1-Allyl- and 1-Benzyl-3-methyl-1,2,3-triazolium Salts via Tandem Click Transformations

James T. Fletcher,* Matthew E. Keeney, Sara E. Walz

Department of Chemistry, Creighton University, Omaha, NE 68178, USA
Fax +1(402)2805737; E-mail: jamesfletcher@creighton.edu

Received 9 March 2010; revised 18 May 2010

Abstract: A series of 1-allylated and 1-benzylated 1,2,3-triazoles with varying substituents at the 4-position were prepared in yields ranging from 74–98% using a two-step one-pot click transformation. This tandem reaction involved the nucleophilic substitution of allyl chloride and benzyl bromide with sodium azide to form organic azide intermediates followed by Cu-catalyzed Huisgen 1,3-dipolar cycloaddition with alkyne reactants in a single reaction pot without the need for sequentially separating reaction steps. 1-Allyl- and 1-benzyl-4-alkyl-1,2,3-triazoles possessing linear alkyl chains underwent efficient N-alkylation at the 3-position with methyl iodide, while *tert*-butyl and phenyl derivatives did not. Each of the 1-allyl- and 1-benzyl-3-methyl-4-alkyl-1,2,3-triazolium iodide salts prepared was a viscous liquid at room temperature with a stable shelf life.

Key words: alkynes, azides, cycloaddition, ionic liquids, tandem reaction

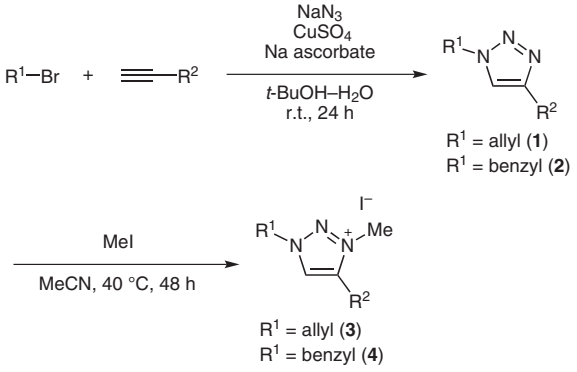
The 1,2,3-triazole heterocycle is an aromatic ring isoelectronic with imidazole. Commonly synthesized via copper-catalyzed Huisgen 1,3-dipolar cycloaddition reactions, variation of substituent identity at the 1- and 4-positions of the ring is trivial due to the high chemospecificity of this transformation.[1–4] While imidazole rings have found widespread utility as components of ionic liquids, few examples of 1,2,3-triazole based ionic salts have been reported.[5–7]

As ionic liquids have been suggested as new organic solvents where the physical properties of the solvent can be engineered via structural variation of its organic building blocks,[8–10] the use of click reaction approaches to prepare new ionic liquid analogues appears attractive in pursuing such investigations. But preparation of new 1,2,3-triazolium salts using a click approach does have inherent conflicting demands. While smaller alkyl substituents on the triazole ring may be desired to help maintain the room temperature liquid properties of its triazolium salt, the explosive potential of such smaller organic azide precursors increases as their size decreases.[11] The common desire to prepare ionic liquid salts in large-scale quantities also adds to the potential danger of preparing 1,2,3-triazolium derivatives directly from organic azide precursors.

To address such issues, the goal of this study was to utilize a two-step one-pot click transformation to prepare 1,2,3-triazole derivatives as precursors to triazolium salts, an approach that avoids the isolation of organic azides and provides practical access to gram-scale quantities of triazolium salts. We report herein the preparation of 1-allylated and 1-benzylated 4-alkyl-1,2,3-triazoles and the formation of their analogous triazolium salts via alkylation with methyl iodide. In addition to investigating how substituent identity impacts ease of preparation, the structure–property relationships resulting from alkyl group variation at the 4-position of 1-allylated and 1-benzylated 1,2,3-triazole rings were examined.

Due to the orthogonal reactivity of the Cu-catalyzed Huisgen 1,3-dipolar cycloaddition, this common click reaction has proven amenable to incorporation within one-pot multi-step transformations. Recent reports include tandem click reactions coupled with azide formation from halide,[12–18] amine,[19–21] boronic acid,[22] epoxide[23,24] and alcohol[25] precursors, as well as with trimethylsilylalkyne deprotection.[26–30]

The general two-step one-pot procedure for preparing the benzylated and allylated target compounds is summarized in Scheme 1. The first reaction, a two-step one-pot tandem process, involves the in situ formation of allyl and benzyl azides followed by the Cu-catalyzed Huisgen 1,3-dipolar cycloaddition with the terminal alkyne co-reactant. Unlike previous reports describing the use of elevated temperatures[12,13,17] or time-delayed introduction of reagents promoting sequential steps,[14,19–22] the tandem reactions involving allyl and benzyl halide reactants proceeded successfully at room temperature and permitted all reagents to be introduced at the onset of the reaction.



