Aprotic Heterocyclic Anion Triazolide Ionic Liquids – A New Class of Ionic Liquid Anion Accessed by the Huisgen Cycloaddition Reaction

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Abstract: The triazole core is a highly versatile heterocyclic ring which can be accessed easily with the Cu(I)-catalyzed Huisgen cycloaddition reaction. Herein we present the preparation of ionic liquids that incorporate a 1,2,3-triazolide anion. These ionic liquids were prepared by a facile procedure utilizing a base-labile pivaloylmethyl group at the 1-position, which can act as precursors to 1*H*-4-substituted 1,2,3-triazole. These triazoles were then subsequently converted into ionic liquids after deprotonation using an appropriate ionic liquid cation hydroxide. The densities and thermal decompositions of these ionic liquids were measured. These novel ionic liquids have potential applications in gas separations and in metal-free catalysis.

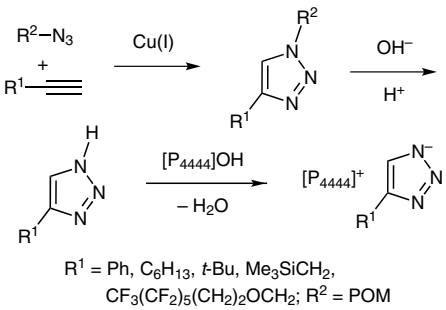
Key words: ionic liquids, triazoles, triazolides, aprotic heterocyclic anions, CO_2 capture, click chemistry

Ionic liquids (ILs) are organic salts which are liquids at room temperature.[1] ILs possess attractive properties including unique solubilities,[2] wide electrochemical windows, negligible vapor pressures, and good thermal stabilities[3] and has resulted in its use in various applications including use as solvents,[4] as catalysts,[5] and in gas separations.[6]

The use of aprotic heterocyclic anions (AHA) in ILs, originally reported by Ogihara,[7] has recently been reported by Wang to efficiently and reversibly capture CO_2 in equimolar stoichiometry.[8] They report that IL prepared from some simple azoles can be tuned for stability, CO_2 absorption enthalpy, and CO_2 capacity based on the pK_a of the azole. AHA-type ILs have also been shown by Gurkan[9] to be a successful general approach to selectively and reversibly react with CO_2 without suffering detrimental increases in viscosity.[10] Inspection of the relative pK_a of tetrazole, 1,2,3-triazole, and 1,2,4-triazole (8.2, 13.9, and 14.8, respectively, in DMSO),[11] shows that 1,2,3-triazole possesses an intermediate pK_a; Wang reported that tetrazole did not successfully capture CO_2, whereas 1,2,4-triazole did. This suggests that 1,2,3-triazoles would be viable candidates for CO_2 capture, particularly in light of the ability to tune the electronics of the anion via ring substitution.

Substituted 1,2,3-triazoles can serve as AHA IL precursors and fortuitously possess a pK_a amenable to the formation of an anion which could react reversibly with CO_2. Azoles which are too basic tend to interact too strongly with H_2O and bind CO_2 irreversibly; those which are not basic enough do not interact with CO_2 strongly enough to bind it. The pK_a of 1,2,3-triazole falls in an intermediate range, where these two trends may tend to balance each other out.

We have prepared triazolide-based ILs utilizing a simple Cu(I)-catalyzed cycloaddition reaction,[12] which is capable of generating a variety of ILs with multiple functional groups located on the 1,2,3-triazole core. The versatility and ease of access of triazole ring has found its use as antifungal agents in medicinal chemistry,[13] in polymer chemistry,[14] and in ILs.[15] The general reaction scheme is shown in Scheme 1. The Huisgen cycloaddition reaction between azide and alkyne is highly tolerant of varying the functional group and requires mild reaction conditions, yielding essentially pure 1,4-difunctional regioisomers.[15a,16] When the azide used possesses a labile group such as pivaloylmethyl (POM), the resulting triazole can easily be transformed into the protonated 4-substituted triazole, which in turn is a facile precursor for a large family of ILs.



