exceeds that of glucopyrannoside (0.117 micromol/l/min) this has not been observed previously



GRAPH 3: Transport of phenyl-β-D-galactopyrannoside by PBA and ILs 3a.

Based on literature data [17] we propose an adequate transport of mechanism. Figure 3 show how the transport of a sugar out of an aqueous departure phase, through a lipophilic membrane and into a slightly aqueous receiving phase can be promoted by an ionic liquid. This transport process is thought to be diffusion with the formation of ILs-sugars complex involving intermolecular bond B-O at the interface being rapid and reversible.

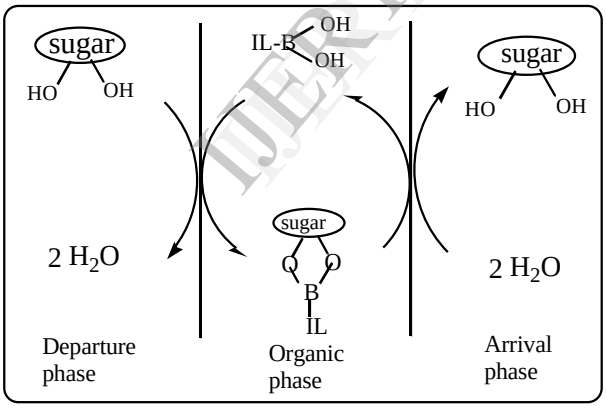


Figure 3: Transport mechanism for the passage of sugars through a lipophilic membrane promoted by ionic liquid.

Conclusion

We have synthesized and studied the ability of some ionic liquids to transfer sugars through liquid organic membrane. Their originality lies that they transport sugars as well as phenyl boronic acid used generally in this type of study. We have also proposed a plausible mechanism to explain this transport.

Experimental

The ^{1}H NMR spectra and ^{13}C NMR were recorded in $CDCl_3$ using a spectrometer BRUKER AC 250 Fourier Transform (250 MHz). The chemical shifts are expressed in parts per million (ppm) relative to tetramethylsilane (TMS). The transfer of different sugars is followed by Waters 600 HPLC coupled with UV detector Waters 480. The data are processed using an integrator Shimadzu C-R4A.

Synthesis of 1a and 1b

In a wide-necked Erlenmeyer flask are introduced 6.8g (0.1 mol) imidazole, 45.5g (0.1 mol) 1-bromohexadecan, 2.4g (7.5 mmol) tertiobutyllammoniumbromid (TBAB). The mixture is adsorbed on mixture of potassium carbonate and potassium hydroxide ratio 1:1 and then irradiated in an open vessel in a domestic microwave oven 300 Watt power for 3 min by period of 20 seconds till it changed to pasty.
After dilution in dichloromethane followed by washing with water, the organic phase is separated and dried over sodium sulfate. After filtration, the solvent is evaporated under vacuum.

1-hexadecyl-imidazole (1a)

Yield: 80%, yellow solid slightly pasty, 1H NMR (CDCl 3) δ ppm: 0.8 (t, 3H, CH3), 1.2 (m, 26H, carbon chain), 1.7 (m, 2H, N-CH2-CH2), 3.87 (t, 2H, N-CH2), 6.8 (s, 1H, H imidazole), 7.0 (s, 1H, H imidazole), 7.4 (s, 1H, H imidazole).

1-decyl-imidazole (1b)

Yield: 91%. yellow solid pasty, 1H NMR (CDCl 3) δ ppm: 0.8 (t, 3H, CH3), 1.2 (m, 14H, carbon chain), 1.7 (m, 2H, N-CH2-CH2), 3.87 (t, 2H, N-CH2), 6.8 (s, 1H, H imidazole), 7.0 (s, 1H, H imidazole), 7.4 (s, 1H, H imidazole).

Synthesis of 2a and 2b

In a necked 50 ml equipped with a condenser, 4.9 ml (57 mmol) of allyl bromide are added dropwise to 0.01 mol of **1a** (2.92g) or **1b** (2.08g) in room temperature and free solvent conditions. The reaction mixture is refluxed and stirred until a solid slightly pasty. This residue is triturated with ether and then filtered under vacuum to obtain a solid dough.

1-hexadecyl-3-allyl-imidazolium (2a)

Yield: 79%, pasty yellow solid; 1H NMR δ ppm 0.8 ppm (t, 3H, CH3), 1.2 ppm (m, 26H, carbon chain), 1.8 ppm (m, 2H, N-CH2-CH2), 4.3 ppm (t, 2H, N-CH2-C15H31), 5.0 ppm (d, 2H, CH2 = CH-CH2-N), 5.3 ppm (d, 1H, H allyl), 5.4 ppm (d, 1H, H allyl), 5.9 ppm (m, 1H, H allyl), 7.5 ppm (s, 2H, 2H imidazolium), 10.3 ppm (s, 1H, imidazolium H).

