

Tripodal “Click” Ligands for Copper-Catalyzed ATRP

Preeyanuch Sangtrirutnugul,^{1,2} Purmpoon Maisopa,^{1,2} Laksamee Chaicharoenwimolkul,^{2,3}
 Atchariya Sunsin,^{2,3} Ekasith Somsook,^{1,2,3} Vichai Reutrakul^{1,2}

¹Faculty of Science, Department of Chemistry, Center for Catalysis, Mahidol University, Rama VI Road, Bangkok 10400, Thailand

²Faculty of Science, Department of Chemistry and Center of Innovation in Chemistry, Mahidol University, Bangkok 10400, Thailand

³Faculty of Science, Department of Chemistry, NANOCAS Laboratory, Mahidol University, Bangkok 10400, Thailand
 Correspondence to: P. Sangtrirutnugul (E-mail: scpsf@mahidol.ac.th)

ABSTRACT: A series of *tris*(*R*-methyltriazolylmethyl)amines [R = C₆H₅ (1), 4-FC₆H₄ (2), 4-MeOC₆H₄ (3), Fc (4)] were prepared and used as ligands for catalytic ATRP of methyl methacrylate (MMA). Despite a lower activity, the CuBr/4 catalyst promoted relatively well controlled polymerization compared to CuBr/1, as evidenced by narrower polydispersity indices. Meanwhile, no polymerization activity was observed with CuBr/2 and CuBr/3 under the catalytic conditions investigated. The CV measurements of CuBr₂ complexes supported 1 and 4 in DMSO showed $E_{1/2}$ values of -0.206 and -0.224 V, respectively, confirming the more electron-rich nature of CuBr/4. Although both CuBr/1 and CuBr/4 catalysts were only partially soluble in several organic solvents used, kinetic studies revealed a pseudo first order linear plot of $\ln[M]_0/[M]_t$ versus time. Addition of CuBr₂ into the polymerization systems led to a decrease in polymer polydispersities and the observed rate constants (k_{obs}). © 2012 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* 000: 000–000, 2012

KEYWORDS: click ligand; ATRP; MMA; copper catalyst

Received 20 October 2011; accepted 27 February 2012; published online

DOI: 10.1002/app.37596

INTRODUCTION

Atom Transfer Radical Polymerization (ATRP)^{1,2} has been intensively researched over the past decade owing to its ability to produce polymers with controlled molecular weights, well-defined architectures, and narrow molecular weight distributions.³ The copper-catalyzed ATRP process involves a reversible one-electron redox reaction catalyzed by a copper complex of the type Cu^IX/L (L = ligand). Halide abstraction from an initiator (R-X) by Cu^IX/L gives the higher oxidation state copper species Cu^{II}X₂/L and the corresponding alkyl radicals (R•), which react with monomers and further propagate to afford polymers (Scheme 1).

Given the crucial roles of a supporting ligand in solubilizing the metal catalysts in organic media and adjusting a redox potential at the metal center, the design and appropriate selection of ligands represent an important research aspect in the development of ATRP. Previous studies have shown that a mixture of CuBr and neutral tetradentate ligands such as *tris*[2-(dimethylaminoethyl)amine (Me₆TREN) or 1,4,8,11-tetraaza-tetramethylcyclotetradecane (Me₄CYCLAM) is an effective ATRP catalyst, affording high poly-

merization activity with narrow polydispersity polymers.⁴ Other related nitrogen-based, tetradentate ligands featuring imidazole⁵ and redox-active ferrocene-containing imine functional groups⁶ were also explored as ligands in copper-catalyzed ATRP.

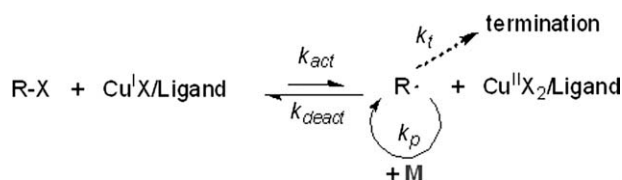
In this study, we were interested in incorporating a 1,2,3-triazole “click” substituent⁷ into the ligand framework via the Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC). Despite the well-established chemistry of click reactions, examples of click-containing ligands involved in catalysis remain relatively limited.^{8,9} Advantages of this type of ligand include ease of preparation and ability to stabilize catalysts at high temperatures with relatively strong metal-ligand interactions.⁹ Herein, we report the preparation of tripodal *tris*(triazolylmethyl)amine compounds and investigate their role as catalyst supports in copper-catalyzed ATRP of methyl methacrylate (MMA).

EXPERIMENTAL

Instruments and Reagents

Manipulations involving air-sensitive reactions were performed using standard Schlenk techniques under an argon atmosphere

© 2012 Wiley Periodicals, Inc.



Scheme 1. The mechanism of copper-catalyzed ATRP.

or in a Braun drybox. Toluene (Fisher Scientific), 2-butanone (Aldrich), DMSO (Labscan) used in air-sensitive reactions were dried with appropriate drying reagents and distilled under N_2 before use. Hexane is commercial grade and distilled prior to use. Diethyl ether, THF, CHCl_3 , CH_2Cl_2 , and CH_3OH were purchased from Lab Scan and used as received. De-ionized (DI) water was obtained from Nanopure[®] Analytical Deionization Water with an electric resistance $\geq 18.2 \text{ M}\Omega/\text{cm}$. CDCl_3 were purchased from Cambridge Isotopes, stored in 4 Å molecular sieves, and used without further purification.

