Research Article

Facile Synthesis of Benzaldehyde-Functionalized Ionic Liquids and Their Flexible Functional Group Transformations

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Three benzaldehyde-functionalized ionic liquids were readily synthesized by quaternization of N-alkylimidazole with benzaldehyde-functionalized alkyl bromides under microwave irradiation in good yield. These aldehyde-functionalized ionic liquids could easily be oxidized in the presence of H₂O₂/KOH or be reduced by NaBH₄ leading to the formation of the corresponding carboxyl-functionalized ionic liquids or benzylic alcohol-functionalized ionic liquids. In addition, the condensations of these functionalized ones with hydrazine hydrate and with aniline under reductive amination conditions were demonstrated.

1. Introduction

Ionic liquids (ILs) have received an increasing interest as green solvent systems in the fields of organic synthesis [1, 2], separation technologies [3], electrochemical devices [4], and materials chemistry [5, 6] because of their advantages over traditional molecular solvents including negligible vapor pressure, broad liquid range, properties modulation, nonflammability, high thermal stability, and so forth [7–9]. Recently, the scope of ILs has been expanded by the introduction of additional functional groups in the ionic liquid structure. These so-called task-specific ionic liquids [10] or a much larger family of task-specific onium salts [11] can be utilized as soluble supports for organic synthesis, supported reagents or catalysts [12], and scavengers in solution phase combinatorial synthesis [13, 14] with high affinity for the ionic liquid phase. Task-specific ionic liquids are compatible with a variety of organic transformations and have proven to be useful for the extraction of specific chemicals [15]. The applications of functionalized ILs for the synthesis of inorganic materials have also been reported by several groups in recent years [16, 17].

Aldehyde-functionalized ILs are important and widely used due to their diverse reactivity. They have been used as soluble supports for various organic reactions such as reductive amination [18], Knoevenagel [19], Biginelli [20], and multicomponent reactions [21, 22]. In this work, we report the synthesis of three benzaldehyde-functionalized ionic liquids and their flexible functional group transformations under simple conditions.

2. Results and Discussion

2.1. Synthesis of Benzaldehyde-Functionalized Ionic Liquids.

The syntheses of N-methylimidazolium based benzaldehyde-functionalized ionic liquids (4a–c) were readily accomplished by alkylation of the phenols (1a–c) with 1,4-dibromobutane (2) and subsequent substitution of benzaldehyde-functionalized alkyl bromides (3a–c) with N-methylimidazole under microwave irradiation, respectively (Scheme 1). Benzaldehyde-functionalized imidazolium bromides (4a–c) (obtained in the yields of 87%, 82%, and 81% over the two steps with the purity of 93%, 97%, and 95% based on HPLC, resp.) could be obtained by the routine post-processing. They can be used as the ionic analogues of the known polymer supports of Wang-aldehyde resin, [23, 24], AMEBA [25], and 3-methoxy-4-benzyloxy benzaldehyde resins reported by our group recently [26], respectively. The intermediate products (3a–c) were prepared by using microwave-assisted phase transfer catalytic technique for
2.2. Functional Group Transformation of Ionic Liquids. In order to illuminate the utility and flexibility of the aldehyde groups in ionic liquids in chemical transformation, some ionic analogue conversions were carried out. Aldehyde-functionalized ionic liquids (4a–c) were readily oxidized by using an aq. H$_2$O$_2$/KOH green system. It afforded the carboxyl-functionalized ionic liquids (5a–c) in a good yield (89%). The oxidation of aromatic aldehydes to their corresponding carboxylic acids with a comparable yield under similar conditions has been reported by Cong and his coworkers [29]. The aldehyde groups in the ionic liquids was also reduced by utilizing conventional NaBH$_4$ leading to the formation of the ionic products bearing benzylic alcohol (6a–c). In addition, the ionic aldehyde compounds (4a–c) were condensed with hydrazine hydrate in an acidic medium leading to the formation of the corresponding ionic hydrazone (7a–c). They were also condensed with aniline under the reductive amination conditions using NaBH$_4$ resulting in the formation of the ionic liquid-supported secondary amines (8a–c). From the above-mentioned reactions represented in Scheme 2, it can be concluded that the ionic liquid-supported benzaldehydes are reactive enough towards many reagents and can therefore be used for many ionic analogue conversions.

3. Conclusion
In conclusion, three benzaldehyde-functionalized ionic liquids were readily synthesized by quaternization of 2-alkylimidazole with benzaldehyde-functionalized alkyl halides under microwave irradiation in good yields. The aldehyde groups supported by the ionic compounds could...
conveniently be transformed to other reactive groups under conventional conditions. These aldehyde-functionalized ionic liquids can be used as task-specific ionic liquids or as intermediate products that can be converted to other functionalized ionic liquids and thus can have other more applications.

