Synthesis and Characterization of Benzimidazolium Salts Bearing Triazole Groups

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Abstract

A propargyl-functionalized salt, 1-(2-methoxyethyl)-3-(prop-2-ynyl)benzimidazolium bromide (**1**), was prepared. 1-(2-methoxyethyl)-3-[(1-phenyl-1H-1,2,3-triazol-4-yl)methyl]benzimidazolium hexafluorophosphate (**2**) and 1-(2-methoxyethyl)-3-[(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methyl]benzimidazolium hexafluorophosphate (**3**) were obtained by Cu(I) catalyzed azide-alkyne cycloaddition reaction of **1** with corresponding azides. Compound **3** was transformed to 1-(2-methoxyethyl)-3-[(1-(4-aminophenyl)-1H-1,2,3-triazol-4-yl)methyl]benzimidazolium hexafluorophosphate (**4**) by reduction reaction with hydrazine monohydrate. The structures of these propargyl- and 1,2,3-triazolyl-functionalized benzimidazolium salts were elucidated by FT-IR, ^{1}H NMR, ^{13}C NMR and elemental analysis methods.

Keywords: Benzimidazolium, N-heterocyclic carbene, Click chemistry, triazole

1. Introduction

Preparation of the first free and stable N-heterocyclic carbene (NHC) was reported in 1991 [1]. NHCs, strong σ-donors and weak π-acceptors, compose NHC-metal complexes stable towards air, moisture and heat. NHC-metal complexes have received excessive attention because of wide applications in homogeneous catalysis.

1,2,3-triazoles are biologically active compounds and so they have been extensively used [2-7]. Although 1,2,3-triazole heterocycle has been known since the end of the 19th century, triazole chemistry has become popular by presenting ″Click chemistry″ concept by Sharpless′ group in 2001 [8]. 1,3-cycloaddition reaction of an alkyne with an azide catalyzed by copper(I) gives 1,4-disubstituted 1,2,3-triazole without byproducts under moderate conditions and in short times (Figure 1). This method has been widely used for synthesizing several ligands comprising 1,4-disubstituted 1,2,3-triazolyl groups [9-14]. The metal complexes of these ligands have drawn attention because of their catalytic activities in many organic transformations [15-18].

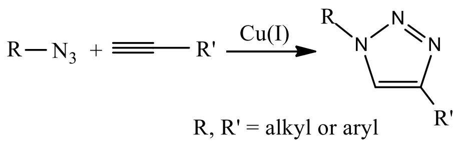

Figure 1. Copper(I) catalyzed 1,3-cycloaddition reaction

There have been limited number of reports regarding bidentate NHC ligands bearing 1,2,3-triazolyl groups and metal complexes. Firstly, Pd(II) complexes were reported by Warsink et al. in 2010 [19]. They exhibit activities in the transfer semihydrogenation of alkynes to Z-alkenes. In another study, cationic rodium and iridium complexes were prepared [20]. Gu et al. synthesized palladium, platinum and copper complexes [21,22]. It was reported that palladium and copper complexes showed high activities in Suzuki-Miyaura cross coupling and azide-alkyne cycloaddition reactions, respectively.

In this paper, preparation of a propargyl benzimidazolium salt and three 1,2,3-triazolyl-functionalized benzimidazolium compounds are reported. The structures of the synthesized compounds are defined by FT-IR, ^{1}H NMR, ^{13}C NMR and elemental analysis methods.

2. Materials and Methods

2.1. General Considerations

All experiments were achieved under air. The reagents and organic solvents were used as purchased. 1-(2-methoxyethyl)benzimidazole, p-nitrophenyl azide and phenyl azide were prepared as reported procedures [23,24]. Elemental analysis measures were achieved on a CHNS-932 (LECO) elemental analyzer. Varian 400 MHz NMR spectrophotometer was used for ^{1}H and ^{13}C NMR. FT-IR spectra were monitored on Perkin Elmer spectrophotometer at 400-4000 cm^{-1}. Melting points were measured in glass capillary tubes under air with Electrothermal 9100 apparatus.