Scheme 1 Preparation of triazoles **1** and **2** from a two-step one-pot reaction, and triazolium salts **3** and **4** from N-alkylation with methyl iodide

SYNTHESIS 2010, No. 19, pp 3339–3345
Advanced online publication: 22.07.2010
DOI: 10.1055/s-0030-1257909; Art ID: M02010SS
© Georg Thieme Verlag Stuttgart · New York

Downloaded by: University of Arizona Library. Copyrighted material.

Overall, product yields are appreciable to one-step methods utilizing organic azides directly.

The second step of the reaction sequence involving the N-alkylation of the 1,2,3-triazole ring to form the desired 1,3,4-trialkyltriazolium salts occurs in analogous manner to preparing 1,3-dialkylimidazolium salts;[31] reacting with excess methyl iodide in acetonitrile at 40 °C.[5,6] In surveying the ratio of reactants to products over time, it was observed that the N-alkylation at the 3-position of the 1,2,3-triazole ring was sensitive to steric bulk at the 4-position. Linear alkyl groups ranging from C3 to C8 each reacted successfully at similar rates, but the *tert*-butyl and phenyl derivatives could not be fully converted to triazolium products under the conditions surveyed, likely due to steric bulk.

Reaction completion was monitored via ^{1}H NMR analysis (Figures 1 and 2), where a singlet at ~4.3 ppm corresponding to the new *N*-methyl group was clearly observed. The N-alkylation at the 3-position of the triazole ring[5,6] also led to a pronounced downfield chemical shift of the aromatic singlet (of approximately 2 ppm) corresponding to the 1,2,3-triazole hydrogen at the 5-position. Minor downfield shifts of hydrogen atoms located in close proximity to the triazole ring were also observed.

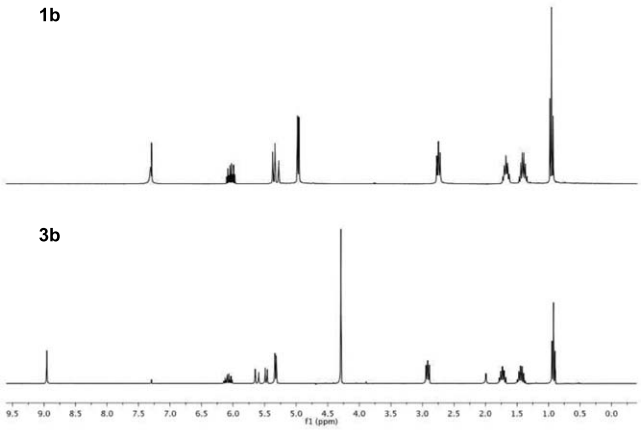


Figure 1 Comparison of ^{1}H NMR spectra of **1b** and **3b** in $CDCl_3$

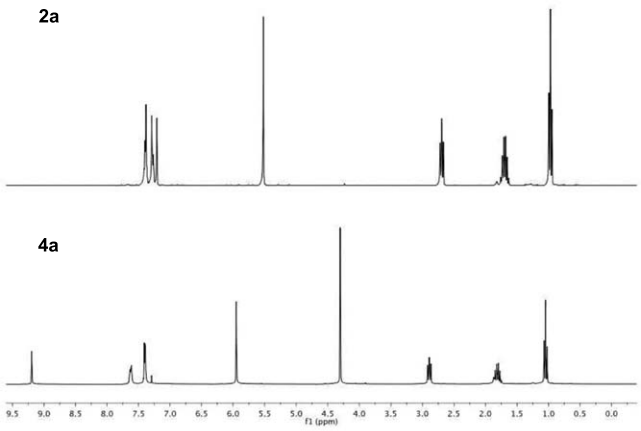


Figure 2 Comparison of ^{1}H NMR spectra of **2a** and **4a** in $CDCl_3$

While a recent report has described the preparation of 1,2,3-triazolium salts with task-specific substituents,[5] the goal of this study was to examine how the systematic variation of simple alkyl substituent identity influenced the room temperature physical state of this family of compounds. It is noteworthy that the allyl group has been reported to impart physical properties[31–34] and reactivity[35] unique to alkyl analogues in imidazolium ionic liquid systems, such as an improved ability to dissolve cellulose. So although in our study the allyl group was utilized for synthetic expediency, it has the potential to also impart novel traits to this class of ionic liquids that warrants future study.