4. Experimental

All chemicals employed were commercially available analytical reagents and were directly used without further purification. Microwave reactions were conducted using a CEM Discover Synthesis Unit. Reactions were performed in glass vessels. Conventional heating reactions were performed using KEM-6 Parallel Synthesizer. Agilent 1100 was used for HPLC. FT-IR spectra (KBr tableting) were recorded on Thermo Nicolet TENSOR AVATAR 360. 1H-NMR spectra were recorded using Bruker AVANCE DRX500 spectrometer. The chemical shifts were recorded in parts per million (δ : ppm) referenced to TMS (δ : 0) as an internal standard and the coupling constants (J) were given in Hertz (Hz).

4.1. Syntheses and Characterization

4.1.1. General Procedure for the Preparation of Compounds (3a–c). 4-Hydroxybenzaldehyde (1a, 6.1 g, 50 mmol) was dissolved in 1,4-dibromobutane (30 mL, 247 mmol). Tetra-n-butylammonium bromide (TBAB, 0.8 g, 2.5 mmol) and 3 M NaOH (30 mL) were added and the reaction mixture was stirred and heated under reflux for 4 hours under microwave irradiation with a power input of 60 W. After cooling, dichloromethane (50 mL) was added and the mixture was rinsed with water (2 × 25 mL). The organic phase was dried (MgSO₄) and concentrated. The oily product was purified by silica gel column chromatography (0 – 30% EtOAc in heptane) to give 4-(4-bromobutoxy)benzaldehyde (3a, 11.4 g, 44.3 mmol, 88.6%). Rf 0.5 (EtOAc/heptane, 1/2, v/v). 1H-NMR (500 MHz, CDCl₃): δ 1.83 (m, 4H), 3.33 (t, 2H, J = 3.8), 4.01 (t, 2H, J = 2.8), 6.93 (dd, 2H, J₁ = J₂ = 6.9), 7.78 (dd, 2H, J₁ = J₂ = 7.8), 9.85 (s, 1H). 4-(4-Bromobutoxy)-2-methoxybenzaldehyde (3b, 12.1 g, 42.2 mmol, 84.4%) and 4-(4-bromobutoxy)-3-methoxybenzaldehyde (3c, 11.8 g, 41.1 mmol, 82.2%) were prepared using the same procedure with 4-hydroxy-2-methoxybenzaldehyde (1b, 7.6 g, 50 mmol) and 4-hydroxy-3-methoxybenzaldehyde (1c, 7.6 g, 50 mmol) as reagents, respectively. 1H-NMR (3b): δ 1.87 (m, 4H), 3.31 (t, 2H, J = 3.7), 3.89 (s, 3H), 4.11 (t, 2H, J = 2.8), 6.47 (d, 1H, J = 7.2), 6.61 (d, 1H, J = 7.2), 7.89 (s, 1H), 10.31 (s, 1H). 1H-NMR (3c): δ 1.89 (m, 4H), 3.28 (t, 2H, J = 3.8), 3.84 (s, 3H), 4.07 (t, 2H, J = 2.8), 6.76 (d, 1H, J = 7.2), 7.12 (s, 1H), 7.38 (d, 1H, J = 8.3), 10.10 (s, 1H).

4.1.2. Benzaldehyde-Functionalized Ionic Liquids (4a–c). 4-(4-Bromobutoxy)benzaldehyde (3a, 5.04 g, 20 mmol) was dissolved in CH₃CN (20 mL) and was treated with N-methylimidazole (4.0 mL, 50 mmol) for 2 hours at reflux under microwave irradiation with a power input of 60 W. The mixture was concentrated and the crude product was rinsed with Et₂O (2 × 15 mL) dried under vacuum at 60°C for 24 hours to give benzaldehyde-functionalized ionic liquid 4a (6.64 g, 19.6 mmol, 98%). 1H-NMR (500 MHz, CD₂OD): δ 1.77 (m, 2H), 1.89 (m, 2H), 3.69 (t, 2H, J = 3.8), 3.91 (s, 3H), 4.19 (t, 2H, J = 2.9), 6.81 (d, 1H, J = 5.3), 6.93 (d, 1H, J = 5.3), 7.09 (dd, 2H, J₁ = J₂ = 7.8), 7.36 (s, 1H), 7.78 (dd, 2H, J₁ = J₂ = 8.2), 9.92 (s, 1H). Ionic liquids (4b, 4c) were synthesized using a similar procedure. 1H-NMR (4b, 97% yield): δ 1.82 (m, 2H), 1.98 (m, 2H), 3.60 (t, 2H, J = 3.7), 3.72 (s, 3H), 3.87 (s, 3H), 4.03 (t, 2H, J = 3.8), 6.89 (d, 2H, J = 5.1), 7.23–7.35 (m, 3H), 7.71 (dd, 1H, J₁ = J₂ = 7.8), 10.21 (s, 1H). 1H-NMR (4c, 99% yield): δ 1.87 (m, 2H), 2.03 (m, 2H), 3.63 (t, 2H, J₁ = J₂ = 3.7), 3.78 (s, 3H), 3.95 (s, 3H), 4.21 (t, 2H, J₁ = J₂ = 2.9), 6.67 (d, 2H), 6.89 (dd, 1H, J₁ = J₂ = 7.2), 7.19 (s, 1H), 7.31 (dd, 1H, J₁ = J₂ = 7.8), 7.48 (s, 1H), 9.92 (s, 1H).

