

# Click Chemistry in Materials Synthesis. 1. Adhesive Polymers from Copper-Catalyzed Azide-Alkyne Cycloaddition

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**ABSTRACT:** The copper(I)-catalyzed cycloaddition reaction between azides and alkynes has been employed to make metal-adhesive materials. Copper and brass surfaces supply the necessary catalytic Cu ions, and thus the polymerization process occurs selectively on these metals in the absence of added catalysts. Alternatively, copper compounds can be added to monomer mixtures and then introduced to reducing metal surfaces such as zinc to initiate polymerization. The resulting materials were found to possess comparable or superior adhesive strength to standard commercial glues, and structure-activity correlations have identified several important properties of the monomers. © 2004 Wiley Periodicals, Inc. *J Polym Sci Part A: Polym Chem* 42: 4392–4403, 2004  
**Keywords:** adhesives; transition metal chemistry; click chemistry; copper; azides; alkynes; cycloaddition

## INTRODUCTION

The collection of supremely reliable and self-directed organic reactions that we have called “click chemistry”<sup>1</sup> has been applied by us and others thus far mostly to targets of biological significance. For example, the identification of the azide-alkyne 1,3-dipolar cycloaddition<sup>2</sup> as a highly reliable molecular connection in water<sup>3</sup> has been used to augment several types of investigations of biomolecular interactions.<sup>4–7</sup> In addition, applications to organic synthesis,<sup>8</sup> drug discovery,<sup>9,10</sup> and the functionalization of surfaces<sup>11–14</sup> have also appeared. Polymer chemistry should be a rich beneficiary of the ability of click reactions to make molecular connections with ab-

solute fidelity. Indeed, the ability of polymerization reactions to create functional species from simple building blocks was one of the original inspirations for the click chemistry concept. Polymer synthesis depends on a limited number of processes that include many of the best examples of click reactivity. However, the champion “click” process, the copper-catalyzed azide-alkyne cycloaddition, has yet to be so employed.<sup>15</sup> Here we describe our first endeavor to use this reaction to build functional materials.

The copper-catalyzed azide-alkyne ligation process has emerged as a unique combination of selective reactivity and “bulletproof” scope.<sup>3,16</sup> The use of Cu(I) catalysts accelerates the process by factors up to 10<sup>7</sup> while preserving the inertness of both azides and alkynes toward the vast majority of functional groups and conditions that are typical of the terrestrial environment.<sup>3,4</sup> Here we employ di-, tri-, and tetravalent azides and alkynes to create robust, crosslinked polymers of

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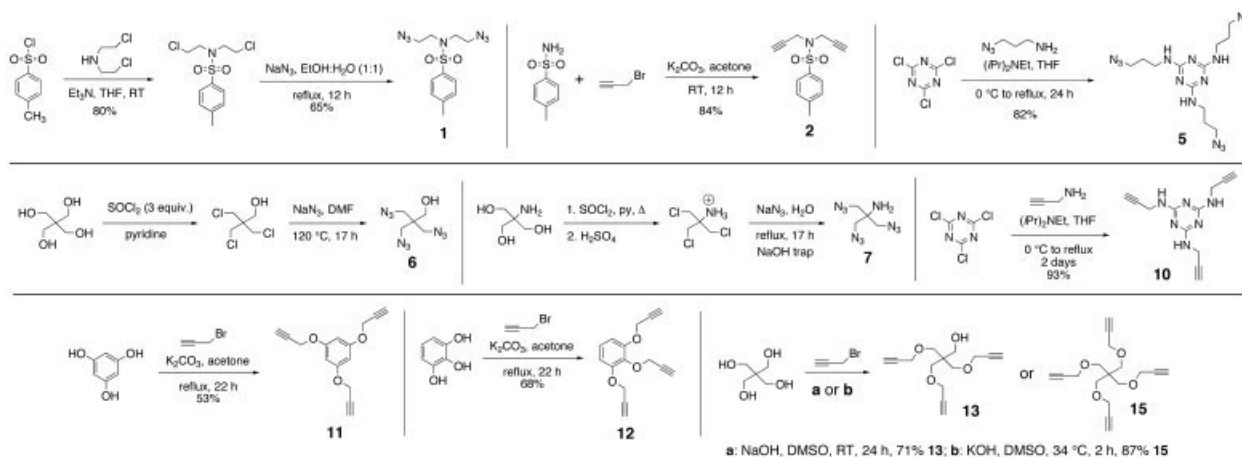


Figure 1. Preparation of monomers.

1,2,3-triazoles that serve to bond metal surfaces to one another. The use of similar components in the remarkably clean synthesis of triazole-containing dendrimers has been recently described.<sup>17</sup>

## EXPERIMENTAL

### General

Solid copper plates (1 in. × 2 in.) were cut from oxygen-free alloy 101 Cu bars (2 in. × 48 in. × 0.125 in., purchased from McMaster-Carr, Inc., Atlanta, GA); brass plates from alloy 260 (68.5–71.5% Cu, 28.38–31.38% Zn, 0.07% Pb, 0.05% Fe; 1 in. × 12 in. × 0.125 in., McMaster-Carr). Zinc plates were cut from commercial carpentry mending plates of 1 in. × 6 in. dimension, obtained from a local hardware store. NMR spectra were obtained at 200 MHz (<sup>1</sup>H) on a Varian Mercury 200 instrument; IR spectra were obtained on a MIDAC FTIR instrument using a horizontal attenuated total reflectance (HATR) accessory (Pike Instruments). Elemental analyses were performed by Midwest Microlabs, Inc. All synthesized monomers were fully characterized and were analytically pure. The commercial glues used for comparison were Weld-It™ (Devcon®, manufactured by ITW Performance Polymers Consumer Division, Riviera Beach, FL), Super Glue™, and Gorilla Glue™, the first being the best and therefore the one used for the majority of tests. “GAP” is GAP Polyol 5527, manufactured by MACH I® Inc., obtained and used as a 40% (w/w) solution in ethyl acetate.