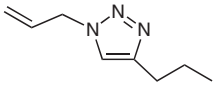
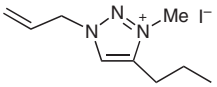
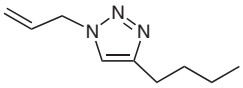
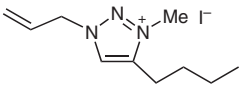
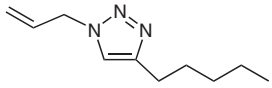
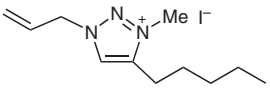
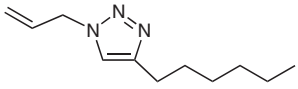
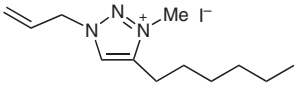
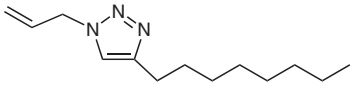
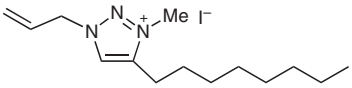
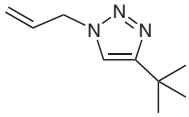
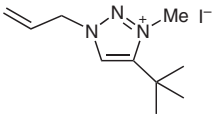
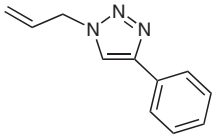
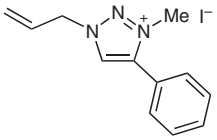
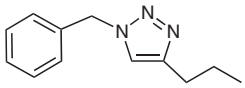
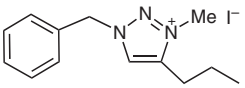
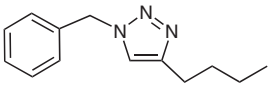
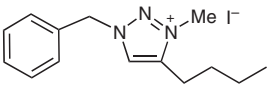
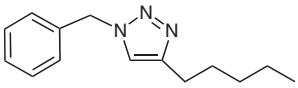
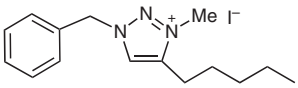
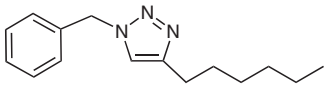
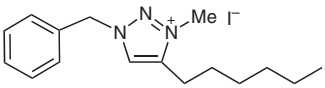
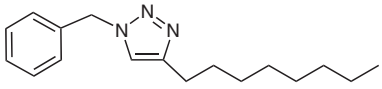
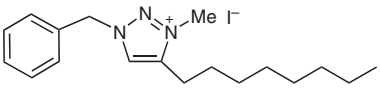
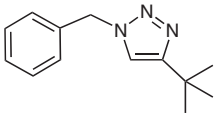
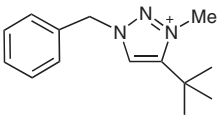
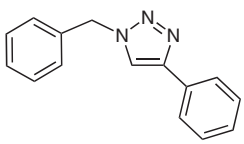
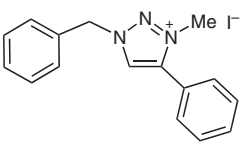
As summarized in Table 1, the majority of the 1-allylated triazoles were room temperature liquids, while the majority of the 1-benzylated derivatives were room temperature solids. Each of the triazolium salts was a viscous liquid and observed to have a stable shelf life. Within twelve months of room temperature storage none of the reported derivatives crystallized upon standing, nor did any derivative show signs of decomposition via NMR analysis.

Circumventing the isolation of triazole reactants not only stands as a practical improvement in reaction efficiency, but it is important from a safety standpoint as well, particularly in applications where the large-scale preparation of target compounds is desired. This strategy was successfully applied towards the multigram scale preparation of 1,2,3-triazolium-based ionic liquid derivatives by conveniently allowing multigram-scale batches of 1-allylated and 1-benzylated 1,2,3-triazoles to be produced. The one significant drawback initially observed for this approach was that the use of typical 20% catalyst loadings complicated product purification due to the formation of emulsions during standard extraction purifications and the presence of solid residue contaminating the resulting triazole products. To address such issues, as well as to minimize the amount of catalyst reagent needed to successfully prepare the desired products, the impact of significantly decreased catalyst loading on gram-scale product preparations was examined.

Table 2 summarizes the results of decreasing the amount of copper catalyst from the typical 20% to 5% or less in the established tandem two-step one-pot reaction conditions. In examining the observed ratio of alkyne reactant to triazole product monitored by GC/MS analysis, 5% catalyst loading led to product formation within 24 hours approaching the isolated yields observed for the milligram scale preparations, while the use of 2% catalyst resulted in essentially half-completed reactions in that timeframe. Interestingly, the use of only 1% catalyst loading resulted in essentially no observed triazole product, even after extended reaction times. Hence, this study indicates that a minimum of 5% catalyst loading is required to prepare 1-allylated and 1-benzylated 1,2,3-triazoles in good yields via tandem two-step one-pot reactions within 24–48 hours reaction times under these conditions.

Downloaded by: University of Arizona Library. Copyrighted material.

Table 1 Summary of Compounds Surveyed[a]

	Compound	Yield (%)[b]	Mp (°C)		Compound	Conversion (%)[c,d]
1a		79	r.t. liq.	**3a**		>98
1b		82	r.t. liq.	**3b**		>98
1c		74	r.t. liq.	**3c**		>98
1d		90	r.t. liq.	**3d**		>98
1e		83	37–39	**3e**		>98
1f		78	r.t. liq.	**3f**		33
1g		91	57–58	**3g**		21
2a		89	r.t. liq.	**4a**		>98
2b		87	58–59	**4b**		>98
2c		76	42–43	**4c**		>98
2d		92	55–56	**4d**		>98
2e		92	69–70	**4e**		>98
2f		89	82–83	**4f**		13
2g		98	128–129	**4g**		7

[a] See the experimental section for conditions.
[b] Isolated yield.
[c] Percent conversion as monitored by ^{1}H NMR spectroscopy.
[d] Each product was a viscous liquid at r.t.

