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REUSABLE POLYMER-SUPPORTED 2,2′-BIARYLPYRIDINE–COPPER COMPLEXES FOR HUISGEN [3+2] CYCLOADDITION IN WATER

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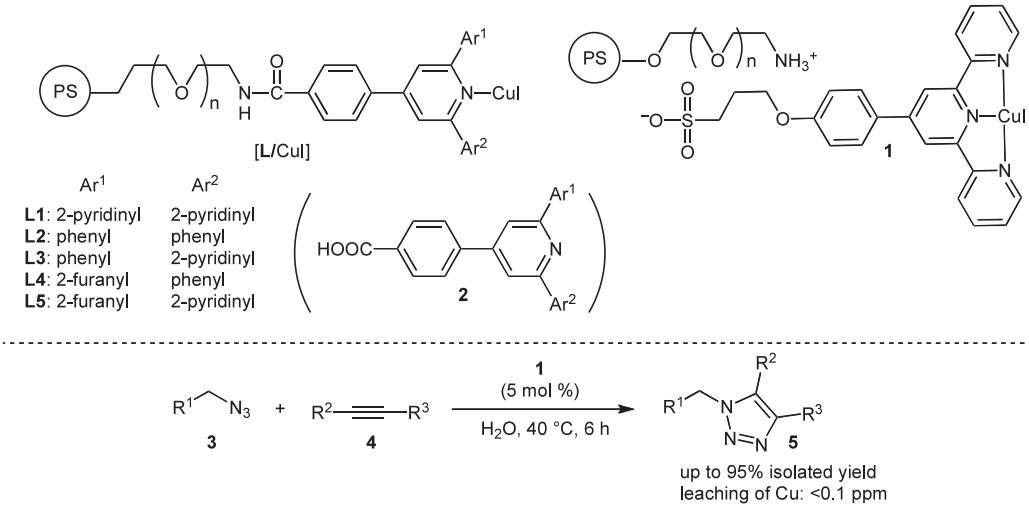
Abstract – Polymer-supported 2,2′-biarylpyridine–copper complexes were prepared and found to promote the Huisgen [3+2] cycloaddition reaction between azides and alkynes in water to give the corresponding triazoles in up to 95% isolated yield. The catalyst was recovered and reused several times without any loss in catalytic activity. ICP-AES analysis of the aqueous phase revealed barely detectable levels of copper residue.

INTRODUCTION

Since the pioneering study by Sharpless *et al*.,[1] the Huisgen 1,3-dipolar cycloaddition reaction has assumed considerable importance in the synthesis of 1,2,3-triazole derivatives,[2] which are key compounds used in agrochemicals and biochemicals.[3] Considerable research has been conducted to improve the efficiency of the homogeneous conditions and applications of this reaction.[4] One of the major problems with the Sharpless *et al*. reaction is the requirement for a copper reagent for promoting the reaction at low temperatures to afford the corresponding 1,4-disubstituted-1,2,3-triazole derivatives with 100% regioselectivity, resulting in the contamination of the coupling products with metal residues. Recently, several studies have been conducted to address this problem. For example, a [3+2] cycloaddition reaction has been carried out with a solid-supported copper(I) catalyst in an organic solvent.[5] Furthermore, we reported a novel polymer-supported terpyridine–copper complex **1**, supported through ionic bonds to the sulfonate group, which efficiently catalyzed the Huisgen [3+2] cycloaddition reaction of azides and acetylenes in water under aerobic conditions to afford the corresponding triazoles in high yield. However, leaching of Cu into the aqueous solution was measured to be 6 ppm (entries 6 and 12, Table 1).[6] In order to reduce leaching of Cu, we have continuously investigated this reaction using novel polymer-supported

terpyridine– or 2,2′-biarylpyridine–copper complexes [**L**/CuI**]**. In this paper, we report the Huisgen [3+2] cycloaddition reaction of azides and acetylenes in water under aerobic conditions using the new polystyrene-poly(ethylene glycol) (PS-PEG)-supported terpyridine– or 2,2'-biarylpyridine–copper complexes formed through covalent bonds to the amino group with resin (Scheme 1).

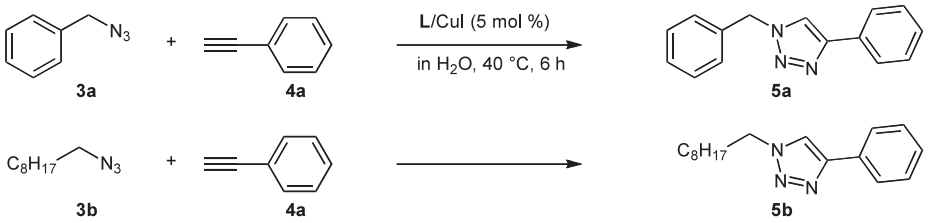


Scheme 1. Polystyrene-poly(ethylene glycol)-supported 2,2′-biarylpyridine–Cu Complex and Application to the [3+2] Cycloaddition Reaction