### Monomer Syntheses

Compounds **8**, **9**, and **14** are commercially available; **16** was kindly provided by Dr. Jun-Cai Meng. The following compounds are known and were prepared by the reported procedures with only slight adjustments: **2**,<sup>18–21</sup> **10**,<sup>22</sup> **11**,<sup>23</sup> **12**,<sup>24</sup> **13**,<sup>25</sup> and **15**.<sup>26</sup> The syntheses of monomers are summarized in Figure 1; synthetic procedures and characterization data for new compounds follow.

#### *N,N*-Bis-(2-azido-ethyl)-4-methylbenzenesulfonamide (**1**)

To a suspension of bis(2-chloroethyl)amine hydrochloride (4.68 g, 26.2 mmol) in dry THF (50 mL) was added Et<sub>3</sub>N (18.3 mL, 131 mmol) at 0 °C and the mixture was stirred for 15 min. *p*-Toluenesulfonyl chloride (5.00 g, 26.25 mmol) and DMAP (a spatula pinch) were added. The reaction mixture was allowed to warm to room temperature and was stirred overnight. When TLC analysis showed complete conversion, the mixture was filtered to remove the Et<sub>3</sub>N·HCl and extracted with EtOAc. The combined organic phases were washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash column chromatography to afford *N,N*-bis(2-chloroethyl)-4-methylbenzenesulfonamide (6.22 g, 80% yield).

To a stirred solution of the above sulfonamide (6.00 g, 20.3 mmol) in EtOH:H<sub>2</sub>O (1:1) (110 mL) was added NaN<sub>3</sub> (13.3 g, 203 mmol) at room temperature and a pinch of 18-crown-6 ether. The mixture was refluxed for 12 h, after which time

the EtOH was removed under vacuum and the aqueous layer was extracted with EtOAc, washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash column chromatography to afford **1** (4.08 g, 65% yield) as a white solid. Mp 47–48 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 2.51 (s, 3H), 3.37 (t, *J* = 6.5 Hz, 4H), 3.61 (t, *J* = 6.0 Hz, 4H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 30.0, 49.4, 51.2, 127.6, 130.4, 136.1, 144.5; IR (thin film, cm<sup>-1</sup>) 2102, 1344, 1302, 1163; MS *m/z* (relative intensity) 332 (M+Na)<sup>+</sup> (100). HRMS calcd for C<sub>11</sub>H<sub>16</sub>N<sub>7</sub>O<sub>2</sub>S 310.1086, found 310.1089.

#### 2,2-Bis(azidomethyl)propane-1,3-diol (**4**)

To a 1 L round-bottomed flask equipped with a stirbar and condenser were added 2,2-bis(bromomethyl)-1,3-propanediol (100 g, 0.38 mol), sodium azide (60 g, 0.92 mol), and DMSO (200 mL). The mixture was heated at 100 °C for 36 h, cooled, and water (300 mL) and brine (100 mL) were added. The mixture was extracted five times with EtOAc, and the combined organic phases were washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The final traces of solvent were removed under vacuum to yield **4** (64 g, 90% yield) as slightly yellow oil. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) 2.65 (br s, 2H), 3.48 (s, 4H), 3.68 (s, 4H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 45.2, 52.1, 63.9; IR (thin film, cm<sup>-1</sup>) 3369, 2934, 2088, 1292, 930; MS *m/z* (relative intensity) 209 (M+Na)<sup>+</sup> (100). HRMS calcd for C<sub>5</sub>H<sub>11</sub>N<sub>6</sub>O<sub>2</sub> 187.0943, found 187.0946.

#### N,N',N''-Tris-(3-azidopropyl)-[1,3,5]triazine-2,4,6-triamine (**5**)

To a solution of 3-chloropropylamine hydrochloride (40 g, 0.31 mmol) in H<sub>2</sub>O (280 mL) at room temperature was added NaN<sub>3</sub> (100 g, 1.54 mol) and a pinch of KI. The reaction mixture was stirred for 72 h at 90 °C. The reaction was cooled to room temperature and NaOH (pellet) was added until ca. pH = 11. Solid NaCl was then added and the mixture was extracted five times with toluene. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>) and filtered, and the solvent was partially evaporated, slowly and carefully, under vacuum in the rotary evaporator at low temperature. The concentration of 3-azidopropylamine in the resulting toluene solution was measured by integration of the <sup>1</sup>H-NMR spectrum (~ 0.6–1.4 M). **Caution!** Small organic azides should never be distilled to dryness.