Downloaded by: University of Arizona Library. Copyrighted material.

Table 2 GC/MS Monitoring of Reaction Completion

	Time (h)	Alkyne/triazole ratio observed		
		5% $CuSO_4$	2% $CuSO_4$	1% $CuSO_4$
1a	1	87:13	95:5	>99:1
	2	41:59	91:9	>99:1
	4	31:69	72:28	>99:1
	24	23:77	67:33	>99:1
	72	18:82	57:43	96:4
2a	1	59:41	86:14	>99:1
	2	22:88	69:31	>99:1
	4	13:87	58:42	>99:1
	24	9:91	56:44	>99:1
	72	9:91	51:49	95:5

In summary, a series of 1-allylated and 1-benzylated 1,2,3-triazoles have been prepared using a two-step one-pot click transformation. This tandem reaction enabled 1,2,3-triazole analogues to be prepared in multigram quantities while circumventing the need to isolate large amounts of intermediate organic azide reactants or sequentially separate reaction steps. 1-Allyl- and 1-benzyl-4-alkyl-1,2,3-triazoles possessing linear alkyl chains underwent efficient N-alkylation with methyl iodide, while 4-*tert*-butyl and phenyl derivatives did not readily form their analogous triazolium salts. Surveying the structure-property relationships between substituents at the 1- and 4-positions of the 1,2,3-triazole ring showed a rational correlation between melting point and substituent identity, with each of the ionic salts prepared existing as liquids at room temperature with stable shelf lives. Future work will examine how additional variations of this class of ionic liquids, including the identity of substituents at the 3-position, the counterion, and substituted benzyl units, impact the physical properties of these compounds.

Reagent grade solvents (Pharmco), alkyne reagents (GFS), NMR solvents (Cambridge Isotopes) and all other reagents (Aldrich) were used as purchased. NMR analyses were obtained on a 300 MHz Varian Inova system. GC/MS was acquired on a Agilent 6850 Series II GC with 5973 MS detector operating at 70 eV. Kinetic GC/MS analysis surveyed a temperature range of 40 to 240 °C. MALDI-TOF MS was acquired on an Applied Biosystems Voyager DE Pro spectrometer using 2,5-dihydroxybenzoic acid as the matrix.

Milligram Scale Tandem Click Preparation of 1,4-Disubstituted 1,2,3-Triazoles 1 and 2; General Procedure

To a 20 mL scintillation vial was added sequentially $CuSO_4$ (64 mg, 0.4 mmol), sodium ascorbate (159 mg, 0.8 mmol), NaN_3 (286 mg, 4.4 mmol), H_2O (10 mL), *t*-BuOH (10 mL), alkyne reactant (4.0 mmol), and either allyl chloride (0.36 mL, 4.4 mmol) or benzyl bromide (0.24 mL, 4.0 mmol). Following the addition of allyl chloride or benzyl bromide reactant, the vial was sealed with a screw cap and stirred rapidly at r.t. After 24 h, the mixture was partitioned between CH_2Cl_2 (50 mL) and 5% aq NH_4OH (50 mL), and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The combined organic layers were dried ($MgSO_4$) and the solution separated via gravity filtration through fluted filter paper into a round-bottomed flask. Volatiles were removed via rotary evaporation to give the final 1,2,3-triazole product (Table 1).

1-Allyl-4-propyl-1,2,3-triazole (1a)

Yield: 476 mg (79%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1 H), 6.02 (m, 1 H), 5.32 (m, 2 H), 4.95 (m, 2 H), 2.70 (t, *J* = 7.5 Hz, 2 H), 1.70 (m, 2 H), 0.98 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.68, 131.80, 120.61, 119.89, 52.71, 27.88, 22.88, 13.93.

MS (EI, 70 eV): *m*/*z* = 151 (calcd for $C_8H_{13}N_3$: 151).

1-Allyl-4-butyl-1,2,3-triazole (1b)

Yield: 542 mg (82%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1 H), 6.02 (m, 1 H), 5.32 (m, 2 H), 4.95 (m, 2 H), 2.73 (t, *J* = 7.5 Hz, 2 H), 1.67 (m, 2 H), 1.40 (m, 2 H), 0.95 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.96, 131.88, 120.58, 119.96, 52.78, 31.82, 25.63, 22.54, 14.05.

MS (EI, 70 eV): *m*/*z* = 165 (calcd for $C_9H_{15}N_3$: 165).

1-Allyl-4-pentyl-1,2,3-triazole (1c)

Yield: 533 mg (74%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1 H), 6.02 (m, 1 H), 5.32 (m, 2 H), 4.95 (m, 2 H), 2.72 (t, *J* = 7.5 Hz, 2 H), 1.68 (m, 2 H), 1.35 (m, 4 H), 0.91 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.92, 131.80, 120.51, 119.88, 52.71, 31.60, 29.32, 25.84, 22.57, 14.15.

MS (EI, 70 eV): *m*/*z* = 179 (calcd for $C_{10}H_{17}N_3$: 179).