CuBr , CuBr_2 , ethyl 2-bromoisobutyrate (EBiB, Aldrich), ascorbic acid (Riedel-de Haën), anhydrous Na_2SO_4 (Carlo Erba Reagenti), ferrocene carboxaldehyde, benzyl bromide, oxalyl chloride (Fluka) were used as received. RCH_2Cl ($\text{R} = 4\text{-FC}_6\text{H}_4$, $4\text{-OMeC}_6\text{H}_4$), NaN_3 , tripropargyl amine were purchased from Aldrich and used without further purification. The reagents FcCH_2OH [$\text{Fc} = (\text{C}_5\text{H}_5)\text{Fe}(\text{C}_5\text{H}_4)$],¹⁰ and $4\text{-XC}_6\text{H}_4\text{CH}_2\text{N}_3$ ($\text{X} = \text{H}$, F , OMe)¹¹ were prepared following the literature procedures with minor modifications. The monomer, methyl methacrylate (MMA), was purchased from Aldrich, dried over CaH_2 under Ar for several days, distilled under reduced pressure, and stored in a Teflon valve sealed storage flask at -5°C .

^1H (500.1 MHz), $^{13}\text{C}\{^1\text{H}\}$ (124.7 MHz), ^{19}F (376.5 MHz) NMR spectra were acquired on Bruker AV-500 spectrometer equipped with a 5 mm proton/QNP probe. All NMR spectra were recorded at room temperature and referenced to protic impurities in the deuterated solvent for ^1H , solvent peaks for $^{13}\text{C}\{^1\text{H}\}$, or CFCl_3 for ^{19}F . Representative DEPT-135 experiments were performed to identify and confirm the $^{13}\text{C}\{^1\text{H}\}$ signals. All melting points were determined using Stuart SMP3 apparatus and were uncorrected. Elemental analyses were conducted by Chemistry Department, Mahidol University. Electrospray mass spectra (ESIMS) were collected on a Bruker Data Analysis Esquire-LC mass spectrometer, ESI mode.

Ligand Preparation and Characterizations

General Synthesis of RCH_2N_3 ($\text{R} = \text{C}_6\text{H}_5$, $4\text{-FC}_6\text{H}_4$, $4\text{-OMeC}_6\text{H}_4$, Fc): Synthesis of $4\text{-XC}_6\text{H}_4\text{CH}_2\text{N}_3$ ($\text{X} = \text{H}$, F , OMe). A 1:1 mixture of $\text{THF}:\text{H}_2\text{O}$ solution (40 mL) of the corresponding RCH_2Cl (15.0 mmol; except $\text{C}_6\text{H}_5\text{CH}_2\text{N}_3$, in which $\text{C}_6\text{H}_5\text{CH}_2\text{Br}$ was used) and NaN_3 (15.0 mmol) was refluxed at 70°C for 1–3 days. The resulting product was extracted with CH_2Cl_2 ($3 \times 10 \text{ mL}$), and the combined organic extracts were dried over anhydrous Na_2SO_4 . The product was then filtered and concentrated under vacuum. Unless otherwise noted, addition of diethyl ether afforded the azide products as colorless or pale yellow oils at 4°C .

$\text{C}_6\text{H}_5\text{CH}_2\text{N}_3$. Reaction time = 1 day. A colorless oil was obtained in 89% yield. $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 7.48–

7.37 (m, 5H, C_6H_5), 4.37 (s, 2H, CH_2). $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): δ 136.3, 129.6, 129.1, 129.0 (aryl carbons), 55.5 (CH_2).

$4\text{-FC}_6\text{H}_4\text{CH}_2\text{N}_3$. Reaction time = 1 day. A pale yellow oil was obtained in 91% yield (approximately or more than 95% pure based on $^1\text{H-NMR}$ spectroscopy). $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 7.25–7.21 (m, 2H, C_6H_5), 7.04–6.99 (m, 2H, C_6H_4), 4.24 (s, 2H, CH_2). $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): δ 163.5 (d, $J_{\text{CF}} = 245 \text{ Hz}$), 132.1, 130.8 (d $J_{\text{CF}} = 8 \text{ Hz}$), 116.6 (d, $J_{\text{CF}} = 22 \text{ Hz}$) (aryl carbons), 54.8 (CH_2). $^{19}\text{F-NMR}$ (376.5 MHz, CDCl_3): δ –114.

$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{N}_3$. Reaction time = 3 day. The $^1\text{H-NMR}$ spectrum of the crude reaction mixture reveals 70% of $4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{N}_3$ and 30% of the remaining alkyl chloride $4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{Cl}$. The resulting pale yellow oil was used in the next step without further purification. $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 7.25 (d $J_{\text{HH}} = 8.7 \text{ Hz}$, 2H, C_6H_4), 6.92 (d $J_{\text{HH}} = 8.7 \text{ Hz}$, 2H, C_6H_4), 4.24 (s, 2H, CH_2), 3.79 (s, 3H, OCH_3). $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): δ 160.3, 130.4, 128.1, 114.9 (aryl carbons), 55.9 (OCH_3), 55.0 (CH_2).

Synthesis of FcCH_2N_3 . The preparation procedure was modified from that reported in the literature.¹² To a 20 mL CH_2Cl_2 solution of FcCH_2OH (0.43 g, 2.0 mmol) was carefully added an ice-cold 10 mL CH_2Cl_2 solution of oxalylchloride (175 μL , 2.0 mmol) at 0°C . The reaction mixture was allowed to warm to room temperature and, after 2 h of stirring, an aqueous solution (30 mL) of NaN_3 (0.13 g, 2.0 mmol) was added. After 15 h, 20 mL of water was added and the solution was extracted with CH_2Cl_2 ($3 \times 20 \text{ mL}$). The organic extracts were then dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. FcCH_2N_3 , which appeared as an orange oil, was obtained in quantitative yield ($>95\%$) and immediately used in the next step without further purification. $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 4.27 (m, 2H, C_5H_4), 4.23 (m, 2H, C_5H_4), 4.20 (br s, 5H, C_5H_5), 4.13 (s, 2H, CH_2). $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): δ 82.9, 69.5, 69.4, 69.3 (Cp carbons), 51.6 (CH_2).