Scheme 1 Synthetic approach used in this work

In this work, we present the synthesis of novel triazolide-based AHA ILs. The 1,4-disubstituted precursor struc-

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tures prepared are shown in Figure 1. These molecules were converted into 1*H*-4-substituted-1,2,3-triazoles, as shown in Figure 2, after alkaline hydrolysis in a methanol–water mixture and were converted into ILs by treatment with tetrabutyl phosphonium hydroxide. The 1*H*-4-substituted 1,2,3-triazole and hydroxide undergo an acid–base reaction to form the IL product. The AHA ILs prepared in this work are shown in Figure 3.

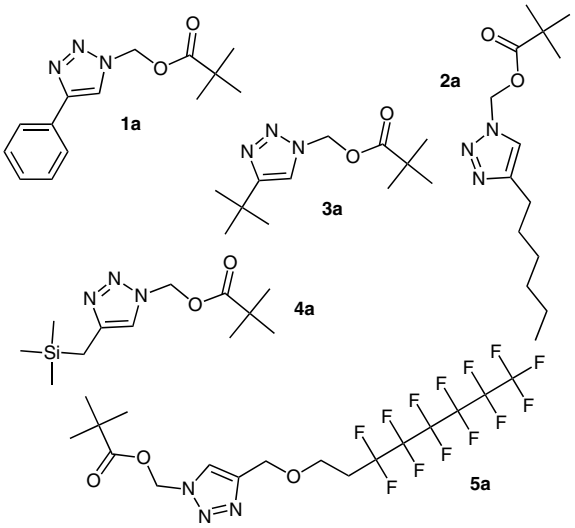

Figure 1 The 1-POM-4-substituted-1,2,3-triazoles **1a**–**5a** synthesized

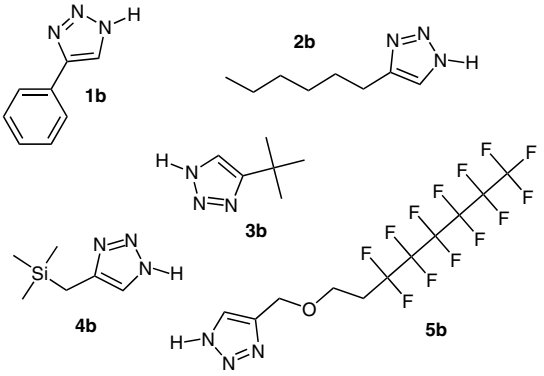

Figure 2 The 1*H*-4-substituted-1,2,3-triazoles **1b**–**5b** synthesized

The IL formation can be extended to any other IL cation by using the appropriate hydroxide. By varying the electronic nature of the substituent at the 4-position on the triazole ring, stabilization of the negative charge on the resulting anion can be affected and increased molar volume can be achieved, which is important for solvent applications. Access to these new triazole precursors are granted by the exceptionally versatile cycloaddition reaction.

A set of five AHA ILs based on 4-substituted-1,2,3-triazole was synthesized and characterized. The triazoles prepared were chosen to include a variety of substituents, with both electron-withdrawing (Ph: **1b**) and electron-donating groups at the 4-position (*n*-Hex and *t*-Bu: **2b** and **3b**). A silyl-substituted and fluorinated ether-substituted triazole (**4b**, **5b**) were also included to observe the effect of hydrophobic substituents on the AHA IL.