RESULTS AND DISCUSSION

2,2′-Biarylpyridine ligands **2** were readily prepared from arylketone, 4-formylbenzoic acid, and NH_4OAc according to the reported procedures (*experimental section*).[7] The amphiphilic PS-PEG resin-bound 2,2′-biarylpyridine ligands **L1-5** were prepared by HOBt/EDCI-mediated amide bond formation between the ligands **2** and a PS-PEG-NH_2 resin. The coordination of the generated polymeric ligands **L1-5** with the copper species gave the PS-PEG resin-supported copper complexes [**L1-5**/CuI], which exhibited good catalytic activity for the Huisgen [3+2] cycloaddition reaction without leaching of Cu into the water (Scheme 1). We have examined several amphiphilic PS-PEG resin-supported 2,2′-biarylpyridine ligands for the Huisgen [3+2] cycloaddition reaction. The coupling of benzyl azide (**3a**) or *n*-nonanyl azide (**3b**) and phenylacetylene (**4a**) was performed with the copper complex bound to the PS-PEG-terpyridine resin **L1-5** (5 mol% Cu) at 40 °C for 6 h in water. The reaction mixture was filtered and the recovered resin beads were rinsed with a small amount of water and extracted with EtOAc to give the organic compounds. The combined extracts were concentrated and the resulting residue was chromatographed on silica gel to give 1-benzyl-4-phenyl-1*H*-1,2,3-triazole (**5a**). The results are summarized in Table 1. The results reveal that the copper complex **L1**/CuI is the best catalyst for the [3+2] cycloaddition reaction of **3a** with **4a**. In this case, the copper complex immobilized by coordination with a terpyridine group, which was anchored on an amphiphilic PS-PEG resin, catalyzed the reaction of **3a** and **4a** in water to give 93% isolated yield of triazole **5a** (entry 1).

Table 1. Catalysts for the Huisgen [3+2] Cycloaddition Reaction[a]



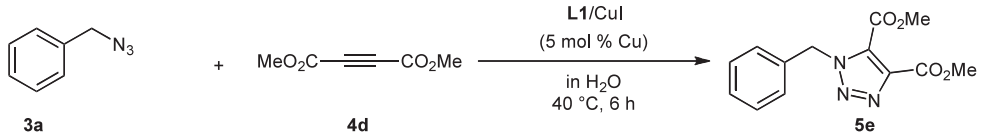
Entry	Catalyst	Product	Yield (%)	Leaching of Cu [c]
1	**L1**/CuI	**5a**	93	<0.1 ppm
2	**L2**/CuI	**5a**	60	<0.1 ppm
3	**L3**/CuI	**5a**	73	<0.1 ppm
4	**L4**/CuI	**5a**	91	<0.1 ppm
5	**L5**/CuI	**5a**	60	<0.1 ppm
6[b]	**1**	**5a**	87	6 ppm
7	**L1**/CuI	**5b**	58	<0.1 ppm
8	**L2**/CuI	**5b**	32	<0.1 ppm
9	**L3**/CuI	**5b**	42	0.2 ppm
10	**L4**/CuI	**5b**	48	<0.1 ppm
11	**L5**/CuI	**5b**	29	0.3 ppm
12[b]	**1**	**5b**	56	6 ppm

[a] All reactions were performed with R-N_3 (**3a**; 0.6 mmol) and phenylacetylene (**4a**; 0.4 mmol) in the presence of polystyrene-poly(ethylene glycol) resin-supported 2,2′-biarylpyridine–copper complexes **L**/CuI in 3.0 mL of solvent at 40 °C for 6 h under aerobic conditions. [b] Our previous results. [c] Leaching of Cu was determined by ICP-AES.

Low catalytic activity was observed in water with the PS-PEG resin-supported biarylpyridine copper complexes **L2**/CuI and **L5**/CuI (entries 2, 5, 8, and 11). The polymeric complex **L4**/CuI exhibited high catalytic activity to afford the triazole **5a** in 91% yield (entry 4), although poor catalytic activity was observed in the reaction of alkyl azide **3b** with **4a** (entry 10). The polymeric complex **L3**/CuI showed good catalytic activity for the reaction of **3a** with **4a** (entry 3), whereas the reaction of **3b** with **4a** gave the triazole **5b** in only 42% yield, with leaching of 0.2 ppm Cu into the water (entry 9).

Note that copper residue could barely be detected by inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis (detection limit of Cu: <3 μg/L) from aqueous and organic filtrates after the reaction of **3a** with **4a** using polymer-supported terpyridine–copper complex **L1**/Cu through formation of a covalent bond to the amino group instead of an ionic bond to the amino group with resin.