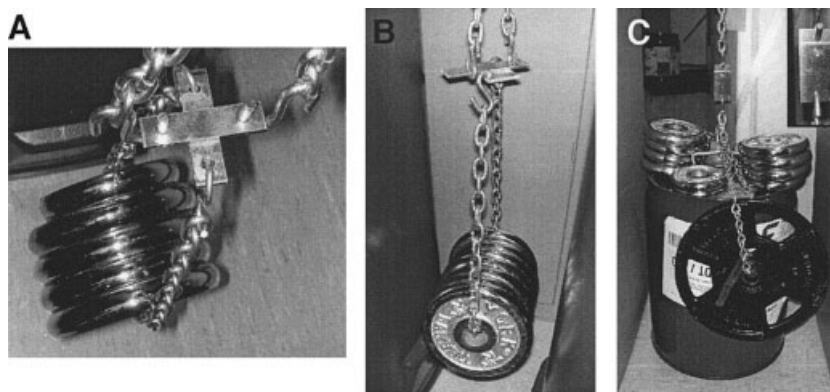
To a solution of cyanuric chloride (10 g, 54.2 mmol) in THF (150 mL) at 0 °C was added diisopropylethylamine (31 mL, 176.18 mmol) in THF (50 mL) and 3-azidopropylamine (128 mL, 1.4 M in toluene, 178.86 mmol). The reaction mixture was stirred under reflux for 50 h. The solvent was then carefully evaporated to the minimum residue, which was extracted with EtOAc. The combined organic layers were washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, concentrated, and purified by flash column chromatography to yield **5** (16.68 g, 82% yield) as slightly yellow gummy syrup. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 1.31 (m, 6H), 1.89 (m, 6H), 3.43 (m, 6H), 3.51 (br s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ 30.0, 38.3, 49.5, 171.6; IR (thin film, cm<sup>-1</sup>) 2137, 2061, 1288, 869; MS *m/z* (relative intensity) 377 (M + 2)<sup>+</sup> (20), 376 (M + 1)<sup>+</sup> (100), 130 (100). HRMS calcd for C<sub>12</sub>H<sub>22</sub>N<sub>15</sub> 376.2177, found 376.2179.

#### 2,2,2-Tris(azidomethyl)ethanol (**6**)

Pentaerythritol was converted to the trichloride by the literature procedure.<sup>27</sup> This intermediate constituted 94% of the crude reaction mixture (analyzed by gas chromatography) and was purified by recrystallization from hexanes. The trichloride was dissolved in DMF, treated with 3.1 equivalents NaN<sub>3</sub>, and heated at 120 °C for 17 h. The crude reaction mixture was cooled, an equivalent volume of water was added, the organic product was extracted into toluene (5x), and DMF was back-extracted into brine. The organic solution was concentrated to remove water by rotary evaporation, but to no greater than 1 M in azide. **Caution!** Small organic azides should never be distilled to dryness. The final concentration of **6** was determined by NMR. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>, toluene peaks omitted) δ 3.58 (s, 2H, CH<sub>2</sub>OH), 3.37 (s, 6H, CH<sub>2</sub>N<sub>3</sub>).

#### Tris(azidomethyl)aminomethane (**7**)

Tris(hydroxymethyl)aminomethane (25.2 g, 200 mmol) was converted to the trichloride ammonium salt using a previously described procedure,<sup>28</sup> and was isolated by treating the solution with NaOH to pH 10 and extracting with CH<sub>2</sub>Cl<sub>2</sub> (5 × 150 mL). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated by rotary evaporation. The concentrate was taken up in diethyl ether (150 mL), and HCl (2.0 M in ether, 114 mL) was slowly added with gentle stirring. The amine salt crystallized out of solution along with an orange semisolid sticking to the sides of the flask.



**Figure 2.** Determination of load-bearing capacity of adhesives: (A) peel test with crossed copper plates; (B) peel test with crossed zinc plates; (C) shear test with parallel aligned copper plates. In (C), the drum was filled with water and, although it is not apparent from the image, was suspended several inches off the floor; the inset shows a close-up of the aligned plates. The adhesive contact areas for the shear and peel tests were the same.

The solid was filtered, crushed, and washed with copious amounts of ether. The final traces of solvent were removed *in vacuo* to yield an off-white solid (36.2 g, 82%,  $m/z$  177.3). An impurity co-crystallizes that can be removed by recrystallization from hot methanol/ether (1:1.5).

This intermediate (8.4 g, 40 mmol) was dissolved in water (200 mL), treated with  $\text{NaN}_3$  (13.2 g, 203 mmol), and gently heated to reflux. The exhaust from the condenser was bubbled through a trap filled with aqueous NaOH to remove any traces of  $\text{HN}_3$  that may have been formed. After 17 h, the mixture was treated with a small amount of 1 M aqueous NaOH to quench any acid, and was then extracted into hexanes ( $2 \times 100$  mL) and ether ( $1 \times 100$  mL). Toluene (200 mL) was added to the combined organics and the solution was concentrated to remove the low boiling solvents and a small amount of the remaining toluene; this solution was then used as obtained. **Caution!** Small organic azides should never be distilled to dryness. The concentration of **7** was determined by NMR.  $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ , toluene peaks omitted)  $\delta$  3.44 (s, 6H,  $\text{CH}_2$ ).