General Synthesis of *Tris*(*R*-methyltriazolylmethyl)amines [$\text{R} = \text{C}_6\text{H}_5$ (1), $4\text{-FC}_6\text{H}_4$ (2), $4\text{-MeOC}_6\text{H}_4$ (3), Fc (4)]. Compounds 1–4 were synthesized following the previously reported preparation of 1.^{8(a)} To a 1:1 mixture of $\text{CH}_2\text{Cl}_2:\text{H}_2\text{O}$ (6 mL) was added RCH_2N_3 (4.06 mmol), tripropargylamine (1.35 mmol), ascorbic acid (0.41 mmol), and 1 M aqueous solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (100 μL), respectively. The reaction mixture was stirred at room temperature for 3 days, after which 20 mL of water was added. The product was extracted using CH_2Cl_2 ($3 \times 20 \text{ mL}$) and the organic extracts were dried under vacuum to afford a brown oil. To this product was added an aqueous solution of 10% (v/v) NH_4OH (20 mL), CH_2Cl_2 (20 mL), and EDTA (0.01 mmol). The reaction mixture was stirred for 3 h upon which it was washed with deionized water ($3 \times 20 \text{ mL}$). The organic layer was then dried over anhydrous Na_2SO_4 . Vacuum evaporation afforded a crude solid product.

***Tris*(4-fluorobenzyltriazolylmethyl)amine (2).** Slow evaporation from 2-butanone at room temperature provided 2 as a colorless, crystalline solid in 90% yield (0.710 g, 1.22 mmol).

¹H-NMR (500 MHz, CDCl₃): δ 7.67(s, 3H, CH=), 7.26–7.22 (m, 6H, C₆H₄), 7.02 (t, 6H, C₆H₄), 5.46 (s, 6H, CH₂C₆H₄), 3.67 (s, 6H, NCH₂). ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ 163.0 (d, J_{CF} = 246 Hz), 144.4, 130.7, 130.0 (d, J_{CF} = 9 Hz), 123.8, 116.2 (d, J_{CF} = 22 Hz) (aryl and triazole carbons), 53.5 (CH₂), 47.1 (CH₂). ¹⁹F-NMR (376.5 MHz, CDCl₃): δ -113. ESIMS (*m/z*): calcd. 584.24 (found: 585.24). Anal. Calcd for C₃₀H₂₇F₃N₁₀: C, 61.64; H, 4.66; N, 23.96. Found: C, 61.58; H, 4.39; N, 24.21. m.p. = 122–125°C.

Tris(4-methoxybenzyltriazolylmethyl)amine (3). Washing the crude product with approximately 50 mL of diethyl ether afforded analytically pure **3** as a white solid in 89% yield (0.745 g, 1.20 mmol). ¹H-NMR (500 MHz, CDCl₃): δ 7.62 (br s, 3H, CH=), 7.20 (d, J_{HH} = 8.6 Hz, 6H, C₆H₄), 6.86 (d, J_{HH} = 8.6 Hz, 6H, C₆H₄), 5.42 (s, 6H, CH₂C₆H₄), 3.79 (s, 9H, OCH₃), 3.66 (br s, 6H, NCH₂). ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ 160.8, 145.2, 130.5, 127.7, 124.5, 115.4 (aryl and triazole carbons), 56.3 (OCH₃), 54.6 (CH₂), 48.1 (CH₂). ESIMS (*m/z*): calcd. 620.30 (found: 621.30). Anal. Calcd for C₃₃H₃₆N₁₀O₃: C, 63.86; H, 5.85; N, 22.57. Found: C, 63.52; H, 5.81; N, 22.20. m.p. = 135–139°C.

Tris(ferrocenylmethyltriazolylmethyl)amine (4). Crystallization by slow evaporation from CHCl₃ at room temperature provided **4** as a brown solid in 91% yield (1.04 g, 1.23 mmol). ¹H-NMR (500 MHz, CDCl₃): δ 7.63 (s, 3H, CH=), 5.24 (s, 6H, CH₂C₅H₄), 4.26 (t, 6H, C₅H₄), 4.17 (t, 6H, C₅H₄), 4.15 (s, 15H, C₅H₅), 3.66 (s, 6H, NCH₂). ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ 143.9, 123.3, 81.3, 69.1, 69.0 (aryl, Cp, and triazole carbons), 50.1 (CH₂), 47.3 (CH₂). ESIMS (*m/z*): calcd. 854.16 (found: 854.17). Anal. Calcd for C₄₂H₄₂Fe₃N₁₀: C, 59.04; H, 4.95; N, 16.39. Found: C, 58.98; H, 5.00; N, 16.25. m.p. = 105–108°C.

Copper-Catalyzed ATRP of Methyl Methacrylate

Bulk Polymerization. Under Ar, the tripodal ligands **1–4** (0.0930 mmol) and CuBr (0.0930 mmol) were added to a dried Schlenk flask equipped with a magnetic stir bar. In the case of varying ratios of [CuBr]:[CuBr₂], at [0.8]:[0.2] and [0.2]:[0.8], CuBr (0.0744 mmol) : CuBr₂ (0.0186 mmol) and CuBr (0.0186 mmol) : CuBr₂ (0.0744 mmol) were used. To this mixture, 2 mL of MMA was added, after which the reaction flask was tightly closed and degassed by three freeze-pump-thaw cycles. The resulting mixture was stirred for 10 min at room temperature, before heating the mixture at 90°C for 10 min. Then, EBiB (0.186 mmol) was added via a syringe to initiate the polymerization. After a given time, the reaction solution was quenched with THF and cooled to room temperature. The resulting THF solution was then passed over an alumina column to remove any remaining copper species. The filtrate was evaporated under vacuum and the remaining polymer product was subsequently washed with an excess amount of methanol and dried *in vacuo*.