The scope of azides and acetylenes was examined for the Huisgen [3+2] cycloaddition reaction in water using the PS-PEG-supported terpyridine–copper complex **L1**/Cu. Representative results are summarized in Table 2. The PS-PEG resin-supported terpyridine–copper complex **L1**/Cu efficiently catalyzed the coupling of benzyl azide (**3a**) and *n*-nonanyl azide (**3b**) with dimethyl acetylenedicarboxylate (**4d**) to afford the dimethyl 1-benzyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**5e**) and dimethyl 1-nonyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**5h**) in 88% and 88% yields, respectively (entries 4 and 8). The Huisgen [3+2] cycloaddition reaction of benzyl azide (**3a**) with various acetylenes **4b**-**c** proceeded to give the corresponding ethyl 1-benzyl-1*H*-1,2,3-triazole-4-carboxylate (**5c**) and 1-benzyl-4-(phenoxymethyl)-1*H*-1,2,3-triazole (**5d**) in 67% and 95% yields, respectively (entries 2–3). The coupling reaction of alkyl azide **3b** with various acetylenes **4b**-**c** also proceeded to give the corresponding ethyl 1-nonyl-1*H*-1,2,3-triazole-4-carboxylate (**5f**) and 1-nonyl-4-phenoxy-1*H*-1,2,3-triazole (**5g**) in 65% and 95% yields, respectively (entries 6–7). The reactivity of each azide derivertives is influenced by its electronic properties. Thus, azides with electron-wtihdrawing substituenets (benzyl azide) react faster than similar azide with a neighboring alkyl group (*n*-nonyl azides).[8]



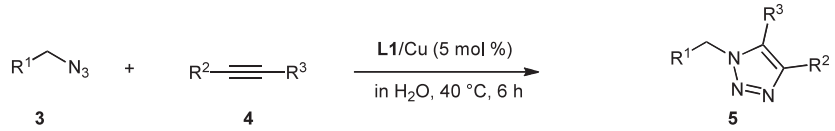
3a 0.6 mmol + **4d** 0.4 mmol → **5e**

88% yield (1st reuse)
89% yield (2nd reuse)
88% yield (3rd reuse)
89% yield (4th reuse)
88% yield (5th reuse)

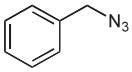
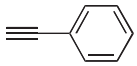
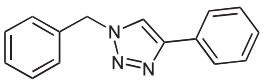
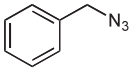
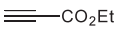
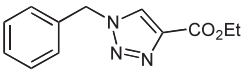
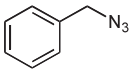
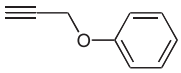
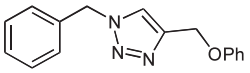
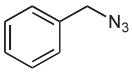
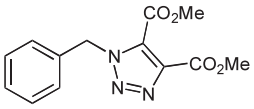
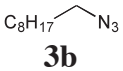
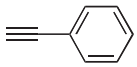
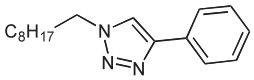
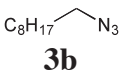
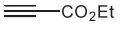
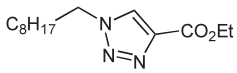
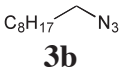
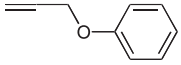
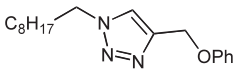
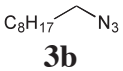
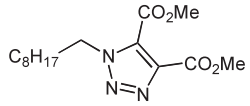
Scheme 2. Catalyst Recycling Experiments

Recyclability of the PS-PEG-supported terpyridine–Cu complex **L1**/CuI was also examined for the Huisgen [3+2] cycloaddition reaction of benzyl azide (**3a**) with dimethyl acetylenedicarboxylate (**4d**). After the first reaction, which gave 88% yield of dimethyl 1-benzyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**5e**), the catalyst was recovered by simple filtration, washed with water, dried under vacuum, and reused five times under similar reaction conditions to give **5e** in 88%, 89%, 88%, 89%, and 88% yields (Scheme 2). Copper residue was barely detected by ICP-AES analysis (detection limit of Cu: <3 μg/L) from aqueous or organic filtrates.

Table 2. Huisgen [3+2] Cycloaddition Reaction of Benzyl Azide and Acetylenes with Polymeric Catalyst **L1**/Cu in Water[a]



3 4 5

Entry	Azide	Alkyne	Product **5**	Yield (%)
1	 **3a**	 **4a**	 **5a**	93
2	 **3a**	 **4b**	 **5c**	67
3	 **3a**	 **4c**	 **5d**	95
4	 **3a**	 **4d**	 **5e**	88
5	 **3b**	 **4a**	 **5b**	58
6	 **3b**	 **4b**	 **5f**	65
7	 **3b**	 **4c**	 **5g**	95
8	 **3b**	 **4d**	 **5h**	88

[a] All reactions were performed with R-N_3 (**3**; 0.6 mmol) and acetylene (**4**; 0.4 mmol) in the presence of polystyrene-poly(ethylene glycol)-supported terpyridine–copper complex **L1**/Cu in 3.0 mL of water at 40 °C for 6 h under aerobic conditions.