#### 5-Dimethylamino-naphthalene-1-sulfonic acid bis(2-azido-ethyl)-amide (**17**)

The same procedure used above to obtain **1** from tosyl chloride was applied to dansyl chloride, yielding **17** in 52% overall yield as a yellow solid. Mp 45–46 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  2.25 (s, 4H), 2.97 (s, 6H), 3.55 (dd,  $J = 13.7, 5.2$  Hz, 4H), 7.28 (d,  $J = 7.4$  Hz, 1H), 7.51–7.71 (m, 2H), 8.27 (d,  $J = 7.3$  Hz, 1H), 8.35 (d,  $J = 8.7$  Hz, 1H), 8.65 (d,  $J$

= 8.5 Hz, 1H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  45.8, 48.3, 50.9, 115.9, 119.4, 123.5, 128.9, 130.2, 130.4, 130.6, 131.4, 134.5, 152.4; IR (thin film,  $\text{cm}^{-1}$ ) 2173, 2057, 1243, 905; MS  $m/z$  (relative intensity) 411 ( $\text{M} + \text{Na}$ )<sup>+</sup> (10), 390 ( $\text{M} + 2$ )<sup>+</sup> (9), 389 ( $\text{M} + 1$ )<sup>+</sup> (58), 130 (100). HRMS calcd for  $\text{C}_{16}\text{H}_{21}\text{N}_8\text{O}_2\text{S}$  389.1503, found 389.1510.

#### Experimental Procedure for Copper Adhesives

Each copper plate was constructed with a drilled hole on each end to facilitate the hanging of weights for load testing. The copper plates were cleaned just before use by brief exposure to  $\text{H}_2\text{SO}_4$ , followed by thorough rinsing with water, ethanol, and acetone; zinc plates were cleaned with organic solvent. The monomers were mixed in concentrated stock solutions using the minimum necessary amount of THF (usually approximately 0.5 M in each monomer). The required amount of stock mixture was then deposited at the center of each plate, and the mixture was manually spread over the relevant region of the plate while the solvent evaporated. The two plates were then crossed at right angles to bring the treated surfaces in contact with each other, and rested flat under a 25-lb weight for the indicated period. The contact area was therefore 1 in.<sup>2</sup> (approximately 650 mm<sup>2</sup>). If GAP was used, the polymer in ethyl acetate was first applied to the two surfaces, the metal pieces were allowed to dry, and then the above procedure was performed with the monomers of choice.

Load testing was performed by attaching one plate to a chain extending over a support rod, and

**Table 1.** Peel Test Results Using 0.1 mmol of the Alkyne Component

Entry	Diazide	Triazide	Dialkyne	Tri-alkyne	Tetra-alkyne	N <sub>3</sub> :CCH <sup>a</sup>	Load (kg) <sup>b,c</sup>	kg Load Per g Adhesive
1a			commercial glue (27 mg) <sup>d</sup>				6.7	248 ± 111
1b			commercial glue (42 mg) <sup>d</sup>				8.9	212 ± 71
1c			commercial glue (65 mg) <sup>d</sup>				6.3	97 ± 46
1d			commercial glue (100 mg) <sup>d</sup>				7.0	70 ± 30
2	<b>1</b>		<b>8</b>			1:1	1.3 [1.3]	32 ± 25
3	<b>17</b>		<b>8</b>			1:1	1.3 [1.3]	27 ± 21
4	<b>4</b>		<b>9</b>			1:1	4.5 [5.7]	161 ± 36
5	<b>1</b>			<b>10</b>		1:1.5	4.0 [6.3]	73 ± 18
6	<b>1</b>			<b>10</b>		1:1	4.8 [7.1]	68 ± 14
7	<b>1</b>			<b>11</b>		1:1.5	5.9 [6.5]	107 ± 18
8	<b>1</b>			<b>12</b>		1:1.5	5.3 [5.9]	96 ± 18
9	<b>1</b>			<b>13</b>		1:1.5	2.5 [3.6]	45 ± 18
10	<b>4</b>			<b>14</b>		1:1.5	5.2 [6.2]	164 ± 32
11	<b>4</b>			<b>14</b>		1:1	11.0[11.5]	268 ± 24
12	<b>1</b>				<b>15</b>	1:2	5.9 [7.0]	99 ± 17
13		<b>5</b>	<b>2</b>			1.5:1	4.0 [4.7]	64 ± 16
14		<b>5</b>	<b>8</b>			1.5:1	1.3 [1.3]	28 ± 21
15		<b>5</b>		<b>10</b>		1:1	7.0 [8.1]	114 ± 16
16		<b>5</b>		<b>11</b>		1:1	6.3 [7.0]	102 ± 16
17		<b>5</b>		<b>12</b>		1:1	5.4 [5.9]	88 ± 16
18		<b>5</b>		<b>13</b>		1:1	4.5 [6.4]	72 ± 16
19		<b>5</b>		<b>14</b>		1:1	7.5 [8.4]	148 ± 20
20		<b>6</b>		<b>14</b>		1:1	5.0	146 ± 29
21		<b>7</b>		<b>14</b>		1:1	5.6	171 ± 31
22		<b>5</b>			<b>15</b>	3:4	5.9 [7.0]	89 ± 15
More complex mixtures								
23	<b>1 + 17</b>		<b>8</b>	<b>10</b>		4:5	3.6 [4.7]	70 ± 19
24	<b>1 + 17</b>			<b>10 + 11</b>		1:1.5	5.9 [5.9]	100 ± 17
Control experiments								
25			monoazide <b>16</b>		<b>10</b>		1:3	1.3
26	<b>1</b>						0 [0]	
27				<b>10</b>			0 [6.5]	
28	<b>1</b>			<b>10</b>		1:1.5	0 [0]	

All values reported are the average of at least two independent experiments of three replicates each, with an error between experiments of ±1 kg. Note that experiments involving Weld-It<sup>®</sup> adhesive were less reproducible, with an error of ±3 kg.