1-Allyl-4-hexyl-1,2,3-triazole (1d)

Yield: 693 mg (90%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1 H), 6.02 (m, 1 H), 5.32 (m, 2 H), 4.95 (m, 2 H), 2.73 (t, *J* = 7.5 Hz, 2 H), 1.68 (m, 2 H), 1.33 (m, 6 H), 0.90 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.01, 131.88, 120.58, 119.95, 52.78, 31.82, 29.67, 29.16, 25.97, 22.79. 14.28.

MS (EI, 70 eV): *m*/*z* = 193 (calcd for $C_{11}H_{19}N_3$: 193).

1-Allyl-4-octyl-1,2,3-triazole (1e)

Yield: 740 mg (83%); white crystalline solid; mp 37–39 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1 H), 6.03 (m, 1 H), 5.34 (m, 2 H), 4.96 (m, 2 H), 2.73 (t, *J* = 7.5 Hz, 2 H), 1.69 (m, 2 H), 1.30 (m, 10 H), 0.90 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.04, 131.89, 120.56, 119.96, 52.79, 32.09, 29.73, 29.58, 29.51, 29.45, 25.98, 22.90. 14.33.

MS (EI, 70 eV): *m*/*z* = 221 (calcd for $C_{13}H_{23}N_3$: 221).

1-Allyl-4-*tert*-butyl-1,2,3-triazole (1f)

Yield: 516 mg (78%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (s, 1 H), 6.03 (m, 1 H), 5.35 (m, 2 H), 4.95 (m, 2 H), 1.37 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.17, 131.90, 119.98, 118.45, 52.76, 30.97, 30.58.

MS (EI, 70 eV): *m*/*z* = 165 (calcd for $C_9H_{15}N_3$: 165).

Downloaded by: University of Arizona Library. Copyrighted material.

1-Allyl-4-phenyl-1,2,3-triazole (1g)
Yield: 671 mg (91%); white crystalline solid; mp 57–58 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87 (m, 2 H), 7.79 (s, 1 H), 7.45 (m, 2 H), 7.36 (m, 1 H), 6.09 (m, 1 H), 5.39 (m, 2 H), 5.04 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.30, 131.60, 130.90, 129.09, 128.41, 125.98, 120.43, 119.66, 53.02.

MS (EI, 70 eV): *m*/*z* = 185 (calcd for $C_{11}H_{11}N_3$: 185).

1-Benzyl-4-propyl-1,2,3-triazole (2a)
Yield: 718 mg (89%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39 (m, 3 H), 7.29 (m, 2 H), 7.21 (s, 1 H), 5.52 (s, 2 H), 2.69 (t, *J* = 7.5 Hz, 2 H), 1.69 (m, 2 H), 0.97 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.95, 135.25, 129.24, 128.78, 128.14, 120.72, 54.16, 27.94, 22.86, 13.97.

MS (EI, 70 eV): *m*/*z* = 201 (calcd for $C_{12}H_{15}N_3$: 201).

1-Benzyl-4-butyl-1,2,3-triazole (2b)
Yield: 746 mg (87%); white crystalline solid; mp 58–59 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (m, 3 H), 7.29 (m, 2 H), 7.21 (s, 1 H), 5.52 (s, 2 H), 2.72 (t, *J* = 7.5 Hz, 2 H), 1.62 (m, 2 H), 1.39 (m, 2 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.20, 135.31, 129.28, 128.82, 128.20, 120.71, 54.20, 31.77, 25.67, 22.57, 14.06.

MS (EI, 70 eV): *m*/*z* = 215 (calcd for $C_{13}H_{17}N_3$: 215).

1-Benzyl-4-pentyl-1,2,3-triazole (2c)
Yield: 692 mg (76%); white crystalline solid; mp 42–43 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39 (m, 3 H), 7.29 (m, 2 H), 7.21 (s, 1 H), 5.52 (s, 2 H), 2.71 (t, *J* = 7.5 Hz, 2 H), 1.62 (m, 2 H), 1.34 (m, 4 H), 0.91 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.22, 135.26, 129.25, 128.80, 128.16, 120.64, 54.18, 31.66, 29.31, 25.93, 22.60, 14.19.

MS (EI, 70 eV): *m*/*z* = 229 (calcd for $C_{14}H_{19}N_3$: 229).

1-Benzyl-4-hexyl-1,2,3-triazole (2d)
Yield: 892 mg (92%); white crystalline solid; mp 55–56 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (m, 3 H), 7.29 (m, 2 H), 7.20 (s, 1 H), 5.52 (s, 2 H), 2.71 (t, *J* = 7.5 Hz, 2 H), 1.66 (m, 2 H), 1.32 (m, 6 H), 0.89 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.19, 135.25, 129.22, 128.76, 128.13, 120.64, 54.15, 31.73, 29.56, 29.10, 25.94, 22.72, 14.22.

MS (EI, 70 eV): *m*/*z* = 243 (calcd for $C_{15}H_{21}N_3$: 243).