Solution Polymerization. The procedure of polymerization followed that described above except that, instead of using 2 mL of neat MMA, toluene (2 mL) or 2-butanone (2 mL) was added to MMA (2 mL) and used as the polymerization solvent.

Polymer Characterizations

The yield percentage of the polymerization was determined by weighing the dried, isolated polymer products. Molecular weight and polydispersity of the polymer products were measured with a Waters e2695 gel permeation chromatograph (GPC) equipped with PLgel 10-mm mixed B 2 columns (molecular weight resolving range = 500–10,000,000). Polystyrene was used as a standard for calibration whereas THF was used as an eluent at 35°C and at a flow rate of 1.0 mL/min.

Kinetic Experiments

To obtain the kinetic data, the polymerization was carried out in bulk MMA or 50% (v/v) 2-butanone:MMA under the same reaction conditions as described in 2.3 with additional 500 μL of anisole as a reference. At timed intervals, an approximately 0.5 mL of the reaction mixture was withdrawn from the flask using a degassed syringe and its ¹H-NMR spectrum in CDCl₃ was taken to determine a percent monomer conversion. The remaining mixture was quenched in 2 mL of methanol and kept at 4°C for further characterizations.

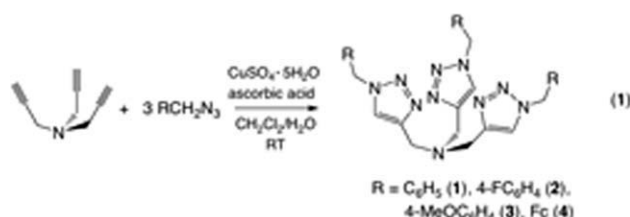
Cyclic Voltammetry

All voltammograms were recorded at ambient temperatures with Autolab PGSTAT 30 potentiostat and GPES software. CuBr₂/L (L = **1**, **4**) (1.0 mM) were dissolved in dry DMSO containing 0.1M [Et₄N][PF₆] electrolyte. Measurements were performed under Ar at a scanning rate of 0.01 V/s with a glassy carbon working electrode, a platinum counter electrode, and a Ag/Ag⁺ reference electrode. Each sample was referenced to the ferrocene internal standard and its potentials were reported versus those of Fc/Fc⁺.

RESULTS AND DISCUSSION

Synthesis and Characterization of Tripodal “Click” Ligands

A series of tripodal ligands featuring 4-*R*-1,2,3-triazole substituents were synthesized following the previously reported literature preparations for *tris*(benzyltriazolylmethyl)amine (TBTA, **1**)^{8(a)} with minor modifications. Reactions of tripropagylamine with freshly prepared RCH₂N₃ in a 1:1 mixture of CH₂Cl₂ and H₂O catalyzed by ascorbic acid and CuSO₄•5H₂O at room temperature afforded the corresponding 1,2,3-triazole products **2–4** [eq. (1)].



The ¹H-NMR spectra of **1–4** in CDCl₃ contain characteristic singlet resonances at approximately δ 7.6 corresponding to CH=C of the 1,2,3-triazole group (see Figure 1 for example). Analytically pure compounds **1–4** were obtained in high yields (i.e., more than 90%) by washing or crystallization from various solvents.

ATRP Catalytic Activity of CuBr/L (L = **1–4**)

Atom Transfer Radical Polymerizations of MMA catalyzed by CuBr/**1–4** systems were conducted under Ar at 90°C, with ethyl

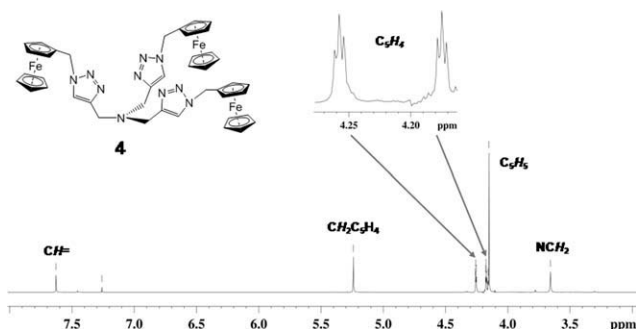


Figure 1. $^1\text{H-NMR}$ spectrum of *tris*(ferrocenylmethyltriazolylmethyl)amine (**4**) in CDCl_3 .

2-bromoisobutyrate (EBiB) as the initiator. Polymerization data of CuBr/1 and CuBr/4 revealed that both copper complexes were active ATRP catalysts (Table I). On the other hand, under the same polymerization conditions, CuBr containing tripodal ligands with a *para*-substituent at the benzyl group (**2** and **3**) exhibited no catalytic activity toward polymerization after 3 d in neat MMA. We speculate that, for ligands **2** and **3**, the heteroatoms (i.e., F and O) present in the 1,2,3-triazole moieties might involve in the coordination at the copper center and, as a result, inhibited the polymerization activity.¹³

At 0.5 mol % CuBr/1 in neat MMA, *p*MMA was isolated in 34% yield after 30 min whereas in 50% (v/v) solution of toluene:MMA and 2-butanone:MMA solvents under similar reaction conditions, the polymer product was obtained in 56% and 45% yields after 3 h, respectively. Despite good catalytic activities, CuBr/1 resulted in poorly controlled polymerizations as evidenced by broad polydispersity polymers with PDI values of 1.8–2.0 (entries 1–3). In comparison, the CuBr/4 catalyst generally required longer reaction times in neat MMA, 50% (v/v) toluene:MMA, and 50% (v/v) 2-butanone:MMA before the reaction mixtures became viscous affording *p*MMA in 95% (15 h),

56% (15 h), and 40% (18 h) yields, respectively (entries 7–9). The GPC data showed that polymers produced from the CuBr/4 catalyst exhibited lower PDI values (1.3–1.5).