In conclusion, we have developed a novel polymer-supported terpyridine–copper complex through formation of a covalent bond to the amino group, which efficiently catalyzed the Huisgen [3+2] cycloaddition reaction of benzyl or alkyl azides with acetylene in water under aerobic conditions to give the corresponding triazoles in high yield and regioselectivity. The catalyst was recovered and reused

several times without any loss of catalytic activity and leaching of Cu into water (<0.1 ppm). Further extensive scope of the Huisgen [3+2] cycloaddition reaction and application of this catalyst to the other organic transformations and the elucidation of ligand effects are in progress in our lab.

EXPERIMENTAL

General Methods

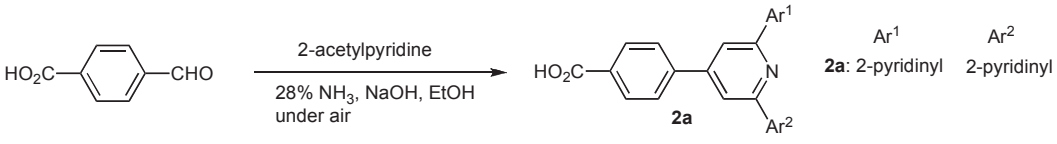
All manipulations were carried out under aerobic conditions. Water was deionized using a Millipore MilliQ gradient A10 to Milli-Q grade. NMR spectra were recorded on a BRUKER AVANCE spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C) and a BRUKER AVANCE spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C), and a HITACHI R1900 spectrometer (90 MHz for ^{1}H and 22 MHz for ^{13}C). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or dimethyl sulfoxide-d_6 (DMSO-d_6) at 25 °C. Chemical shifts of ^{13}C NMR were given relative to $CDCl_3$ and DMSO-d_6 as an internal standard (δ 77.0 ppm and 39.7 ppm). Mass spectral data were obtained on a JEOL JMS-T100GCv MS detector (GC-MS) and a JEOL JMS-T100LP MS detector (LC-MS); the abbreviation 'bp' is used to denote the base peak. GC analysis was performed on a Shimadzu GC-2014 GC. IR analysis was performed on a JASCO FTIR-410 spectrometer. ICP-AES spectral data were obtained on a Shimadzu ICPE-9000 spectrometer. Elemental analysis was performed on a J-Science, JM10 elemental analyzer.

Materials

The PS-PEG amino-resin (Tenta Gel S NH_2, average diameter 90 mm, 1% divinylbenzene cross-linked, loading value of amino residue 0.31 mmol/g) was purchased from RAPP POLYMERE.

*Synthesis of **L1** (One-Step Method)*[7f]

Preparation of 4′-(4-carboxyphenyl)-2,2′:6′,2″-terpyridine (**2a**)

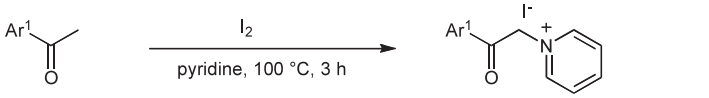


To a solution of 4-methoxycarbonylbenzaldehyde (164 mg, 1.0 mmol) and 2-acetylpyridine (242 mg, 2.0 mmol) in EtOH (4.1 mL), 28% NH_4OH solution (0.2 mL) and NaOH (80 mg, 2.0 mmol) dissolved in a minimum amount of water were added. After the addition of NaOH, the solution turned yellow and then red after 1 h. The solution was stirred vigorously at room temperature in a flask exposed to air for 17 h, after which a yellow suspension was obtained. Then, water (50 mL) was added and the solution was neutralized with conc. HCl to yield a light yellow precipitate and a red solution. The precipitate was collected by filtration and washed with water. For further purification, the precipitate was refluxed for 1 h in EtOH (10 mL) before 77.6 mg (22% yield) of **2a** was collected by filtration. ^{1}H NMR (DMSO-d_6): δ

13.2 (br s, 1H), 8.79–8.76 (m, 4H), 8.69 (d, *J* = 7.9 Hz, 2H), 8.14 (d, *J* = 8.4 Hz, 2H), 8.05 (td, *J* = 7.6, 1.8 Hz, 4H), 7.56–7.53 (m, 2H); ^{13}C NMR (DMSO-d_6): δ 166.6, 155.8 (2C), 154.9 (2C), 149.0 (2C), 148.4, 141.0, 136.9 (2C), 132.4, 129.8 (2C), 126.6 (2C), 124.0 (2C), 120.7 (2C), 117.9 (2C); IR (ATR) (cm^{-1}): *v* 3414 (br), 3122, 1684, 1565; HR-ESI-MS: calcd for $C_{22}H_{15}N_3O_2Na$ (M+Na) 376.1062, found 376.1061. CAS registry number: 158014-74-5.