4.2. Functional Group Transformation of Ionic Liquids

4.2.1. Oxidation of Ionic Liquids (4a–c). The typical procedure is presented as follows. Aqueous hydrogen peroxide (30%, 2.4 mL, 24 mol) was added dropwise to a stirred solution of 50% aq. KOH (1.0 mL, 13.6 mmol) and ionic liquid 4a (1.02 g, 3 mmol) in methanol (5 mL) under reflux for 10 min. Then the mixture was stirred at the same temperature for 30 min, cooled, and acidified with concentrated hydrochloric acid to give carboxyl-functionalized ionic liquid 5a (0.95 g, 2.68 mmol, 89%). 1H-NMR (500 MHz, CD₂OD): δ 1.72 (m, 2H), 1.81 (m, 2H), 3.61 (t, 2H, J = 3.8), 3.79 (s, 3H), 4.13 (t, 2H, J = 2.8), 6.62 (d, 1H, J = 5.4), 6.83 (d, 1H, J = 5.4), 7.03 (dd, 2H, J₁ = J₂ = 7.8), 7.30 (s, 1H), 8.53 (dd, 2H, J₁ = J₂ = 8.3), 10.78 (s, 1H). IR (KBr): 1705 cm⁻¹ (C = O), 2740 cm⁻¹ (H-bonded, O-H stretching).

4.2.2. Reduction of Ionic Liquids (4a–c). The typical procedure is presented as follows. Aqueous NaBH₄ (10%, 4.5 mL, 12.8 mmol) was added dropwise to a stirred solution of ionic liquid 4a (1.02 g, 3 mmol) in methanol (5 mL) at room temperature for 10 min. Then the mixture was stirred for 2 hours and acidified with 5% hydrochloric acid to give benzyl alcohol-functionalized ionic liquid 6a (0.97 g, 2.84 mmol, 95%). 1H-NMR (500 MHz, CD₂OD): δ 1.72 (m, 2H), 1.83 (m, 2H), 2.37 (t, 1H), 3.69 (t, 2H, J = 3.6), 3.78 (s, 3H), 3.98 (t, 2H, J = 3.8), 4.83 (d, 2H, J = 4.7), 6.77–6.83 (m, 4H), 7.11 (dd, 2H, J₁ = J₂ = 7.9), 7.36 (s, 1H). IR (KBr): 1050 cm⁻¹ (C–OH stretching), 3310 cm⁻¹ (O–H stretching).

4.2.3. Condensation Reaction of 4a with Hydrazine. Aqueous N₂H₄·H₂O (25%, 2.0 mL, 10.3 mmol) and a catalytic amount of glacial acetic acid were added to a stirred solution of ionic liquid 4a (1.02 g, 3 mmol) in methanol (5 mL). Then the mixture was heated under reflux for 2 hours, cooled, and concentrated with a rotary evaporator under vacuum to give hydrazono-functionalized ionic compound 7a (0.98 g, 2.78 mmol, 93%). 1H-NMR (500 MHz, CD₂OD): δ 1.69 (m, 2H), 1.78 (m, 2H), 2.87 (s, 2H), 3.70 (s, 3H), 3.83 (t, 2H, J = 3.7), 4.01 (t, 2H, J = 2.6), 6.67–6.74 (m, 4H), 7.36 (s,
1H), 7.61 (dd, 2H, \( J_1 = J_2 = 8.2 \)), 8.22 (s, 1H). IR (KBr): 1674 cm\(^{-1}\) (C=N), 3440 cm\(^{-1}\) (N–H stretching).

4.2.4. Reductive Amination of 4a with Aniline. Aniline (0.3 mL, 3.3 mmol) and 4a (1.02 g, 3 mmol) were mixed in ethanol (5 mL) and the reaction mixture was stirred at 60°C for 60 min followed by the addition of sodium borohydride (0.175 g, 4.5 mmol) for another 60 min, cooled, and concentrated with a rotary evaporator under vacuum. The remainder was solubilized in acetonitrile (10 mL) and filtered to separate sodium borohydride. The acetonitrile solution was dried (MgSO\(_4\)) and concentrated to give compound 8a (1.05 g, 2.53 mmol, 84%). \(^1\)H-NMR (500 MHz, CD\(_3\)OD): \( \delta \) 1.67 (m, 2H), 1.79 (m, 2H), 2.07 (s, 1H), 3.69 (s, 3H), 3.78–3.83 (m, 6H), 4.07 (t, 2H, \( J = 3.8 \)), 6.61–6.73 (m, 4H), 6.93–7.07 (m, 5H), 7.26 (dd, 2H), \( J_1 = J_2 = 8.2 \)), 7.42 (s, 1H). IR (KBr): 3370 cm\(^{-1}\) (N–H stretching).

Acknowledgments

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