It must be noted that the copper species supported by ligand **1** or **4** are not completely soluble in the solvents studied. As a result, actual concentrations of copper species in the solution cannot be easily determined. In an attempt to increase the solubility of copper species, the 50% (v/v) DMSO:MMA solvent was employed for both CuBr/1 and CuBr/4 polymerization systems affording green, homogeneous reaction mixtures. Unfortunately, despite narrower polydispersity of polymers, very slow polymerization activities (i.e., 21% and 55% of *p*MMA after 36 h for CuBr/1 and CuBr/4, respectively) and a bimodal GPC trace was resulted for the CuBr/4 catalyst (entries 4 and 10).

Effect of Ligands on ATRP

According to the Hammett substituent constant (σ), electron-donating ability of the ferrocenyl group ($-\text{Fc}$) is higher compared to the phenyl substituent ($-\text{C}_6\text{H}_5$).¹⁴ To confirm their relative basicity, cyclic voltammetry (CV) measurements of the *in situ*-generated CuBr_2 complexes of ligands **1** and **4** were carried out in DMSO to achieve homogeneity of the solution. Referenced to the internal ferrocene standard, the CV profile of $\text{CuBr}_2/1$ shown in Figure 2 exhibits a quasi-reversible Cu(I)/Cu(II) redox wave at $E_{1/2} = -0.206$ V with the cathodic-anodic peak separation (ΔE_p) of 235 mV. Note that redox potentials of $\text{CuBr}_2/1$ are similar to those of the previously reported $\text{CuCl}_2/1$ in DMSO ($E_{1/2} = -0.18$ V).¹⁵ In comparison, the $\text{CuBr}_2/4$ complex contains two redox waves: a reversible wave with $E_{1/2}$ potential of 0.0985 V, assignable to the Fe(II)/Fe(III) couples of the ferrocenyl substituents, and a quasi-reversible Cu(I)/Cu(II) redox wave at $E_{1/2} = -0.224$ V.

In general, stronger electron-donating groups on supporting ligands (i.e., more reducing complexes) often lead to more active ATRP catalysts and, often times, result in faster

Table I. ATRP of MMA with CuBr/L (L = 1, 4)

Entry	Ligand (L)	[CuBr]:[CuBr ₂]:[L]	Time (h)	% Conv. ^e	M_n (theo) ^f	M_n (GPC)	M_w/M_n
1	1 ^a	1/-/1	0.5	34	3,599	171,432	2.05
2	1 ^b	1/-/1	3	56	5,802	80,907	1.95
3	1 ^c	1/-/1	3	45	4,700	46,699	1.84
4	1 ^d	1/-/1	36	21	2,298	7,105	1.27
5	1 ^c	0.8/0.2/1	4	71	7,304	61,270	1.59
6	1 ^c	0.2/0.8/1	3	49	5,100	56,002	1.42
7	4 ^a	1/-/1	15	95	9,707	29,127	1.37
8	4 ^b	1/-/1	15	56	5,802	17,375	1.53
9	4 ^c	1/-/1	18	40	4,200	8,013	1.33
10	4 ^d	1/-/1	36	55	5,702	36,913/6,706	1.52/1.19
11	4 ^a	0.8/0.2/1	12	76	7,804	26,421	1.30
12	4 ^a	0.2/0.8/1	24	38	4,000	19,904	1.15

Polymerization conditions: 90°C, initiator = ethyl 2-bromoisobutyrate (EBiB), molar ratio of [MMA]:[EBiB]:[CuBr]:[L] = 200 : 2 : 1 : 1.

^a Neat MMA, ^b 50% (v/v) toluene:MMA, ^c 50% (v/v) 2-butanone:MMA, ^d 50% (v/v) DMSO:MMA, ^e Determined by $^1\text{H-NMR}$ spectroscopy,

^f M_n (theo) = $\frac{[(\text{Monomer})_0]/[\text{Initiator}]_0 \times \text{Conversion} \times \text{MW}_{\text{monomer}}}{\text{MW}_{\text{initiator}}}$, where $\text{MW}_{\text{monomer}}$ is the monomer molecular weight and $\text{MW}_{\text{initiator}}$ is the initiator molecular weight.

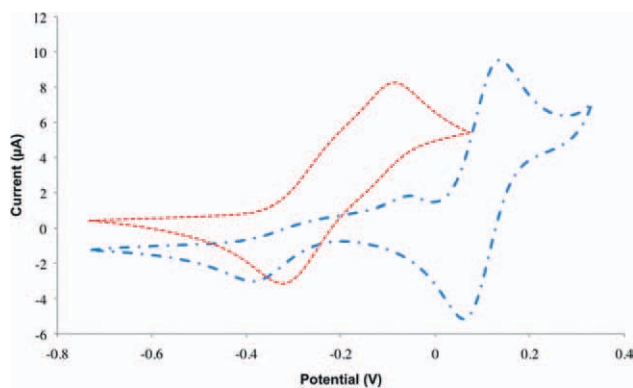


Figure 2. Cyclic voltammograms of CuBr₂/1 and CuBr₂/4 in DMSO, 0.1 mol/L [NBu₄][PF₆], scan rate = 0.01 V/s. Potentials quoted against Fc/Fc⁺. [Color figure can be viewed in the online issue, which is available at www.onlinelibrary.com.]