1-Benzyl-4-octyl-1,2,3-triazole (2e)
Yield: 1.00 g (92%); white crystalline solid; mp 69–70 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (m, 3 H), 7.29 (m, 2 H), 7.20 (s, 1 H), 5.52 (s, 2 H), 2.71 (t, *J* = 7.5 Hz, 2 H), 1.66 (m, 2 H), 1.28 (m, 10 H), 0.90 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.25, 135.32, 129.29, 128.82, 128.19, 120.71, 54.20, 32.08, 29.67, 29.56, 29.51, 29.44, 26.01, 22.90, 14.34.

MS (EI, 70 eV): *m*/*z* = 271 (calcd for $C_{17}H_{23}N_3$: 271).

1-Benzyl-4-*tert*-butyl-1,2,3-triazole (2f)
Yield: 762 mg (89%); white crystalline solid; mp 82–83 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (m, 3 H), 7.29 (m, 2 H), 7.18 (s, 1 H), 5.51 (s, 2 H), 1.35 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.43, 135.33, 129.28, 128.80, 128.27, 118.61, 54.17, 31.03, 31.61.

MS (EI, 70 eV): *m*/*z* = 215 (calcd for $C_{13}H_{17}N_3$: 215).

1-Benzyl-4-phenyl-1,2,3-triazole (2g)
Yield: 948 mg (98%); white crystalline solid; mp 128–129 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83 (m, 2 H), 7.70 (s, 1 H), 7.39 (m, 8 H), 5.60 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.50, 134.97, 130.82, 129.42, 129.07, 129.04, 128.42, 128.33, 125.97, 119.76, 54.49.

MS (EI, 70 eV): *m*/*z* = 235 (calcd for $C_{15}H_{13}N_3$: 235).

Multigram Scale Tandem Click Preparation of 1,4-Disubstituted 1,2,3-Triazoles; General Procedure
To a 200 mL round-bottomed flask was added sequentially $CuSO_4$ (399 mg, 2.5 mmol), sodium ascorbate (991 mg, 5.0 mmol), NaN_3 (3.576 g, 55 mmol), H_2O (50 mL), *t*-BuOH (50 mL), alkyne reactant (50 mmol), and either allyl chloride (4.08 mL, 50 mmol) or benzyl bromide (5.95 mL, 50 mmol). Following the addition of allyl chloride or benzyl bromide reactant, the flask was sealed with a rubber septum and stirred rapidly at r.t. After 48 h, the mixture was partitioned between CH_2Cl_2 (100 mL) and 5% aq NH_4OH (100 mL), and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layers were dried ($MgSO_4$) and the solution separated via gravity filtration through fluted filter paper into a round-bottomed flask. Volatiles were removed via rotary evaporation to give the final 1,2,3-triazole product. Representative analogues prepared in this manner: **1a** (81%, 6.09 g); **2a** (91%, 9.16 g).

Methyliodonium Salts 3 and 4; General Procedure
To a 20 mL scintillation vial was added sequentially 4-substituted 1-allyl- **1a–g** or 1-benzyl-1,2,3-triazole **2a–g** (1.0 mmol), MeCN (5 mL), and MeI (0.31 mL, 5.0 mmol). The vial was sealed with a screw cap and stirred at 40 °C. After 48 h, the contents of the vial were transferred to a round-bottomed flask and volatiles were removed via rotary evaporation, resulting in isolated 1-allyl- and 1-benzyl-3-methyl-4-alkyl-1,2,3-triazolium iodide salts as pale yellow to yellow viscous liquids. Isolated yields for those reactions reaching completion as observed by ^{1}H NMR (**3a–e** and **4a–e**) was >98% (Table 1).

1-Allyl-3-methyl-4-propyl-1,2,3-triazolium Iodide (3a)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.93 (s, 1 H), 6.06 (m, 1 H), 5.58 (dd, *J* = 16.2, 0.6 Hz, 1 H), 5.44 (dd, *J* = 9.9, 0.6 Hz, 1 H), 5.29 (d, *J* = 6.6 Hz, 2 H), 4.26 (s, 3H), 2.87 (t, *J* = 7.8 Hz, 2 H), 1.77 (m, 2 H), 1.00 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.55, 128.86, 128.10, 123.99, 55.97, 38.92, 25.66, 20.47, 13.60.

MS (MALDI): *m*/*z* $[M - I]^+$ calcd for $C_9H_{16}N_3$: 166; found: 166.

1-Allyl-4-butyl-3-methyl-1,2,3-triazolium Iodide (3b)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.95 (s, 1 H), 6.07 (m, 1 H), 5.62 (dd, *J* = 16.2, 0.6 Hz, 1 H), 5.48 (dd, *J* = 9.9, 0.6 Hz, 1 H), 5.32 (d, *J* = 6.6 Hz, 2 H), 4.29 (s, 3 H), 2.92 (t, *J* = 7.8 Hz, 2 H), 1.72 (m, 2 H), 1.44 (m, 2 H), 0.92 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.83, 128.89, 128.16, 124.14, 56.09, 38.99, 28.93, 23.73, 22.14, 13.61.

MS (MALDI): *m*/*z* $[M - I]^+$ calcd for $C_{10}H_{18}N_3$: 180; found: 180.