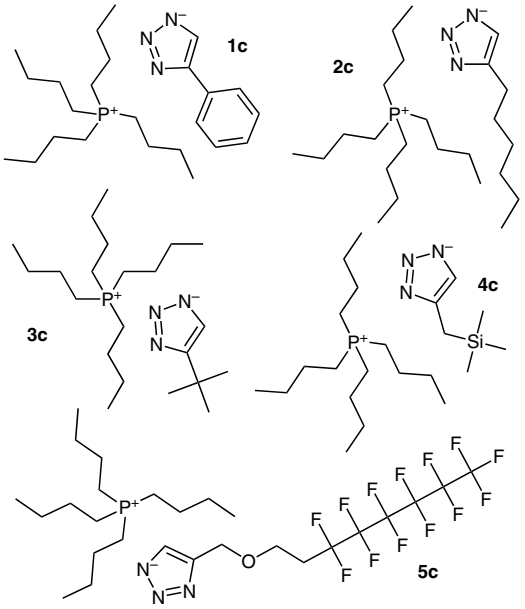

Figure 3 The tetrabutyl phosphonium 4-substituted-1,2,3-triazolide ILs **1c**–**5c** synthesized

The physical properties of the resulting AHA ILs were measured, the results are listed in Table 1. The densities (ρ) of all of the ILs, except for the fluorinated **5c**, were approximately 1 g/mL; the molar volumes (V_m) listed were calculated from these density values. Karl Fisher (KF) titration of the ILs revealed that after vacuum drying to constant weight at 50 °C, 0.9–2.4 wt% water still remained in the ILs. In addition, preliminary experiments measuring the viscosities and CO_2 absorption abilities were conducted (see Supporting Information).

T_{onset}: **3c** > **2c** > **4c** > **1c** > **5c**

electron-donating ability: **3c** ~ **2c** > **4c** > **1c** > **5c**

Scheme 2 Comparison of T_{onset} and electron-donating ability for ILs **1c**–**5c**

Thermal analysis of the decomposition of the ILs **1c**–**5c** shows that electron-donating groups (**1c**, **5c**) on the triazole ring begin to decompose (T_{onset}) at lower temperatures than those with electron-withdrawing groups (**2c**–**4c**). Alkyl groups on **2c** and **3c** cause the ILs to begin thermal decomposition about 75 °C cooler than for **1c** and **5c**. A comparison of T_{onset} and substituent electron-donating ability for ILs **1c**–**5c** is shown in Scheme 2. The onset of thermal decomposition for ILs **1c**–**5c** were found to be comparable with results reported by Wang, et al. for [P_{66614}][imidazolide] and [P_{66614}][pyrazolide] (T_{dec} = 252 °C and 182 °C, respectively).[8]

The relative effect of electron-donating and withdrawing-substitution at the 4-position is also observed in the ^{1}H NMR chemical shift of the triazole ring proton at the 5-po-

Table 1 Physical Properties of Triazolide ILs **1c**–**5c**

IL	FW (g/mol)	ρ[a] (g/mL)	V_m (mL/mol)	T_{onset} (°C)	H_2O (wt%, by KF)	H_2O (mol%, by KF)	Mol absorbed (CO_2/mol IL)	η[a] (cP)
1c	403.58	0.9836	402.7	238	1.06	23.7	0.10	2255
2c	411.65	0.9324	431.2	185	2.35	53.7	0.40	1357
3c	383.59	0.9290	401.2	151	0.914	19.5	0.07	2414
4c	413.70	0.9400	416.6	227	1.04	23.9	0.30	1659
5c	704.61	1.2141	578.6	263	0.973	38.0	0.23	8275

[a] Densities and viscosities were measured at ambient temperature (19–24 °C) and were not controlled.

sition. The shifts in 1,2,3-triazolides with electron-donating groups in **2c**, **3c**, and **4c** (δ = 7.12–7.23 ppm in $CDCl_3$) are observed upfield from those of the electron-withdrawing groups in **1c** and **5c** (δ = 7.36–7.59 ppm), reflecting the less shielded environment for the protons in the latter cases. Related effects are also reflected in the relative chemical shifts for the H_5 proton in the 1*H*-1,2,3-triazoles **1b**–**5b** and in the 1,2,3-triazolide ILs **1c**–**5c**, depicted in Figure 4. The H_5 signal shifted upfield 0.1–0.4 ppm for all five triazoles after conversion into ILs, indicating that the electronic environment of the azole ring was more electron rich after being converted into anionic form.