polymerization.^{13(a),16} For example, CuBr/Me₆TREN catalyzed the ATRP of methyl acrylate at a much faster rate than CuBr/TREN affording polymers with narrower polydispersity.^{16(b)} In fact, a linear correlation between observed polymerization rates and measured $E_{1/2}$ values has previously been reported for copper complexes of various supporting ligands including Me₆TREN.¹⁷ However, for our catalytic system, even though the CV data from Table II suggested that CuBr/4 was more reducing than CuBr/1, kinetic studies (vide infra) revealed that ATRP catalyzed by CuBr/4 was significantly slower than those with CuBr/1 under various polymerization conditions. It is possible that the steric hindrance imposed by bulky ferrocenyl substituents may reduce the accessibility of the copper ions and consequently impede the efficiency of the halide exchange process resulting in slow polymerizations. Furthermore, since the overall rate of polymerization is governed by the relative concentration of [CuBr/L]:[CuBr₂/L] in solution,¹⁸ the solubility of Cu(I) and Cu(II) species supported by 1 and 4 may also be responsible for differences in the observed rates.

Effect of Added CuBr₂

Broad polydispersities resulted from CuBr/L (L = 1, 4) under reaction conditions studied thus far (entries 1–4 and 7–10; Table I) may be attributed to the persistent radical effect¹⁹ which involves high concentration of active radicals (R•) at the initial stage of polymerization. This phenomenon leads to an irreversible radical termination before the system reaches equilibrium resulting in poorly controlled polymerization and limited monomer conversion. In an attempt to improve the M_w/M_n values and increase the polymer yields, different amounts of CuBr₂

Table II. CV Data for CuBr₂/L (L = 1, 4) in DMSO^a

Complex	$E_{p, a}$ [V]	$E_{p, c}$ [V]	ΔE_p [mV]	$E_{1/2}$ [V] ^b
CuBr ₂ /1	-0.0885	-0.324	235	-0.206
CuBr ₂ /4	-0.0625	-0.386	324	-0.224
CuBr ₂ /4	0.129	0.0685	60	0.0985

^a 0.1M [NBu₄][PF₆], 1.0 mM CuBr₂/L complex, scan rate 0.01 V/s; potentials reported versus Fc/Fc⁺; $E_{p, a}$ and $E_{p, c}$ are the peak potentials of the oxidation and reduction waves, respectively, ^b $E_{1/2} = (E_{p, a} + E_{p, c})/2$.

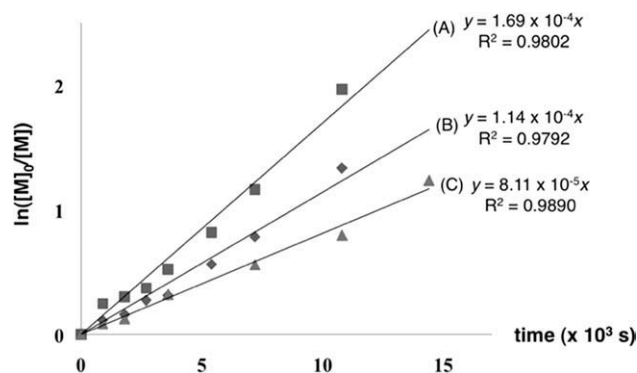


Figure 3. Kinetic plots for polymerizations of MMA by CuBr/1. General polymerization conditions: molar ratio of [MMA]:[EBiB]:[L] = 200:2:1, 90°C, initiator = ethyl 2-bromoisobutyrate (EBiB) in 2-butanone: (A) [CuBr]:[CuBr₂] = [1.0]:[0] ($k_{obs} = 1.69 \times 10^{-4} \text{ s}^{-1}$), (B) [CuBr]:[CuBr₂] = [0.8]:[0.2] ($k_{obs} = 1.14 \times 10^{-4} \text{ s}^{-1}$), (C) [CuBr]:[CuBr₂] = [0.2]:[0.8] ($k_{obs} = 8.11 \times 10^{-5} \text{ s}^{-1}$).

were added into the reaction to reduce the concentration of active radicals at the beginning of the reaction and speed up the rate of deactivation (Scheme 1).²⁰

$$\frac{M_w}{M_n} = 1 + \left[\frac{k_p[\text{RX}]}{k_{\text{deact}}[\text{Cu}^{\text{II}}\text{X}]} \right] \left[\frac{2}{q} \cdot 1 \right] \quad (2)$$

where [RX] is the initiator concentration, [Cu^{II}X] is the Cu(II) concentration, k_p and k_{deact} are the rate constants of propagation and deactivation, respectively, and q is the monomer conversion.

To investigate the effect of added Cu(II) species, polymerization experiments were performed in 50% (v/v) 2-butanone:MMA solution for CuBr/1 and in neat MMA for CuBr/4, with [0.8]:[0.2] and [0.2]:[0.8] ratios of [CuBr]:[CuBr₂] (entries 5, 6 and 11, 12). We have found that narrower polydispersity polymers were obtained as the amount of CuBr₂ increased. For example, compared to the polymerizations without added CuBr₂, when the ratio of [CuBr]:[CuBr₂] was [0.2]:[0.8], the PDI values of the resulting polymers reduced from 1.84 to 1.49

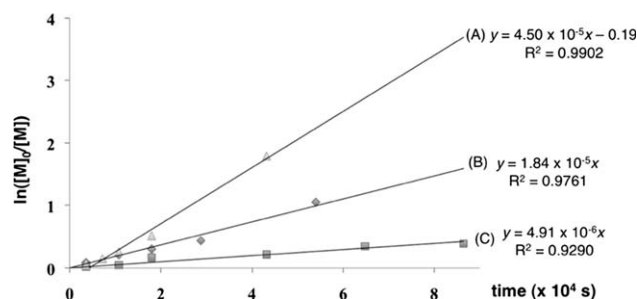


Figure 4. Kinetic plots for polymerizations of MMA by CuBr/4. General polymerization conditions: molar ratio of [MMA]:[EBiB]:[L] = 200:2:1, 90°C, initiator = ethyl 2-bromoisobutyrate (EBiB) in neat MMA: (A) [CuBr]:[CuBr₂] = [1.0]:[0] ($k_{obs} = 4.50 \times 10^{-5} \text{ s}^{-1}$), (B) [CuBr]:[CuBr₂] = [0.8]:[0.2] ($k_{obs} = 1.84 \times 10^{-5} \text{ s}^{-1}$), (C) [CuBr]:[CuBr₂] = [0.2]:[0.8] ($k_{obs} = 4.91 \times 10^{-6} \text{ s}^{-1}$).