2.2. Synthesis of 1-(2-methoxyethyl)-3-(prop-2-ynyl)benzimidazolium bromide (1)

Propargyl bromide (2.20 mL, 20.24 mmol, 80 wt% toluene solution) was added to the solution of 1-(2-methoxyethyl)benzimidazole (1.43 g, 8.10 mmol) in CH_3CN (20 mL). The mixture was refluxed overnight. The solvent was removed. The crude was washed with Et_2O (3x5 mL). The product was recrystallized from EtOH. Yield: 1.58 g, 66%. mp: 149-150 °C. ^1H NMR (400MHz, DMSO-d6): δ = 9.86 (s, 1H, NCHN), 8.14-8.02 (m, 2H, Ar-H), 7.75-7.68 (m, 2H, Ar-H), 5.56 (d, 2H, J = 2.35 Hz, $CH_2C{\equiv}CH$), 4.75-4.72 (m, 2H, $CH_2\underline{CH_2}OCH_3$), 3.85 (t, 1H, J = 2.54 Hz, $C{\equiv}CH$), 3.79-3.77 (m, 2H, $\underline{CH_2}CH_2OCH_3$), 3.25 (s, 3H, $CH_2CH_2O\underline{CH_3}$) ppm. ^{13}C NMR (100MHz, DMSO-d6): δ = 142.83, 131.81, 130.76, 127.32, 127.27, 114.66, 114.23, 79.67, 76.06, 69.51, 58.66, 47.23, 37.23 ppm. FT-IR (KBr) $\nu_{(C\equiv C)}$: 2124 cm^{-1}, $\nu_{(NCN)}$: 1566 cm^{-1}. Anal. Calc. for $C_{13}H_{15}N_2OBr$: C, 52.89; H, 5.13; N 9.49%. Found: C, 52.15; H, 4.86; N, 9.34%.

2.3. Synthesis of 1-(2-methoxyethyl)-3-[(1-phenyl-1H-1,2,3-triazol-4-yl)methyl]benzimidazolium hexafluorophosphate (2)

A mixture of phenyl azide (0.14 g, 1.2 mmol), **1** (0.30 g, 1 mmol), sodium L-ascorbate (0.02 g, 0.1 mmol) and $CuSO_4{\cdot}5H_2O$ (0.012 g, 0.05 mmol) was stirred in tert-butyl alcohol and water (6 mL, 1/1) for 24h at 50 °C. After filtration, a methanolic solution of NH_4PF_6 (0.20 g, 1.2 mmol) was added to the filtrate. The mixture was stirred for 2h at room temperature. Water (10 mL) was added to the solution. The powder pink solid was collected by filtration and washed with water (2x5mL). The product was recrystallized from CH_2Cl_2/Et_2O. Yield: 0.48 g, 62%. mp: 142-143 °C. ^1H NMR (400MHz, DMSO-d6): δ = 9.88 (s, 1H, NCHN), 8.98 (s, 1H, triazole), 8.15-8.07 (m, 2H, Ar-H), 7.86-7.83 (m, 2H, Ar-H), 7.72-7.67 (m, 2H, Ar-H), 7.60 (t, 2H, J = 7.83 Hz, Ar-H), 7.52-7.48 (m, 1H, Ar-H), 6.00 (s, 2H, CH_2), 4.73 (t, 2H, J = 4.70 Hz, $CH_2\underline{CH_2}OCH_3$), 3.80 (t, 2H, J =4.89 Hz, $\underline{CH_2}CH_2OCH_3$), 3.26 (s, 3H, $CH_2CH_2O\underline{CH_3}$) ppm. ^{13}C NMR (400MHz, DMSO-d6): δ = 143.22, 141.49, 136.77, 131.82, 131.23, 130.43, 129.52, 127.23, 127.20, 123.59, 120.70, 114.47, 114.38, 69.50, 58.64, 47.21, 42.13 ppm. FT-IR (KBr): $\nu_{(NCN)}$: 1563 cm^{-1}. Anal. Calc. for $C_{19}H_{20}N_5OPF_6$: C, 47.60; H, 4.21; N 14.61%. Found: C, 47.23; H, 4.27; N, 14.55%.