(a) Ratio of azide groups to alkyne groups.

(b) Maximum load supported by the plates for one minute.

(c) Values in brackets were obtained with the use of GAP as described above.

(d) Weld-It<sup>®</sup>, manufactured by Devcon, Inc.

the other to a chain on which weights could be hung (Fig. 2A,B). Weight was added in 1-lb increments and allowed to hang from the assembly for 1 min, after which the weight was increased. Care was taken to introduce the load at each increment without imposing a sharp stress on the apparatus. Failure of the adhesive was reached when the plates separated within one minute of the load being applied. This can be regarded as a simple “peel”-type test, and was chosen because highly reproducible results were obtained. Shear-type testing (Fig. 2C) gave much greater supported

loads, but was less reproducible. For example, a shear test on a mixture of **1+10** supported a maximum load of 31 kg, compared to 4.8 kg in the peel test. The results represented in Figure 2 are provided in Table 1. In that table are also listed “normalized” values of adhesive strength (maximum load sustained per gram of adhesive). While not discussed above, this offers a different way to compare the performance of different mixtures.

Dansyl diazide **17** (Scheme 2) was used with **1** to test the relative effectiveness of mixtures of monomers (i.e., more than one azide or alkyne) when

**Table 2.** Adhesives Formed Between Zinc Plates. In Each Case, the Ratio of Total Azide to Alkyne Groups Was 1:1.

Entry	Monomers (mmol)	Additive (mmol) <sup>a</sup>	Max. Load (kg) <sup>b</sup>	kg Load Per g Adhesive <sup>c</sup>
1a		Weld-It® (27 mg)	7.8	289 ± 111
1b		Weld-It® (42 mg)	8.1	193 ± 71
1c		Weld-It® (65 mg)	6.1	94 ± 46
1d		Weld-It® (100 mg)	7.8	78 ± 30
2	<b>1</b> + <b>10</b> (0.15 + 0.10)	None	0	–
3	<b>1</b> + <b>10</b> (0.15 + 0.10)	CuI (0.015)	6.2	88 ± 14
4	<b>1</b> + <b>10</b> (0.15 + 0.10)	CuI (0.03)	8.2	116 ± 14
5	<b>1</b> + <b>10</b> (0.15 + 0.10)	CuI (0.30)	4.5	64 ± 14
6	<b>1</b> + <b>10</b> (0.15 + 0.10)	CuI (0.40)	5.0	71 ± 14
7	<b>1</b> + <b>10</b> (0.15 + 0.10)	CuSO <sub>4</sub> · 5H <sub>2</sub> O (0.30)	4.7	67 ± 14
8	<b>5</b> + <b>10</b> (0.10 + 0.10)	None	0	–
9	<b>5</b> + <b>10</b> (0.10 + 0.10)	CuI (0.03)	10.5	101 ± 16
10	<b>4</b> + <b>10</b> (0.15 + 0.10)	CuI + sodium ascorbate (0.03 + 0.03)	6.0	119 ± 19
11	<b>4</b> + <b>14</b> (0.15 + 0.10)	None	0	–
12	<b>4</b> + <b>14</b> (0.15 + 0.10)	CuI (0.03)	0	–
13	<b>4</b> + <b>14</b> (0.15 + 0.10)	CuI + hydroquinone (0.03 + 0.03)	0	–
14	<b>6</b> + <b>14</b> (0.10 + 0.10)	CuI (0.03)	0	–
15	<b>7</b> + <b>14</b> (0.10 + 0.10)	CuI (0.03)	0	–
16	<b>6</b> + <b>10</b> (0.10 + 0.10)	CuI (0.03)	0	–
17	<b>7</b> + <b>10</b> (0.10 + 0.10)	CuI (0.03)	0	–

(a) Cu(I) was dissolved in acetonitrile; CuSO<sub>4</sub>·5H<sub>2</sub>O and hydroquinone were dissolved in water before mixing with the monomers.

(b) Determined by three independent replicates; ±1 kg, except for entries 1a–d, which is ±3 kg. A value of zero indicates that no adhesive was formed.

(c) Determined as in Table 1.

compared to standard pairwise compositions; entries 23 and 24 show that no difference in adhesive performance was realized. When alkyne **10** was used with GAP and no additional azide, a moderately strong adhesive was produced (entry 27), showing that the side-chain azide polymer can be stitched together into a networked structure with only a multivalent alkyne. When two standard runs were annealed at 60 °C instead of room temperature, little difference in the strength of the resulting material was observed (data not shown).