Synthesis of ***L2-5*** *(Two-step Krohnke Method)*[7e]

Preparation of 1-(2-oxo-2-phenylethyl)pyridinium iodide (**7a**)



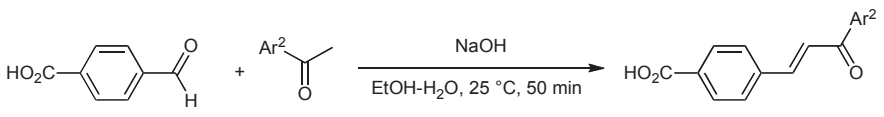
6a: Ar^1 = phenyl
6b: Ar^1 = 2-furanyl

7a: Ar^1 = phenyl (80% yield)
7b: Ar^1 = 2-furanyl (41% yield)

To a stirred warmed (60 °C) solution of I_2 (469.5 mg, 3.7 mmol) in pyridine (2.7 mL), acetophenone (**6a**) (222 mg, 1.8 mmol) was added under N_2, which was stirred at 100 °C for 1 h. The crystals that formed upon cooling were filtered and washed with $CHCl_3$ and Et_2O to give 480.2 mg (80% yield) of the iodide salt **7a**. ^{1}H NMR (DMSO-d_6): δ 8.99 (dd, *J* = 6.6, 1.2 Hz, 2H), 8.80–8.72 (m, 1H), 8.30–8.26 (m, 2H), 8.08–8.06 (m, 2H), 7.83–7.77 (m, 1H), 7.69–7.66 (m, 2H), 6.48 (s, 2H); ^{13}C NMR (DMSO-d_6): δ 190.8, 146.6, 146.4 (2C), 134.9, 133.6, 129.3 (2C), 128.4 (2C), 128.0 (2C), 66.4; IR (ATR) (cm^{-1}): *v* 3047, 2816, 1695, 1484; HR-ESI-MS: calcd for $C_{13}H_{12}NO$ (M-I) 198.0918, found 198.0915. CAS registry number: 1137-94-6.

1-(2-Oxo-2-(2′-furanyl))pyridinium iodide (**7b**) (41% yield). ^{1}H NMR (DMSO-d_6): δ 8.98 (dd, *J* = 6.5, 1.2 Hz, 1H), 8.91 (dd, *J* = 6.5, 1.5 Hz, 1H), 8.73 (tt, *J* = 7.8, 1.3 Hz, 1H), 8.26 (td, *J* = 7.8, 1.4 Hz, 1H), 8.22–8.21 (m, 1H), 8.05–8.01 (m, 1H), 7.71 (dd, *J* = 3.6, 0.5 Hz, 1H), 6.89 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.24 (s, 2H); ^{13}C NMR (DMSO-d_6): δ 179.1, 149.3, 146,7, 146.5 (3C), 128.0 (2C), 120.4, 113.5, 65.2; IR (ATR) (cm^{-1}): *v* 3054 (br), 2892, 1671, 1631; HR-ESI-MS: calcd for $C_{11}H_{10}NO_2$ (M-I) 188.0711, found 188.0714. CAS registry number: 53676-94-1.

Preparation of (*E*)-4-(3-oxo-3-phenylprop-1-enyl)benzoic acid (**8a**)



6a: Ar^2 = phenyl
6c: Ar^2 = 2-pyridinyl

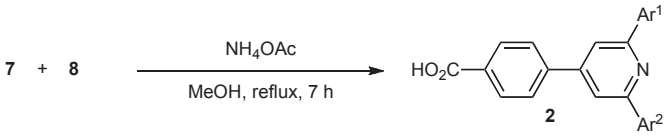
8a: Ar^2 = phenyl (55% yield)
8b: Ar^2 = 2-pyridinyl (38% yield)

To a solution of 4-formylbenzoic acid (496 mg, 3.31 mmol) and NaOH (180 mg, 4.50 mmol) in EtOH/H_2O (5.0 mL, 1:1), a solution of acetophenone (**6a**) (397 mg, 3.31 mmol) in EtOH (0.5 mL) was added dropwise over 10 min with vigorous stirring. A thick yellow solid precipitated 10 min after addition was complete. The reaction mixture was stirred for a further 50 min at 25 °C and was neutralized

to pH 6 in HCl solution to generate a yellow solid. The yellow solid was collected by filtration, washed with aqueous MeOH, and dried *in vacuo*. Recrystallization of the yellow solid from MeOH furnished 458 mg (55% yield) of (*E*)-4-(3-oxo-3-phenylprop-1-enyl)benzoic acid (**8a**). ^{1}H NMR ($CDCl_3$): δ 13.1 (br s, 1H), 8.19–8.17 (m, 2H), 8.06 (d, *J* = 15 Hz, 1H), 8.01–7.98 (m, 4H), 7.79 (d, *J* = 15.6 Hz, 1H), 7.71–7.67 (m, 1H), 7.58 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (DMSO-d_6): δ 189.3, 167.0, 142.7, 138.9, 137.5, 133.5, 132.2, 129.9 (2C), 129.1 (2C), 129.0 (2C), 128.8 (2C), 124.4: IR (ATR) (cm^{-1}): *v* 3415 (br), 2817, 2544, 1665; HR-ESI-MS: calcd for $C_{16}H_{11}O_3$ (M-H) 251.0708, found 251.0706. CAS registry number: 20118-38-1.