2.4. Synthesis of 1-(2-methoxyethyl)-3-[(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methyl]benzimidazolium hexafluorophosphate (3)

A mixture of p-nitrophenyl azide (0.20 g, 1.2 mmol), **1** (0.30 g, 1 mmol), sodium L-ascorbate (0.020 g, 0.1 mmol) and $CuSO_4{\cdot}5H_2O$ (0.012 g, 0.05 mmol) was stirred in tert-butyl alcohol and water (6 mL, 1/1) for 24h at 50 °C. Water (20 mL) was added to the mixture. After filtration, an aqueous solution of NH_4PF_6 (0.20 g, 1.2 mmol) was added to the filtrate. The resulting suspension was stirred for 2h at room temperature. The yellow precipitate was collected by filtration and washed with water (2x5mL). The product was recrystallized from CH_2Cl_2/Et_2O. Yield: 0.41 g, 79%. mp: 150-151 °C. ^1H NMR (400MHz, DMSO-d6): δ = 9.89 (s, 1H, NCHN), 9.18 (s, 1H, triazole), 8.47-8.43 (m, 2H, Ar-H), 8.19-8.16 (m, 2H, Ar-H), 8.14-8.09 (m, 2H, Ar-H), 7.72-7.68 (m, 2H, Ar-H), 6.03 (s, 2H, CH_2), 4.74-4.72 (m, 2H, $CH_2\underline{CH_2}OCH_3$), 3.81-3.79 (m, 2H, $\underline{CH_2}CH_2OCH_3$), 3.26 (s, 3H, $CH_2CH_2O\underline{CH_3}$) ppm. ^{13}C NMR (100MHz, DMSO-d6): δ = 147.41, 143.27, 142.10, 140.97, 131.80, 131.22, 127.26, 127.23, 126.08, 124.10, 121.31, 114.49, 114.38, 69.50, 58.65, 47.24, 42.02 ppm. FT-IR(KBr) $\nu_{(NCN)}$: 1569 cm^{-1}, $\nu_{(NO)}$: 1526 and 1340 cm^{-1}. Anal. Calc. for $C_{19}H_{19}N_6O_3PF_6$: C, 43.52; H, 3.66; N 16.03%. Found: C, 44.05; H, 3.68; N, 16.19%.

2.5. Synthesis of 1-(2-methoxyethyl)-3-[(1-(4-aminophenyl)-1H-1,2,3-triazol-4-yl)methyl]benzimidazolium hexafluorophosphate (4)

Hydrazine monohydrate (3.0 mL, excess) and palladium on carbon (10% (w/w), 0.015 g) were added to the solution of **3** (0.78 g, 1.44 mmol) in MeOH (30 mL) and THF (15 mL). The mixture was refluxed overnight and cooled to the room temperature. THF (30 mL) was added. The mixture was filtrated and rinsed with THF (3x15 mL). After removing of the solvent, the product was washed with Et_2O (3x10 mL). It was recystallized from $MeOH/Et_2O$ (1/3) at room temperature. Yield: 0.50 g, 71%. mp: 188-189 °C. ^1H NMR (400MHz, DMSO-d6): δ = 9.85 (s, 1H, NCHN), 8.69 (s, 1H, triazole), 8.12-8.06 (m, 2H, Ar-H), 7.71-7.66 (m, 2H, Ar-H), 7.43-7.40 (m, 2H, Ar-H), 6.67-6.63 (m, 2H, Ar-H), 5.92 (s, 2H, CH_2), 5.53 (s, 2H, NH_2), 4.72-4.69 (m, 2H, $CH_2\underline{CH_2}OCH_3$), 3.79-3.76 (m, 2H, $\underline{CH_2}CH_2OCH_3$), 3.24 (s, 3H, $CH_2CH_2O\underline{CH_3}$) ppm. ^{13}C NMR (100MHz, DMSO-d6): δ = 150.12, 143.16, 140.85, 131.81, 131.20, 127.20, 127.17, 125.93, 123.00, 122.17, 114.47, 114.40, 114.22, 69.51, 58.65, 47.18, 42.20 ppm. FT-IR (KBr) $\nu_{(NH2)}$: 3400 and 3495 cm^{-1}, $\nu_{(NCN)}$: 1563 cm^{-1}. Anal. Calc. for $C_{19}H_{21}N_6OPF_6$: C, 46.15; H, 4.29; N, 17.00%. Found: C, 46.52; H, 4.21; N, 16.89%.