Table 2 summarizes the preliminary measurements of adhesive strength for zinc plates. Note that for zinc no adhesion was observed in the absence of added copper salts.

### Linear Polymers Made in Solution

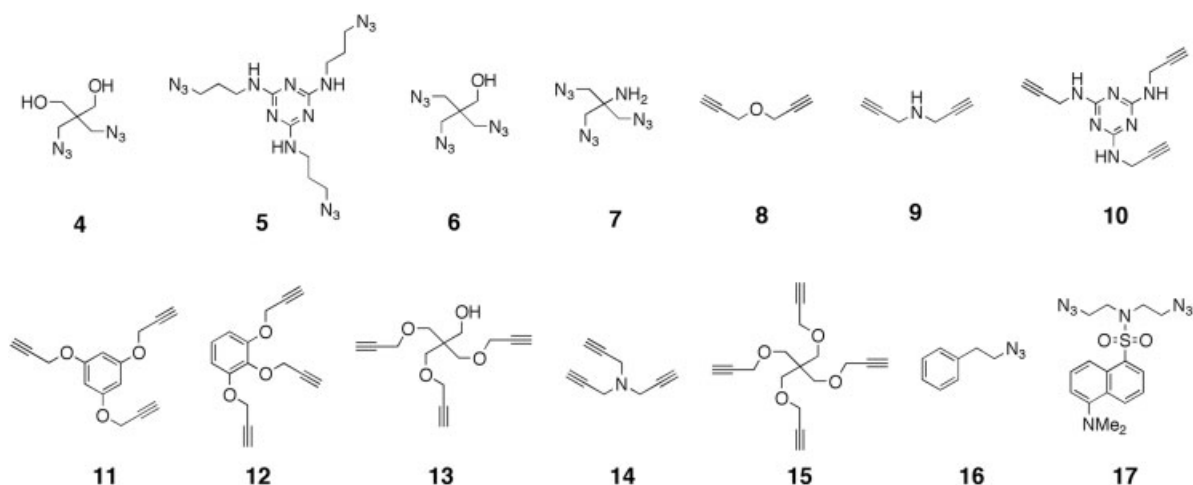
Bifunctional monomers **1** and **2** were condensed in 1:1 *t*-BuOH:H<sub>2</sub>O (0.3 M in each monomer) at room temperature for 10 h in the presence of 5% CuSO<sub>4</sub> and 10% sodium ascorbate. The solvent was poured off, leaving a gummy solid that was

washed sequentially with water, methanol, chloroform, THF (3x), and dried under vacuum. A small portion was removed by scraping (designated **3a**). The remainder was dissolved in hot DMSO and precipitated by the addition of methanol. The resulting solid was collected and washed again with water, methanol, chloroform, and THF (designated **3b**). This latter material represented the major component of the mixture, approximately 70%, and was insoluble in a wide selection of solvents other than hot DMSO. Spectroscopic data (IR and NMR) were consistent with the presence of relatively short chains (unreacted azide and alkyne being sensitively detected by their overlapping signatures at ~ 2100 cm<sup>-1</sup> in the infrared), but neither sample was sufficiently soluble for GPC analysis.

## RESULTS AND DISCUSSION

That the copper-catalyzed 1,3-dipolar cycloaddition can provide polymers was shown by the con-





**Scheme 2.** Polyvalent azide and alkyne building blocks.

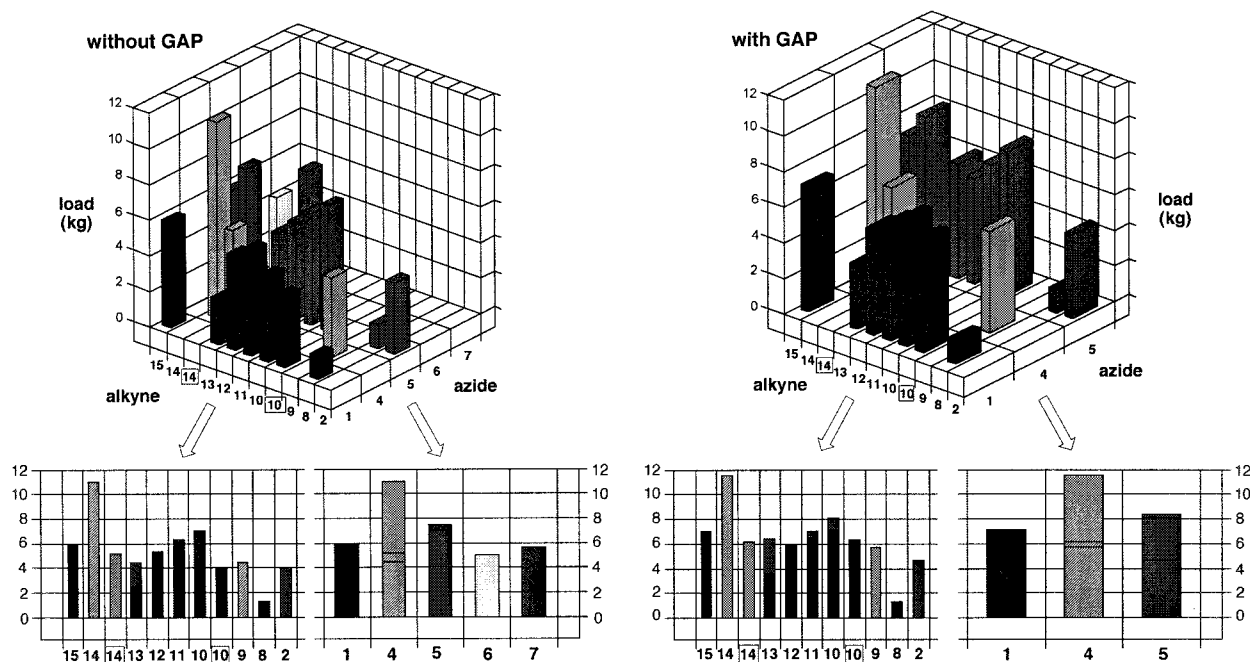
metal adhesive qualities; indeed, triazoles incorporated into polymer structures have been found to enhance binding to copper.<sup>37–39</sup> Since such polymers could be generated selectively on copper surfaces, we anticipated that the use of trifunctional (and higher) monomers would give rise to crosslinked networks on copper-containing materials.