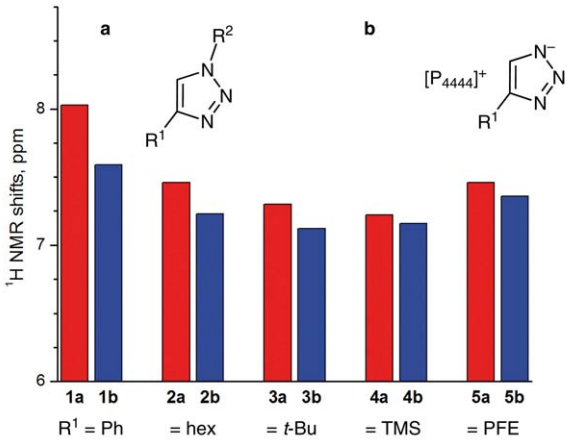

Figure 4 The ^1H NMR chemical shifts (in $CDCl_3$) for triazoles **1b**–**5b** and triazolide ILs **1c**–**5c**

The mass spectra of 1,2,3-triazolide IL solutions in methanol were all obtained, and the results are listed in the Supporting Information (SI Table 1). In all five cases, the molecular ion for the tetrabutyl phosphonium cation was observed in the positive mode, and the molecular ion for the triazolide anion was observed in the negative mode, confirming the identities of all products.

In conclusion, we have synthesized a series of five novel, tunable ILs based on substituted-1,2,3-triazoles, prepared via Huisgen cycloaddition chemistry. These AHA ILs possess densities and thermal stabilities which are comparable to other AHA ILs cited in the literature.[7–9] By careful selection of the substituent at the 4-position, control over the physical properties and reactivity of the resulting 1,2,3-triazolide anions is realized, depending upon the electronic nature and steric bulk of the substituent. The electronic changes in the azole rings are reflected in the chemical-shift changes observed in the ^1H NMR spectra of the azole ring protons. Characterization of these new ILs by mass spectrometry confirms their compositions. Current work is under way to study the viscosity of these ILs and to study their reactivity with H_2O and CO_2 using both laboratory experiments and computational chemistry.

General Method for the Synthesis of 1-POM-4-Phenyl-1,2,3-triazole (1a)

Azidomethyl pivalate was synthesized from NaN_3 and chloromethyl pivalate in H_2O according to literature procedures.[17] Azidomethyl pivalate (5.00 g, 31.8 mmol), phenyl acetylene (4.12 g, 40.4 mmol), Et_3N (3.63 g, 35.9 mmol), and 3% Cu/charcoal (3.05 g, 1.44 mmol) were placed in a Schlenk tube, dissolved in dioxane (15 mL), and heated overnight at 80 °C. This mixture was filtered to remove the catalyst, and then evaporated and vacuum dried to give a brown solid. The residue was dissolved in minimal Et_2O, filtered through a 0.2 μm syringe filter, evaporated, and vacuum dried to give **1a** as a white solid (7.25 g, 28.0 mmol, 88% yield). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.04 (s, 1 H, triazole CH), 7.87 (m, 2 H, 2-Ph), 7.45 (m, 2 H, 3-Ph), 7.42 (m, 1 H, 4-Ph), 6.29 (s, 2 H, piv-CH_2), 1.21 (s, 9 H, piv-CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 178.0 (C=O), 148.3 (triazole), 130.0 (triazole), 128.9, 128.5, 125.8, 120.9, 69.7, 38.8, 26.8. FTIR (ATR film): 1737 (C=O) cm^{-1}. MS: *m/z* calcd for $C_{14}H_{18}N_3O_2^+$ $[M + H]^+$: 260; found: 260.