1-decyl-3-allyl-imidazolium (2b)

Yield: 86% Appearance: pasty yellow solid, ^{1}H NMR (CDCl 3) δ ppm: 0.8 (t, 3H, CH3), 1.2 (m, 14H, carbon chain), 1.8 (m, 2H, N-CH2-CH2), 4.2 (t, 2H, N-CH2-C9H19), 5.0 (d, 2H, CH2 = CH-CH2-N), 5.3 (d, 1H, H allyl), 5.4 (d, 1H, H allyl), 5.9 (m, 1H, H allyl), 7.49 ppm (s, 1H, imidazolium H), 7.52 ppm (s, 1H, imidazolium H), 10.3 (s, 1H, imidazolium H).

Synthesis of 3a and 3b

In a three-necked flask fitted with a condenser and under argon, 10 mmol allylimidazole are added to 50 ml of chloroform in an ice bath. We added 1.15 ml (12 mmol) of BH_3 borane dimethyl sulfide (BMS). Then allowed to stir at room temperature for 3 hours. 5 ml of methanol are added dropwise to the reaction mixture before hydrolysis with 5 ml of 1M hydrochloric acid. The aqueous phase is washed with chloroform. The organic phases are combined, dried over sulfate and evaporated under vacuum.

3 - (3-hexadecylimidazolium)-propylboronic acid (3a)

Yield: 81% Appearance: orange yellow resinous solid, ^{1}H NMR (CDCl 3) δ ppm: 0.8 (t, 3H, CH3), 0.9 (m, 2H, (OH) 2B-CH2), 1.2 (m, 26H, chain carbon), 1.9 (m, 2H, N-CH2-CH2-C14H29), 1.9 (m, 2H, (OH) 2B-CH2-CH2-CH2-N), 4.2 (m, 2H, (OH) 2B-CH2 -CH2-CH2-N), 4.2 (t, 2H, N-CH2-C15H 31), 7.4 (s, 2H, 2H imidazolium), 10.3 (s, 1H, imidazolium H). ^{13}C RMN ($CDCl_3$) δ ppm: 14 (CH3) 19 ((OH) 2B-CH2-CH2-CH2-N), 23 (CH2-CH3), 26 (OH) 2B-CH2-CH2-CH2-N), 28-30 (N-C13H26-CH2-CH2-CH3), 49 (N-CH2-C15H31), 50 ((OH) 2B-CH2-CH2-CH2-N), 122 (2C imidazolium), 136ppm (1C imidazolium).

3 - (3-decylimidazolium)-propylboronic acid (3b)

M = 374.8 g / mol, Yield: 85% Appearance: Yellow viscous oil-orange, ^{1}H NMR (CDCl 3) δ ppm: 0.8 (t, 3H, CH3), 0.9 (m, 2H, (OH) 2B-CH2), 1.2 (m, 14H, carbon chain), 1.9 (m, 2H, N-CH2-C8H17), 1.9 (m, 2H, (OH) 2B-CH2-CH2 -CH2-N), 4.2 (m, 2H, (OH) 2B-CH2-CH2-CH2-N), 4.2 (t, 2H, N-CH2-C9H19), 7.4 (s, 2H, 2H imidazolium), 10.3 (s, 1H, H imidazoulium). ^{13}C NMR ($CDCl_3$) δ ppm: 14 (CH3), 19 ((OH) 2B-CH2-CH2-CH2-N), 23 (CH2-CH3), 26 (OH) 2-B-CH2-CH2-CH2 - N), 28-30 (N-CH2-C7H14-CH2-CH3), 49 (N-CH2-C9H19), 50 ((OH) 2-B-CH2-CH2-CH2-N), 122 (1C imidazolium) , 136 (imidazolium 2C).

Transport of glycopyrannosides

For different tests, we use a U-tube system represented in figure 4 (capacity of 170 mL, height of 19 cm) in which two aqueous phases (starting and receiving phases) 30 ml each are separated by 130 ml of an organic phase CH_2Cl_2. The organic phase is under a magnetic stirring and the receiving phase is under mechanical stirring. Regular samples of the receiving phase were analyzed by HPLC equipped with a column Hypersil ODS C_{18} reversed phase coupled with UV detection (214 nm). Eluent: water/ acetonitrile 85/15. Flow rate: 1.5 mL / min.

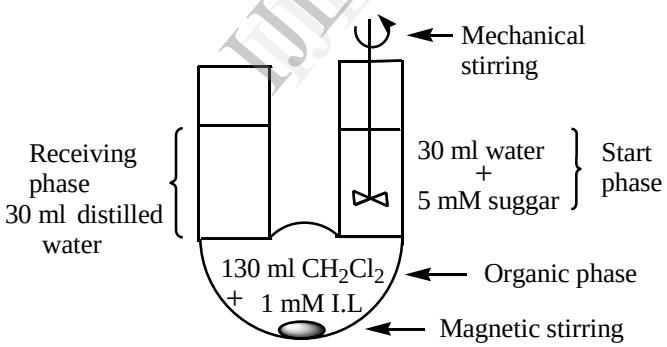


Figure 4: U-tube system used in different test.

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Graphical Abstract

The synthesized Ionic Liquids 3 - (3-hexadecylimidazolium)-propylboronic acid (3a) and 3 - (3-decylimidazolium)-propylboronic acid (3b) can transport phenyl-β-D-glucopyrannoside through Liquid Organic Membrane as well as phenyl boronic PBA acid used generally in this type of study.

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