1-Allyl-3-methyl-4-pentyl-1,2,3-triazolium Iodide (3c)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.87 (s, 1 H), 6.02 (m, 1 H), 5.55 (dd, *J* = 16.2, 0.6 Hz, 1 H), 5.42 (dd, *J* = 9.9, 0.6 Hz, 1 H), 5.26 (d, *J* = 6.6 Hz, 2 H), 4.23 (s, 3 H), 2.84 (t, *J* = 7.8 Hz, 2 H), 1.67 (m, 2 H), 1.28 (m, 4 H), 0.80 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.63, 128.62, 127.99, 123.87, 55.84, 38.87, 30.80, 26.47, 23.75, 21.89, 13.65.

Downloaded by: University of Arizona Library. Copyrighted material.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{11}H_{20}N_3$: 194; found: 194.

1-Allyl-4-hexyl-3-methyl-1,2,3-triazolium Iodide (3d)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.74 (s, 1 H), 5.93 (m, 1 H), 5.46 (dd, *J* = 16.2, 0.6 Hz, 1 H), 5.24 (dd, *J* = 9.9, 0.6 Hz, 1 H), 5.17 (d, *J* = 6.6 Hz, 2 H), 4.13 (s, 3 H), 2.75 (t, *J* = 7.8 Hz, 2 H), 1.57 (m, 2 H), 1.24 (m, 2 H), 1.11 (m, 4 H), 0.66 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.31, 128.24, 127.77, 123.44, 55.52, 38.58, 30.62, 28.10, 26.43, 23.45, 21.83, 13.46.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{12}H_{22}N_3$: 208; found: 208.

1-Allyl-3-methyl-4-octyl-1,2,3-triazolium Iodide (3e)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.75 (s, 1 H), 5.96 (m, 1 H), 5.49 (dd, *J* = 16.2, 0.6 Hz, 1 H), 5.34 (dd, *J* = 9.9, 0.6 Hz, 1 H), 5.20 (d, *J* = 6.6 Hz, 2 H), 4.17 (s, 3 H), 2.78 (t, *J* = 7.8 Hz, 2 H), 1.61 (m, 2 H), 1.26 (m, 2 H), 1.08 (m, 8 H), 0.69 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.41, 128.33, 127.83, 123.58, 55.64, 38.68, 31.23, 28.56, 26.61, 23.58, 22.09, 13.46.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{14}H_{26}N_3$: 236; found: 236.

1-Benzyl-3-methyl-4-propyl-1,2,3-triazolium Iodide (4a)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.20 (s, 1 H), 7.63 (m, 2 H), 7.40 (m, 3 H), 5.95 (s, 2 H), 4.30 (s, 3 H), 2.98 (t, *J* = 7.9 Hz, 2 H), 1.80 (m, 2 H), 1.05 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.64, 131.51, 130.01, 129.73, 129.50, 129.15, 57.36, 39.00, 25.90, 20.69, 13.81.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{13}H_{18}N_3$: 216; found: 216.

1-benzyl-4-butyl-3-methyl-4-1,2,3-triazolium Iodide (4b)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.16 (s, 1 H), 7.63 (m, 2 H), 7.41 (m, 3 H), 5.96 (s, 2 H), 4.30 (s, 3 H), 2.91 (t, *J* = 7.9 Hz, 2 H), 1.74 (m, 2 H), 1.45 (m, 2 H), 0.94 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.85, 131.52, 130.04, 129.77, 129.53, 129.07, 57.40, 38.99, 29.07, 23.87, 22.31, 13.71.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{14}H_{20}N_3$: 230; found: 230.

1-benzyl-3-methyl-4-pentyl-1,2,3-triazolium Iodide (4c)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 7.59 (m, 2 H), 7.35 (m, 3 H), 5.92 (s, 2 H), 4.28 (s, 3 H), 2.87 (t, *J* = 7.9 Hz, 2 H), 1.72 (m, 2 H), 1.33 (m, 4 H), 0.84 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.99, 131.67, 130.11, 129.86, 129.61, 129.11, 57.47, 39.28, 31.30, 26.93, 24.22, 22.33, 14.11.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{15}H_{22}N_3$: 244; found: 244.

1-Benzyl-4-hexyl-3-methyl-1,2,3-triazolium Iodide (4d)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 7.60 (m, 2 H), 7.38 (m, 3 H), 5.94 (s, 2 H), 4.28 (s, 3 H), 2.88 (t, *J* = 7.9 Hz, 2 H), 1.72 (m, 2 H), 1.39 (m, 6 H), 0.83 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.75, 131.43, 129.90, 129.64, 129.40, 128.89, 57.26, 38.98, 31.14, 28.70, 27.01, 24.03, 22.39, 13.98.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{16}H_{24}N_3$: 258; found: 258.

1-Benzyl-3-methyl-4-octyl-1,2,3-triazolium Iodide (4e)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.09 (s, 1 H), 7.60 (m, 2 H), 7.38 (m, 3 H), 5.94 (s, 2 H), 4.28 (s, 3 H), 2.87 (t, *J* = 7.9 Hz, 2 H), 1.72 (m, 2 H), 1.38 (m, 2 H), 1.22 (m, 8 H), 0.83 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.74, 131.43, 129.89, 129.65, 129.39, 128.87, 57.26, 38.97, 31.68, 29.07, 29.03, 28.99, 27.08, 24.04, 22.56, 14.07.