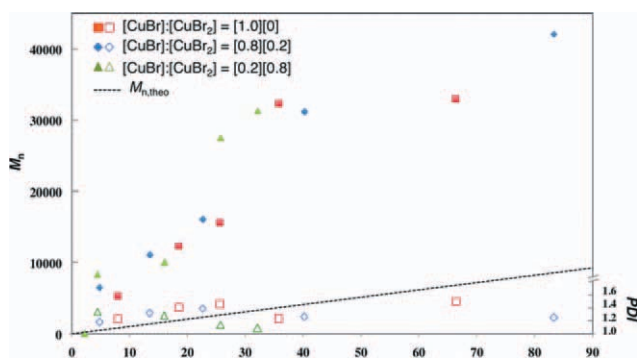


Figure 5. Variation of *p*MMA molecular weight (M_n) and polydispersity (M_w/M_n) on MMA conversion at three different ratios of [CuBr]:[CuBr₂]. For the polymerization conditions, see Figure 4. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

for CuBr/1 (entries 3 and 6) and from 1.33 to 1.15 for CuBr/4 (entries 7 and 12).

Kinetic studies were carried out to evaluate the efficiency of tripodal click compounds **1** and **4** as ligands for ATRP. The kinetic plots in Figures 3 and 4 show a linear relationship between $\ln([M]_0/[M]_t)$ versus reaction time for both catalysts CuBr/1 and CuBr/4 with three different ratios of [CuBr]:[CuBr₂] (entries 3, 5, 6 and 7, 11, 12). The linear first-order kinetic plots indicate a constant concentration of active propagating species, despite the heterogeneous nature of the polymerization system. In addition, as expected, an increased amount of CuBr₂ generally leads to a decrease in the observed rate constants (k_{obs}).

The relations of polymer masses ($M_{n, GPC}$) and polydispersity (M_w/M_n) values to monomer conversion for the CuBr/4 catalyst at three different [CuBr]:[CuBr₂] ratios are shown in Figure 5. In general, experimental M_n values ($M_{n, GPC}$) increase linearly with monomer conversion while the PDI values slightly decrease as the polymerization progressed. However, the polymer molecular weights are significantly higher than the theoretical values ($M_{n, theo}$), indicating low initiation efficiencies, which may be attributed to inefficient deactivator species (CuBr₂/L) or initiator (EBiB) employed in our polymerization systems. Despite a difference between the theoretical and the measured polymer masses, monomer conversions of >60% were achieved with [1.0]:[0] and [0.8]:[0.2] ratios of [CuBr]:[CuBr₂]. On the other hand, when the [CuBr]:[CuBr₂] ratio was [0.2]:[0.8], only 38% monomer conversion was obtained after 24 h.

CONCLUSIONS

A series of *tris*(*R*-methyltriazolylmethyl)amines [R = C₆H₅ (**1**), 4-FC₆H₄ (**2**), 4-MeOC₆H₄ (**3**), Fc (**4**)] were successfully prepared and, for the first time, employed as catalyst supports for ATRP of MMA. On the basis of the observed rates constants, polymerization activities were better with CuBr/1 compared to CuBr/4 whereas CuBr/2 and CuBr/3 catalysts exhibited insignificant ATRP catalytic activity. However, broad polydispersities were obtained in the presence of CuBr/1 (PDI = 1.3–2.0) compared to CuBr/4 (PDI = 1.2–1.5). Apparently, the substituents at the 1,2,3-triazole rings exert a dramatic effect both on the ac-

tivity of copper catalysts and the well-controlled nature of polymerization. Because of the heterogeneity nature of the polymerization systems presented in this study, it is difficult to quantify the effect of added CuBr₂. However, we observed that lower initial ratio of [CuBr]:[CuBr₂] (i.e., increased amount of CuBr₂) used generally led to narrower polymer polydispersities with reduced overall polymerization rates.

It should be emphasized that solvent polarity also played an important role in terms of solubilizing copper species. For the CuBr/1 catalyst, ATRP of MMA in 2-butanone resulted in lower PDI values while, with the CuBr/4 catalyst, narrower polydispersities of *p*MMA were obtained from polar solvents such as MMA and 2-butanone. Interestingly, for both CuBr/1 and CuBr/4, the polar DMSO solvent afforded very low polymerization activity and, for CuBr/4, *p*MMA with bimodal GPC traces. Given this substantial solvent effect for these copper catalysts, it is of interest to further explore the type of solvents, with regard to their ability to solubilize Cu(I) and Cu(II) species, that will eventually lead to more active catalysts and better controlled radical polymerization. In addition, to improve solubility of copper species in the polymerization media, further investigations of this catalytic system which include changing the R group of *tris*(*R*-methyltriazolylmethyl)amines to more non-polar organic substituents such as long alkyl chains are currently being explored.