(*E*)-4-(3-Oxo-3-(pyridin-2-yl)prop-1-enyl)benzoic acid (**8b**) (38% yield). ^{1}H NMR ($CDCl_3$): δ 13.0 (br s, 1H), 8.78–8.76 (m, 1H), 8.40 (d, *J* = 16 Hz, 1H), 8.21 (td, *J* = 7.8, 1.0 Hz, 1H), 8.13 (d, *J* = 6.6 Hz, 2H), 7.94 (d, *J* = 17 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.54–7.51 (m, 1H); ^{13}C NMR (DMSO-d_6): δ 188.8, 166.9, 153.3, 149.4, 142.7, 138.8, 138.0, 132.4, 130.1, 128.9 (2C), 128.0 (2C), 123.1, 122.7; IR (ATR) (cm^{-1}): *v* 3410 (br), 2830, 2549, 1682; HR-ESI-MS: calcd for $C_{15}H_{10}NO_3$ (M-H) 252.0660, found 252.0659. CAS registry number: 227286-59-1.

Preparation of 2,2′-biarylpyridine ligands **2**



	Ar^1	Ar^2	
2b:	phenyl	phenyl	33% yield
2c:	phenyl	2-pyridinyl	47% yield
2d:	2-furanyl	phenyl	71% yield
2e:	2-furanyl	2-pyridinyl	50% yield

An excess of ammonium acetate (770 mg, 10 mmol) was added to a mixture of (*E*)-4-(3-oxo-3-phenylprop-1-enyl)benzoic acid (**8a**) (252 mg, 1.0 mmol) and 1-(2-oxo-2-phenylethyl)pyridinium iodide (**7a**) (198 mg, 1.0 mmol) in MeOH (6.1 mL). After refluxing for 7 h, the reaction mixture was allowed to cool (5 °C) to generate the pure product as yellow needles. The solid was collected by filtration, washed with cold MeOH, and dried *in vacuo* to give 4-(2,6-diphenylpyridin-4-yl)benzoic acid **2b** in 33% yield (115 mg). ^{1}H NMR (DMSO-d_6): δ 13.2 (br, 1H), 8.34 (d, *J* = 7.1 Hz, 4H), 8.21 (s, 2H), 8.07 (d, *J* = 6.8 Hz, 2H), 8.00 (d, *J* = 6.8 Hz, 2H), 7.56–7.45 (m, 6H); ^{13}C NMR (DMSO-d_6): 169.1, 156.7 (2C), 149.6, 139.8, 139.0 (2C), 138.5, 129.9 (2C), 129.4 (2C), 128.9 (4C), 127.1 (4C), 126.6 (2C), 116.7 (2C); IR (ATR) (cm^{-1}): *v* 3317 (br), 1592, 1550, 1384. HR-ESI-MS: calcd for $C_{24}H_{18}NO_2$ (M+H) 352.1337, found 352.1328. CAS registry number: 161121-56-8.

4-(6-Phenyl-2,2′-bipyridin-4-yl)benzoic acid (**2c**) (47% yield). ^{1}H NMR ($CDCl_3$): δ 13.1 (br, 1H), 8.83–8.82 (m, 1H), 8.75–8.72 (m, 2H), 8.24–8.21 (m, 4H), 8.03 (d, *J* = 1.5 Hz, 1H), 7.95–7.92 (m, 3H), 7.57–7.41 (m, 4H); ^{13}C NMR (DMSO-d_6): 167.2, 156.8, 156.0, 155.2, 149.5, 148.6, 141.8, 138.5, 137.7, 131.6, 130.3 (2C), 129.6, 129.0 (2C), 127.6 (2C), 127.2 (2C), 124.7, 121.1, 118.4, 116.8. IR (ATR)

(cm^{-1}): *v* 3317 (br), 1697, 1589, 1569. HR-ESI-MS: calcd for $C_{23}H_{17}N_2O_2$ (M+H) 353.1290, found 353.1279. CAS registry number: 227286-58-0.

4-(2-(Furan-2-yl)-6-phenylpyridin-4-yl)benzoic acid (**2d**) (71% yield). ^{1}H NMR ($CDCl_3$): δ 13.2 (br, 1H), 8.27 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 7.0 Hz, 2H), 7.90–7.82 (m, 4H), 7.58–7.46 (m, 4H), 7.27 (d, *J* = 3.4 Hz, 1H), 6.59 (dd, *J* = 3.3, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): 170.8, 157.9, 153.8, 149.9, 148.7, 144.0, 143.4, 139.0, 130.9 (2C), 129.5, 129.3, 128.7 (2C), 127.3 (2C), 127.1 (2C), 116.8, 114.9, 112.1, 109.3; IR (ATR) (cm^{-1}): *v* 3316 (br), 1692, 1607; HR-ESI-MS: calcd for $C_{22}H_{15}NO_3$ (M+H) 342.1130, found 342.1118.