A selection of di-, tri-, and tetravalent alkynes and azides (**1**, **2**, **4–15**, Scheme 2) was tested for the ability to form adhesive polymers.<sup>40</sup> The experimental procedure consisted of spreading a mixture of monomers dissolved in the minimum amount of solvent over the surface of two metal plates, and pressing the crossed plates together under well-defined conditions of pressure, temperature, and time after evaporation of the solvent. The approximate adhesive power of each material formed was determined by measuring the force normal to the surface required to separate the adhered plates (a simplified “peel” test). It should be emphasized that these studies represent the preliminary evaluation and screening of such materials; more in-depth analysis is in progress and will be reported separately.

The maximum loads supported are shown in Figure 4; the error of these averaged measurements (three independent replicates per experiment) was found to be a relatively small  $\pm 1$  kg.<sup>41</sup> We also tested the use of a polymer containing side-chain azides (“glycidyl azide polymer,” GAP, a commercially-available product of azide substitution on the ring-opening polymer of glycidyl chloride) by pretreating the metal surfaces with the polymer and then depositing additional mono-

mers as before. This was done to test the notion that precoating the metal surface with an azide-containing polymer might lead to a higher density of triazoles at the metal interface, and therefore to greater adhesive power. The results of these tests are also shown in Figure 4. While the general observed trend was toward better adhesive properties, the effect of GAP was not dramatic and no structure-activity trends were changed with its use. While many samples formed strong bonds to copper, mixtures involving tripropargylamine (**14**) and, to a lesser extent, trialkyne (**10**), significantly outperformed the commercial glues.

Two factors appear to be most important in determining the power of azide/alkyne adhesive mixtures: the number of “arms” of the monomeric units, and the presence of an amine group. The former factor is presumably related to the degree of crosslinking of the resulting polymer. Thus, combinations of diazides with dialkynes (such as **1**+**8**) gave poor results, since such reactions should produce linear, rather than covalently crosslinked, polymers analogous to **3**. It is unlikely that catenated structures are formed efficiently by ring closure, but such possibilities are being explored separately. The efficacy of amine-containing monomers was demonstrated by comparisons of **9** versus **8**, and **14** versus other tripodal alkynes (**10–13**). Amines are beneficial to the copper-catalyzed process because they assist in the production of Cu-acetylide intermediates and contribute to productive chelating interactions with the metal center. Indeed, the Cu(I) complexes of



**Figure 4.** Maximum loads supported by adhesives made from the indicated mixtures of monomers, at 0.1 mmol scale in the alkyne. The observed trends are very similar for adhesives made with and without precoating with GAP polymer. Rows marked with boxed designations of alkyne (**10** and **14**) denote the use of a 1:1.5 ratio of total azide groups to alkyne groups in the mixture. Under the three-dimensional plots are shown projections along the alkyne and azide axes.

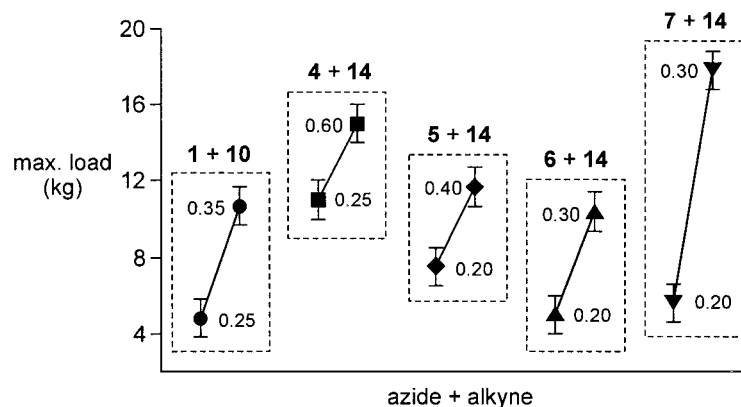
tris(triazolylamine) compounds derived from **14** are highly active catalysts in solution-phase triazole-forming reactions for organic synthesis and bioconjugation.<sup>4,42</sup>

The length and molecular weight distributions of condensation polymers are extremely sensitive to the functional group ratio, with longer chains being produced the closer the ratio approaches unity.<sup>43</sup> It might therefore be expected that the nature of the crosslinked adhesives produced here would also reflect this parameter. Indeed, the material formed from [**4**+**14**] was quite sensitive to functional group stoichiometry, showing far better strength at a 1:1 ratio of azides to alkynes than at a 1:1.5 ratio of functional groups. In contrast, the mixture of [**1**+**10**] was relatively insensitive to changes in the monomer ratio (Fig. 4).