ACKNOWLEDGMENTS

The authors acknowledge the Thailand Research Fund and Commission on Higher Education for financial support under Grant No. MRG5180070. This work was also supported in part by funding from the Center of Excellence for Innovation in Chemistry (PERCH-CIC), Faculty of Science, Mahidol University, and the Office of Higher Education Commission and Mahidol University under the National Research Universities Initiative. In addition, we are grateful to Dr. Waret Veerasai for helpful suggestions regarding cyclic voltammetry.

REFERENCES

- Wang, J.S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614.
- Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 1721.
- (a) Pintauer, T.; Matyjaszewski, K. *Coord. Chem. Rev.* **2005**, *249*, 1155; (b) Tang, H.; Arulsamy, N.; Radosz, M.; Shen, Y.; Tsarevsky, N.V.; Braunecker, W.A.; Tang, W.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2006**, *128*, 16277; (c) Tsarevsky, N.V.; Matyjaszewski, K. *Chem. Rev.* **2007**, *107*, 2270; (d) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921; (e) Cao, J.; Chen, J.; Zhang, K.; Shen, Q.; Zhang, Y. *Appl. Catal. A* **2006**, *311*, 76; (f) Becer, C.R.; Hooogenboom, R.; Fournier, D.; Schubert, U.S. *Macromol. Rapid Commun.* **2007**, *28*, 1161.
- Tang, W.; Kwak, Y.; Braunecker, W.A.; Tsarevsky, N.V.; Coote, M.L.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2008**, *130*, 10702.
- Yamamura, Y.; Matyjaszewski, K. *J. Polym. Sci. A Polym. Chem.* **2008**, *46*, 2015.

6. Sunsin, A.; Wisutsri, N.; Suriyarak, S.; Teanchai, R.; Jindabot, S.; Chaicharoenwimolkul, L.; Somsook, E. *J. Appl. Polym. Sci.* **2009**, *113*, 3766.
7. (a) Rostovtsev, V.V.; Green, L.G.; Fokin, V.V.; Sharpless, K.B. *Angew Chem. Int. Ed.* **2002**, *41*, 2596; (b) Meldal, M.; Tornøe, C.W. *Chem. Rev.* **2008**, *108*, 2952.
8. (a) Chan, T.R.; Hilgraf, R.; Sharpless, K.B.; Fokin, V.V. *Org. Lett.* **2004**, *6*, 2853; (b) Özçubukçu, S.; Ozkal, E.; Jimeno, C.; Pericas, M.A. *Org Lett* **2009**, *11*, 4680; (c) Liu, D.; Gao, W.; Dai, Q.; Zhang, X. *Org Lett* **2005**, *7*, 4907; (d) Detz, R.J.; Heras, S.A.; de Gelder, R.; van Leeuwen, P.W.N.M.; Hiemstra, H.; Reek, J.N.H.; van Maarseveen, J.H. *Org Lett* **2006**, *8*, 3227; (e) Kelly, J.K.; Paul, U.S.D.; Lee, A.L.; Crowley, J.D. *Chem. Commun.* **2011**, *47*, 328.
9. Duan, H.; Sengupta, S.; Petersen, J.L.; Akhmedov, N.G.; Shi, X. *J. Am. Chem. Soc.* **2009**, *131*, 12100.
10. Germaneau, R.; Chavignon, R.; Tranchier, J.-P.; Rose-Munch, F.; Rose, E.; Collot, M.; Duhayon, C. *Organometallics* **2007**, *26*, 6139.
11. Campbell-Verduyn, L.; Elsinga, P.H.; Mirfeizi, L.; Dierckx, R.A.; Feringa, B.L. *Org. Biomol. Chem.* **2008**, *6*, 3461.
12. Bellouard, F.; Chuburu, F.; Yaouanc, J.-J.; Handel, H.; Mest, Y.L. *N.J. Chem.* **1999**, *23*, 1133.
13. (a) Clark, A.J.; Battle, G.M.; Heming, A.M.; Haddleton, D.M.; Bridge, A. *Tetrahedron Lett.* **2001**, *42*, 2003; (b) Tang, C.; Kowalewski, T.; Matyjaszewski, K. *Macromolecules* **2003**, *36*, 1465.
14. (a) Nesmeyanov, A.N.; Perevalova, E.G.; Gubin, S.P.; Grandberg, K.I.; Kozlovsky, A.G. *Tetrahedron Lett.* **1966**, *22*, 2381; (b) McDaniel, D.H.; Brown, H.C. *J. Org. Chem.* **1958**, *23*, 420.
15. Donnelly, P.S.; Zanatta, S.D.; Zammit, S.C.; White, J.M.; Williams, S.J. *Chem. Commun.* **2008**, 2459.
16. (a) Xia, J.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 7697; (b) Xia, J.; Gaynor, S.G.; Matyjaszewski, K. *Macromolecules* **1998**, *31*, 5958.
17. Qiu, J.; Matyjaszewski, K.; Thouin, L.; Amatore, C. *Macromol. Chem. Phys.* **2000**, *201*, 1625.
18. Min, K.; Jakubowski, W.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2006**, *27*, 594.
19. (a) Fischer, H. *J. Polym. Sci. A Polym. Chem.* **1999**, *37*, 1885; (b) Ohno, K.; Tsujii, Y.; Miyamoto, T.; Fukuda, T.; Goto, M.; Kobayashi, K.; Akaike, T. *Macromolecules* **1998**, *31*, 1064; (c) Tang, W.; Tsarevsky, N.V.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2006**, *128*, 1598.
20. (a) Matyjaszewski, K.; Wei, M.; Xia, J.; Gaynor, S.G. *Macromol. Chem. Phys.* **1998**, *199*, 2289; (b) Zhang, H.; Klumperman, B.; Ming, W.; Fischer, H.; van der Linde, R. *Macromolecules* **2001**, *34*, 6169.