4-(6-(Furan-2-yl)-2,2′-bipyridin-4-yl)benzoic acid (**2e**) (50% yield). ^{1}H NMR (DMSO-d_6): δ 13.1 (br, 1H), 8.74–8.73 (m, 1H), 8.58–8.54 (m, 2H), 8.13–7.99 (m, 6H), 7.92 (s, 1H), 7.53–7.50 (m, 1H), 7.40 (d, *J* = 3.3 Hz, 1H), 6.74–6.73 (m, 1H); ^{13}C NMR (DMSO-d_6): 167.1, 156.1, 154.8, 153.0, 149.5, 149.3, 148.4, 144.7, 141.7, 137.6, 131.7, 130.3 (2C), 127.4 (2C), 124.8, 121.0, 116.4, 116.2, 112.6, 110.1; IR (ATR) (cm^{-1}): *v* 3317 (br), 1703, 1595, 1481; HR-ESI-MS: calcd for $C_{21}H_{15}N_2O_3$ (M+H) 343.1082, found 343.1078.

Preparation of PS-PEG resin-supported 2,2′-biarylpyridine–copper complex (**L1**/CuI)

A Merrifield vessel was charged with PS-PEG-NH_2 (0.80 g, 0.24 mmol), **2a** (127 mg, 0.36 mmol), EDCI (138 mg, 0.72 mmol), HOBt (130 mg, 0.96 mmol), and *N*,*N*-dimethylformamide (DMF) (10 mL). The reaction mixture was shaken on a shaking machine (EYELA CM-1000) at 25 °C for 6 h. Complete consumption of the primary amino residue of the resin was monitored by a Kaiser negative test. The reaction mixture was filtered and the resin was washed with DMF and CH_2Cl_2. The resin was dried under reduced pressure to give the polymer-supported 2,2′-biarylpyridine **L1** (loading value of **L**: 0.27 mmol/g, as determined by elemental analysis). A Merrifield vessel was charged with resin-supported 2,2′-biarylpyridine (**L1**; 442 mg, 0.12 mmol) and 10 mL of CH_2Cl_2. To this suspension was added copper iodide (35.4 mg, 0.19 mmol) and the mixture was shaken on a shaking machine (CM-1000) at 25 °C for 3 h. After filtration, the resin was washed with CH_2Cl_2 and H_2O. The resin thus obtained was dried under reduced pressure to give polymer-supported copper complex **L1**/CuI (loading value of Cu: 0.26 mmol/g). Loading value of Cu: (**L2**/CuI; 0.26 mmol/g, **L3**/Cu; 0.26 mmol/g; **L4**/Cu; 0.26 mmol/g, **L5**/Cu; 0.26 mmol/g). IR (ATR) (cm^{-1}); **L1**/CuI; *v* 2880, 1454, 1342; **L2**/CuI; *v* 2877, 1454, 1342; **L3**/CuI; *v* 2881, 1454, 1342; **L4**/CuI; *v* 2881, 1453, 1342; **L5**/CuI; *v* 2879, 1454, 1342.

Copper-Catalyzed Cycloaddition Reaction of Benzyl Azide with Phenylacetylene

To a mixture of the polymeric catalyst (**L1**/CuI; 78.4 mg, 0.020 mmol) and benzyl azide (**3a**; 79.8 mg, 0.60 mmol) in H_2O (3.0 mL), phenylacetylene (**4a**; 40.8 mg, 0.40 mmol) was added. The reaction mixture was shaken at 40 °C for 6 h and filtered. The recovered resin beads were rinsed with water and the rinsed aqueous layer was extracted three times with EtOAc (6 mL). The EtOAc layer was separated and the aqueous layer was extracted with EtOAc (5 mL). The combined EtOAc extracts were washed with brine (2 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was chromatographed on silica gel (hexane-EtOAc, 10:1) to give 87.8 mg (93% yield) of 1-benzyl-4-phenyl-1*H*-1,2,3-triazole (**5a**). ^{1}H NMR ($CDCl_3$): δ 7.81–7.78 (m, 2H), 7.66 (s, 1H), 7.41–7.37 (m, 5H), 7.33–7.30 (m, 3H), 5.57 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 148.1, 134.6, 130.4, 129.0 (2C), 128.7, 128.7 (2C), 128.0 (2C), 127.9 (2C), 125.6, 119.4, 54.1; MS (EI) *m/z* (rel%): 235 (8, M^+), 206 (30), 116 (bp), 91 (87); IR (ATR) (cm^{-1}); *v* 2928, 1725, 1493, 1467. CAS registry number: 108717-96-0.

1-Nonyl-4-phenyl-1*H*-1,2,3-triazole (**5b**). ^{1}H NMR ($CDCl_3$): δ 7.85–7.81 (m, 2H), 7.74 (s, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.35–7.32 (m, 1H), 4.40 (t, *J* = 7.3 Hz, 2H), 1.97–1.92 (m, 2H), 1.35–1.26 (m, 12H), 0.87 (t, *J* = 7.0 Hz, 3H): ^{13}C NMR ($CDCl_3$) δ 147.6, 130.6, 128.8 (2C), 128.0, 125.6 (2C), 119.3, 50.4, 31.7, 30.3, 29.3, 29.1, 28.9, 26.4, 22.6, 14.0. MS (EI) *m/z* (rel%): 271 (8, M^+), 242 (8), 172 (20), 145 (29), 117 (bp), 104 (35); IR (ATR) (cm^{-1}): *v* 3120, 2951, 1462. CAS registry number: 853052-50-3.