MS (MALDI): *m/z* [M – I]$^+$ calcd for $C_{18}H_{28}N_3$: 286; found: 286.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis. Included are ^{1}H NMR, ^{13}C NMR and GC/MS characterization of each compound described in this study.

Acknowledgment

This research was supported by an award from Research Corporation.

References

(1) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596.
(2) Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.
(3) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51.
(4) Meldal, M.; Tornoe, C. W. *Chem. Rev.* **2008**, *108*, 2952.
(5) Hanelt, S.; Liebscher, J. *Synlett* **2008**, 1058.
(6) Khan, S. S.; Hanelt, S.; Leibscher, J. *ARKIVOC* **2009**, *(xii)*, 193.
(7) Drake, G.; Kaplan, G.; Hall, L.; Hawkins, T.; Larue, J. *J. Chem. Cryst.* **2007**, *37*, 15.
(8) Welton, T. *Chem. Rev.* **1999**, *99*, 2071.
(9) Forsyth, S. A.; Pringle, J. M.; MacFarlane, D. R. *Aust. J. Chem.* **2004**, *57*, 113.
(10) Ohno, H. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1665.
(11) Brase, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem. Int. Ed.* **2005**, *44*, 5188.
(12) Feldman, A. K.; Colasson, B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 3897.
(13) Appukkuttan, P.; Dehaen, W.; Fokin, V. V.; Van der Eycken, E. *Org. Lett.* **2004**, *6*, 4223.
(14) Kacprzak, K. *Synlett* **2005**, 943.
(15) Zhao, Y. B.; Yan, Z. Y.; Liang, Y. M. *Tetrahedron Lett.* **2006**, *47*, 1545.
(16) Odlo, K.; Hoydahl, E. A.; Hansen, T. V. *Tetrahedron Lett.* **2007**, *48*, 2097.
(17) Li, P. H.; Wang, L. *Lett. Org. Chem.* **2007**, *4*, 23.
(18) Sreedhar, B.; Reddy, P. S. *Synth. Commun.* **2007**, *37*, 805.
(19) Beckmann, H. S. G.; Wittmann, V. *Org. Lett.* **2007**, *9*, 1.
(20) Barral, K.; Moorhouse, A. D.; Moses, J. E. *Org. Lett.* **2007**, *9*, 1809.
(21) Smith, N. M.; Greaves, M. J.; Jewell, R.; Perry, M. W. D.; Stocks, M. J.; Stonehouse, J. P. *Synlett* **2009**, 1391.
(22) Tao, C. Z.; Cui, X.; Li, J.; Liu, A. X.; Liu, L.; Guo, Q. X. *Tetrahedron Lett.* **2007**, *48*, 3525.
(23) Yadav, J. S.; Reddy, B. V. S.; Reddy, G. M.; Chary, D. N. *Tetrahedron Lett.* **2007**, *48*, 8773.
(24) Sharghi, H.; Beyzavi, M. H.; Safavi, A.; Doroodmand, M. M.; Khalifeh, R. *Adv. Synth. Catal.* **2009**, *351*, 2391.
(25) Yadav, J. S.; Reddy, B. V. S.; Reddy, G. M.; Anjum, S. R. *Tetrahedron Lett.* **2009**, *50*, 6029.
(26) Thibault, R. J.; Takizawa, K.; Lowenheilm, P.; Helms, B.; Mynar, J. L.; Frechet, J. M. J.; Hawker, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 12084.
(27) Aucagne, V.; Leigh, D. A. *Org. Lett.* **2006**, *8*, 4505.
(28) Luu, T.; McDonald, R.; Tykwinski, R. R. *Org. Lett.* **2006**, *8*, 6035.
(29) Fletcher, J. T.; Bumgarner, B. J.; Engels, N. D.; Skoglund, D. A. *Organometallics* **2008**, *27*, 5430.
(30) Fletcher, J. T.; Walz, S. E.; Keeney, M. E. *Tetrahedron Lett.* **2008**, *49*, 7030.
(31) Mizumo, T.; Marwanta, E.; Matsumi, N.; Ohno, H. *Chem. Lett.* **2004**, *33*, 1360.

Downloaded by: University of Arizona Library. Copyrighted material.

(32) Wu, J.; Zhang, J.; Zhang, H.; He, J. S.; Ren, Q.; Guo, M. *Biomacromolecules* **2004**, *5*, 266.
(33) Zhang, H.; Wu, J.; Zhang, J.; He, J. S. *Macromolecules* **2005**, *38*, 8272.
(34) Zhang, X. J.; Hsung, R. P.; You, L. F. *Org. Biomol. Chem.* **2006**, *4*, 2679.
(35) Zhao, D. B.; Fei, Z. F.; Geldbach, T. J.; Scopelliti, R.; Laurenczy, G.; Dyson, P. J. *Helv. Chim. Acta* **2005**, *88*, 665.

Downloaded by: University of Arizona Library. Copyrighted material.