3. Results and Discussion

The methods for synthesizing of the compounds **1-4** are given in Figure 2. **1** was prepared by refluxing of 1-(2-methoxyethyl)benzimidazole with propargyl bromide in acetonitrile. Copper(I) catalyzed alkyne-azide cycloaddition reaction of **1** with phenyl azide and p-nitrophenyl azide gave the benzimidazolium salts containing triazole groups, **2** and **3**, respectively. In this reaction, $CuSO_4{\cdot}5H_2O$ and sodium L-ascorbate were employed as catalyst system. **2-3** were obtained as PF_6^- salts by counter-anion exchange. The compound **4** was prepared by the reduction of **3** with hydrazine hydrate.

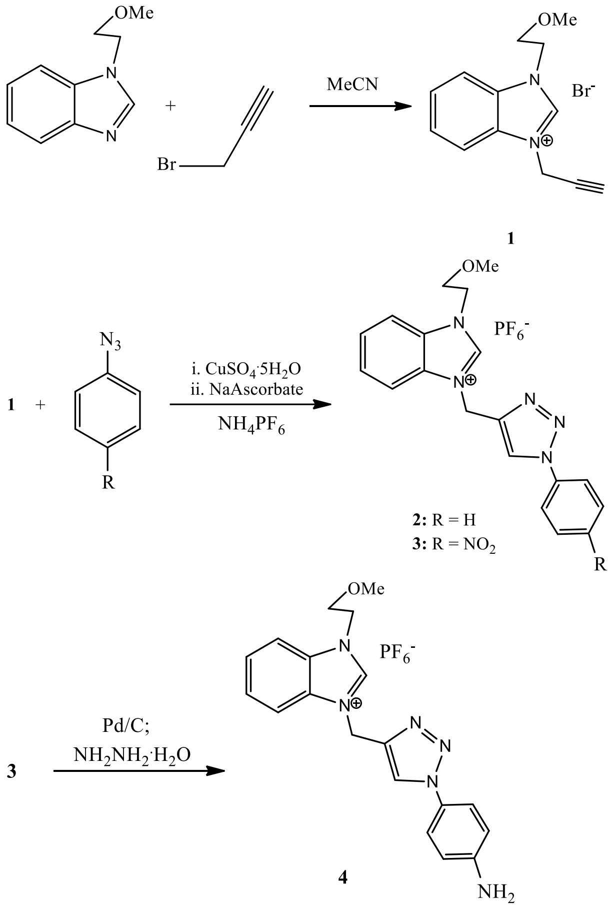

Figure 2. Synthesis of the salts **1-4**

FT-IR peaks at 1563-1569 cm^{-1} concern the stretching vibrations of –C=N– groups for compounds **1-4**. These values are consistent with the literature [25,26]. **1** has a sharp band at around 2124 cm^{-1} assigned to ν(C≡C) of the alkyne group. The extinction of this alkyne peak and the formation of the peaks appeared at 3150-3170 cm^{-1} related to the stretching frequencies of C–H bond in the spectra of **2-4** confirm the formation of triazole groups. In the spectrum of **3** having nitro group, symmetric and asymmetric nitro stretching frequencies are observed at 1525 and 1339 cm^{-1}. The peaks existing at 3490 and 3400 cm^{-1} in the spectrum of **4** relate to primer amine group.

NMR data confirm the suggested structures. In the ^{1}H NMR spectra of the all synthesized compounds, acidic NCHN proton resonances appear at 9.85-9.90 ppm. These resonance values are characteristic for NCHN protons of benzimidazolium salts [25,26]. For **1**, terminal alkynyl proton is observed at 3.85 ppm with a triplet signal. Singlet signals appeared at 8.98, 9.18 and 8.69 ppm in the ^{1}H NMR spectra of **2-4**, respectively, show the formation of 1,2,3-triazole ring. ^{13}C NMR spectrum of **1** exhibits two signals at 79.67 and 76.06 ppm for alkynyl carbons and a signal at 142.83 ppm for NCN carbon. For the all compounds the signals attributed to aliphatic carbons of (2-methoxy)ethyl groups appear at almost the same values at 47-70 ppm. In the ^{13}C NMR spectra of **2-4**, methylene carbons bound to 1,2,3-triazole ring are observed around 42 ppm.

4. Conclusion

Benzimidazolium salts bearing propargyl and triazole groups were prepared. The structures of the compounds were determined by spectroscopic methods and elemental analysis. Further studies on synthesizing of transition metal-NHC complexes of these NHC precursors are in progress.

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