Ethyl 1-benzyl-1*H*-1,2,3-triazole-4-carboxylate (**5c**). ^{1}H NMR ($CDCl_3$): δ 8.02 (s, 1H), 7.39–7.37 (m, 3H), 7.30–7.28 (m, 2H), 5.57 (s, 2H), 4.38 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 160.5, 140.4, 133.6, 129.1 (2C), 128.9 (2C), 128.1, 127.2, 61.1, 54.3, 14.1; MS (EI) *m/z* (rel%): 231 (1, M^+), 202 (2), 174 (18), 130 (25), 91 (bp); IR (ATR) (cm^{-1}): *v* 3117, 1724, 1213. CAS registry number: 126800-24-6.

1-Benzyl-4-phenoxy-1*H*-1,2,3-triazole (**5d**). ^{1}H NMR ($CDCl_3$): δ 7.53 (s, 1H), 7.38–7.35 (m, 3H), 7.30–7.26 (m, 4H), 6.96–6.95 (m, 3H), 5.53 (s, 2H), 5.19 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 158.1, 144.5, 134.2, 129.5 (2C), 129.1 (2C), 128.8, 128.1 (2C), 122.6, 121.2, 114.7 (2C), 61.9, 54.3; MS (EI) *m/z* (rel%): 265 (7, M^+), 172 (13), 144 (41), 91 (bp). IR (ATR): (cm^{-1}) *v* 3132, 2922, 1218. CAS registry number: 478555-18-9.

Dimethyl 1-benzyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**5e**). ^{1}H NMR ($CDCl_3$): δ 7.35–7.32 (m, 3H), 7.26–7.25 (m, 2H), 5.81 (s, 2H), 3.96 (s, 3H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 160.3, 158.7, 140.1, 133.1, 129.1 (2C), 128.9 (2C), 128.8, 127.9, 53.9, 53.2, 52.6; MS (EI) *m/z* (rel%): 216 (2, M^+ – COOMe), 214 (6), 174 (6), 156 (10), 130 (12), 91 (bp). IR (ATR) (cm^{-1}): *v* 2954, 1727, 1217. CAS registry number:

73500-16-0.

Ethyl 1-nonyl-1*H*-1,2,3-triazole-4-carboxylate (**5f**). ^{1}H NMR ($CDCl_3$): δ 8.09 (s, 1H), 4.46–4.40 (m, 4H), 2.07–1.90 (m, 2H), 1.41 (t, *J* = 7.0 Hz, 3H), 1.32–1.26 (m, 12H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 160.7, 140.1, 127.1, 61.1, 50.6, 31.6, 30.0, 29.1, 29.0, 28.8, 26.2, 22.5, 14.2, 13.9; MS (EI) *m*/*z* (rel%): 222 (16, M^+ – OEt), 210 (14), 168 (45), 154 (62), 152 (75), 130 (50), 96 (83), 83 (bp). IR (ATR) (cm^{-1}): *v* 3114, 2952, 1722. CAS registry number: 1222558-93-1.

1-Nonyl-4-phenoxy-1*H*-1,2,3-triazole (**5g**). ^{1}H NMR ($CDCl_3$): δ 7.59 (s, 1H), 7.31–7.27 (m, 2H), 7.00–6.95 (m, 3 H), 5.22 (s, 2 H), 4.34 (t, *J* = 7.0 Hz, 2 H), 1.91–1.89 (m, 2H), 1.31–1.25 (m, 12H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 158.1, 144.0, 129.5 (2C), 122.4, 121.2, 114.7 (2C), 61.9, 50.6, 31.7, 30.2, 29.2, 29.1, 28.9, 26.4, 22.6, 14.0; MS (EI) *m*/*z* (rel%): 301 (13, M^+), 180 (bp), 94 (51). IR (ATR) (cm^{-1}): *v* 2952, 2846, 1600. CAS registry number: 1222558-94-2.

Dimethyl 1-nonyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**5h**). ^{1}H NMR ($CDCl_3$): δ 4.58 (t, *J* = 7.3 Hz, 2H), 4.00 (s, 3H), 3.97 (s, 3H), 1.92–1.86 (m, 2H), 1.31–1.25 (m, 12H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 160.5, 159.0, 139.8, 129.8, 53.3, 52.6, 50.6, 31.7, 30.2, 29.2, 29.0, 28.8, 26.2, 22.5, 14.6. MS (EI) *m*/*z* (rel%): 280 (6, M^+–OMe), 252 (bp), 224 (25), 154 (37), 140 (37), 126 (27); IR (ATR): (cm^{-1}) *v* 2925, 1731, 1466. CAS registry number: 1222558-92-0.

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