General Method for the Synthesis of 1*H*-4-Phenyl-1,2,3-triazole (1b)

The general procedure for removal of the methyl pivalate leaving group was based on that described by Loren et al.[17] The structures for all molecules synthesized by this method are shown in Figure 3. KOH (7.46 g, 133 mmol) and **1a** (7.25 g, 28.0 mmol) were stirred in MeOH–H_2O (50 mL, 1:1) in air for 2 h at r.t., then was neutralized with 1 M HCl (100 mL, 100 mmol) to form a cloudy white solution. The mixture was filtered and the solids were rinsed with H_2O (300 mL) and vacuum dried to give off-white solids (3.48 g, 24.1 mmol, 86% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1 H, triazole CH), 7.83 (m, 2 H, 2-Ph), 7.47 (m, 2 H, 3-Ph), 7.40 (m, 1 H, 4-Ph). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.9 (triazole), 132.2 (triazole), 129.0, 128.9, 126.2, 126.1. FTIR (ATR film): 3159, 3114, 2845, 1466, 1453, 1131, 1082, 1003, 972, 915, 873, 764, 693, 517 cm^{-1}. ESI-MS (+/–, MeOH): *m/z* calcd for $C_8H_8N_3^+$ $[M + H]^+$: 146.17; found: 145.95.

General Method for the Synthesis of Tetrabutyl Phosphonium 4-Phenyl-1,2,3-triazolide ($[P_{4444}][4\text{-Ph-}1,2,3\text{-TZ}]$, 1c)

The general procedure for the synthesis of 1,2,3-triazolide IL was derived from that described by Fukumoto.[18] The structures for all IL synthesized by this method are shown in Figure 4. A solution of **1b** (1.63 g, 11.2 mmol) in EtOH (25 mL) was treated with 40% tetrabutyl phosphonium hydroxide ($[P_{4444}]OH$) in H_2O (7.84 g, 11.3 mmol) and was stirred at 50 °C for 6 h. The solvent was then evaporated, and the residue was vacuum dried at 50 °C until constant weight. The product was taken up in EtOAc (10 mL), filtered through a 0.2 µm syringe filter, evaporated, and vacuum dried to give a brown liquid (4.81 g, 106% yield). This liquid was then purified as described by Burrell,[19] by refluxing over activated charcoal in MeOH at 65 °C for 24 h. Evaporation and vacuum drying at 50 °C gave a pale red-brown liquid. ^{1}H NMR (700 MHz, DMSO): δ = 7.69 (m, 2 H, 2-Ph), 7.60 (s, 1 H, triazole CH), 7.26 (m, 2 H, 2-Ph), 7.04 (m, 1 H, 4-Ph), 2.16 (m, 8 H, PCH_2), 1.41 (m, 16 H, PCH_2), 0.90 (t, 12 H, PCH_3). ^{13}C NMR (101 MHz, DMSO): δ = 142.8 (triazole), 135.7 (triazole), 128.1, 126.9, 124.4, 124.3, 23.2 (dd, PCH_2), 17.3 (d, 48.5 Hz, PCH_2), 13.2 (PCH_3). ^{31}P NMR (162 MHz, DMSO): δ = 33.6. FTIR (ATR film): 2958, 2928, 2871, 1603, 1465, 1379, 1096, 1047, 965, 906, 763, 718, 696, 682, 605, 512 cm^{-1}. ESI-MS (+/–, MeOH): *m/z* calcd for $C_{22}H_{43}N_3P$: 403.58; *m/z* calcd for cation $C_{16}H_{36}P^+$ [M^+]: 259.43; found: 259.27; *m/z* calcd for anion $C_8H_6N_3^-$ [M^-]: 144.15; found: 144.07.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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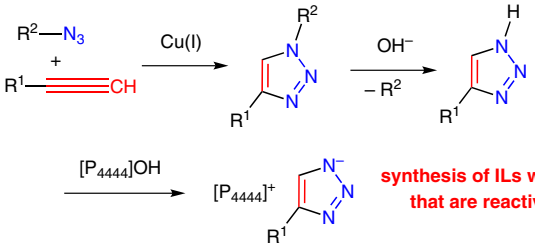

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