Given equal coverage of adhered surfaces, the use of increasing amounts of elastic adhesive often results in less overall bonding strength. Such was the case with the commercial glue used for comparison testing (Fig. 4). In contrast, all five monomer combinations gave improved performance when used in larger amounts, as shown in Figure 5. The most dramatic example was pro-

vided by **7**+**14**: the mixture containing 0.10 mmol of each monomer on copper supported 5.6 kg whereas the use of 50% more material (0.15 mmol of each monomer) gave nearly three times the strength (17.8 kg). The latter value represents the best performance observed in this study, between two and three times the measured strength of the commercial metal adhesive.<sup>44</sup> Visual inspection of the plates after separation revealed complete coverage of the metal surface in each case, with failure occurring in the bulk of the adhesive rather than at the polymer-metal interface, a property characteristic of brittle materials. Such preliminary measurements have pointed the way to more complete studies, which are currently underway.

We had previously observed that polymers made in solution using soluble Cu(I) species retain a substantial amount of copper in the bulk of the material (unpublished results). Three representative adhesive samples ([**1**+**8**], [**1**+**10**], and [**4**+**14**]) were removed from the copper surface after separation of the plates in load testing, and analyzed for copper after dissolving the polymer in sulfuric acid. The results showed copper present at levels approximately 5–15% of the



**Figure 5.** Maximum load (kg) as a function of the amounts of monomers used. The value beside each point is the total mmoles of the combined monomers; each reaction contains an equimolar ratio of azide and alkyne groups. Adhesive layer thicknesses were approximately 20–100 microns.

number of triazole units potentially formed in each matrix (2–5 wt % of the adhesive mixture).<sup>29</sup> While the relationship between copper content and adhesive properties remains to be explored, studies of bulk polymers show little change in melting properties before and after removal of copper by vigorous treatment with metal chelating agents (data not shown).

Variables such as annealing pressure, annealing time, added copper salts, and the addition of a dendrimeric poly(alkyne) were explored as well, each having a modest effect on the outcome.<sup>29</sup> Control experiments established that no adhesion was obtained with the monodentate azide **16** and trialkyne **10**, nor with polydentate azide or alkyne alone. Copper-electroplated zinc performed analogously to solid copper, but differences in surface roughness caused larger variations (approximately  $\pm 20\%$ ) in adhesive performance. Brass, which is approximately 70% copper, was found to make an adhesive polymer with strengths that are 60–90% of those reported here for pure copper.

Zinc metal surfaces do not mediate the cycloaddition reaction and therefore are not adhered to one another by these monomers alone. However, polytriazoles bind to metals of various kinds, so the addition of copper ions to monomer mixtures on zinc was explored. The addition of Cu(I) or Cu(II) salts promoted the formation of adhesive materials, with Zn metal as the reducing agent to generate and preserve Cu(I) in the mixture. The observed load-bearing capacities were comparable to those of the commercial glue and in the range of many of the mixtures tested on copper.<sup>29</sup>

The addition of Cu at 10 mol % (relative to the total number of azide or alkyne groups) made for the maximum strength in a series of experiments using **1+10**, presumably due to a balancing of overall cycloaddition rate (proportional to Cu concentration) and the length of the polymer chains (inversely proportional to Cu concentration). Most striking is the fact that, with the exception of **[4+10]**, no adhesive polymer was formed with monomers derived from pentaerythritol (**4**, **6**, and **7**), which performed well on copper metal. While the reasons for this are not yet clear, these observations suggest that structure-activity relationships depend upon the type of surface and/or the method by which the catalytic Cu(I) centers are introduced.

In summary, the copper-promoted azide-alkyne cycloaddition is a convenient method for the synthesis of new types of bulk polymers, in this case with adhesive properties. It should be noted also that some of the same monomers create adhesive bonds to glass and plastic, allowing for fusion of these materials to each other and to metals. The ease of introduction of azides and alkynes into organic building blocks, and their nearly complete inertness toward other functional groups, confer similar advantages of generality and practicality to materials synthesis with click chemistry methods as are afforded to the making of bonds in biological systems. The full characterization of these types of materials and further optimization of their adhesive and coating functions are currently under investigation.

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- in pencil) while the solvent evaporated. The two plates were then crossed at right angles to bring the treated surfaces in contact with each other, and allowed to anneal under controlled conditions.
41. Measurements with the commercial adhesive most often tested in this work were less reproducible, with an error of  $\pm 3$  kg.
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  44. Preliminary experiments were also performed with extra large copper plates (surface contact area of  $2 \times 2$  inches = 2581 mm<sup>2</sup>) and 100 mg of monomer mixtures. The most effective system, supporting at least 25 kg in a peel test for at least 10 hours, was composed of a 1.5:1 mixture of **4** and **14** (azide: alkyne ratio = 1:1).