รายงานวิจัยฉบับสมบูรณ์

โครงการ การสังเคราะห์ วิเคราะห์ และศึกษาคุณสมบัติการเร่งปฏิกิริยาของสารประกอบเชิงซ้อนคอปเปอร์ที่มีอนุพันธ์ 1,2,3-triazole เป็นส่วนประกอบของลิแกนด์

Synthesis, Characterization, and Catalytic Study of Copper Complexes Featuring 1,2,3-triazole Ligands

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สัญญาเลขที่ MRG5180070

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สนับสนุนโดยสำนักงานคณะกรรมการการอุดมศึกษา และสำนักงานกองทุนสนับสนุนการวิจัย

(ความเห็นในรายงานนี้เป็นของผู้วิจัย สกอ. และ สกว. ไม่จำเป็นต้องเห็นด้วยเสมอไป

หน้าสรุปโครงการ (Executive Summary)

1. ความสำคัญและที่มาของปัญหา

Multidentate ligands with a rigid geometry have been found to support transition metal complexes that mediate interesting chemical transformations such as alkane dehydrogenation, C-H bond activation, and polymerization. Such observations have generated considerable interests in the development and exploration of metal complexes containing novel, easy-to-synthesize ligands, which exhibit exceptional catalytic activities. Chelating ligands featuring “click” or 1,2,3-triazole substituents are of particular interest due to their ease of preparation and chemically robust property. Despite the well-established chemistry of click compounds, examples of transition metal complex supported by such ligand derivatives remained limited. Thus, we aimed at the synthesis of copper complexes featuring a neutral, tetradentate ligand of the type *tris*(alkyl-1,2,3-triazolylmethyl)amine and investigating their catalytic acitivities towards Atom Transfer Radical Polymerization (ATRP).

2. วัตถุประสงค์

To prepare a series of tetradentate *tris*(alkyl-1,2,3-triazolylmethyl)amine ligands and investigate their ability as catalyst supports in copper-catalyzed ATRP of methylmethacrylate (MMA).

3. ระเบียบวิธีวิจัย

This two-year project consisted of four phases:

(1) Preparation and characterizations of a series of *tris*(alkyl1,2,3-triazolylmethyl)amine compounds were prepared and characterized.

(2) Copper(I) complexes supported by *tris*(alkyl1,2,3-triazolylmethyl)amine derivatives were generated and their catalytic activities towards Atom Transfer Radical Polymerization (ATRP) of methylmethacrylate (MMA) were investigated.

(3) Kinetic studies of these copper complexes were determined. The electronic effect of different substituents on 1,2,3-triazole groups on the rate of ATRP were assessed.

(4) Optimal polymerization conditions were explored in order to produce polymethylmethacrylate (*p*MMA) with narrow polydispersities (low PDI).

4. แผนการดำเนินงานวิจัยตลอดโครงการ (2 ปี)

กิจกรรม	ปีที่ 1				ปีที่ 2			
	เดือน 1-3	เดือน 4-6	เดือน 7-9	เดือน 10-12	เดือน 13-15	เดือน 16-18	เดือน 19-21	เดือน 22-25
1. Preparation and Characterizations of *tris*(alkyl1,2,3-triazolylmethyl)amine ("click") compounds								
2. Investigation of catalytic ATRP activities of CuBr supported by click ligands								
3. Kinetic studies of copper catalysts								
4. Finding optimal polymerization conditions for new catalysts obtained								

5. ผลงาน/หัวข้อเรื่องที่คาดว่าจะตีพิมพ์

ปีที่ 2: ชื่อเรื่องที่คาดว่าจะตีพิมพ์ : Tripodal "Click" Ligands for Copper-Catalyzed ATRP

ชื่อวารสารที่คาดว่าจะตีพิมพ์ : Applied Catalysis A: General กำลังอยู่ในขั้นเตรียม manuscript

บทคัดย่อ

รหัสโครงการ: MRG5180070

ชื่อโครงการ: การสังเคราะห์ วิเคราะห์ และศึกษาคุณสมบัติการเร่งปฏิกิริยาของสารประกอบเชิงซ้อนคอปเปอร์ที่มีอนุพันธ์ของ 1,2,3-triazole เป็นส่วนประกอบของลิแกนด์

ชื่อนักวิจัย: ปรียานุช แสงไตรรัตน์นุกูล เพิ่มพูน ใหม่โสภา อัฉริยา สวนสิน และ วิชัย ริ้วตระกูล

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คลิ๊กลิแกนด์ประเภท *tris*(R-methyltriazolylmethyl)amines [R = C_6H_5 (**1**), $SiMe_3$ (**2**), 4-FC_6H_4 (**3**), 4-$MeOC_6H_4$ (**4**), Fc (**5**)] ได้ถูกสังเคราะห์และนำมาใช้เป็นตัวยึดคอปเปอร์ เพื่อศึกษาการเร่งปฏิกิริยา ATRP ของเมทิลเมทาคริเลท (methylmethacrylate; MMA) โมโนเมอร์ ผลการทดลองพบว่าที่อุณหภูมิ 90 องศาเซลเซียส ตัวเร่งปฏิกิริยา CuBr/**1** และ CuBr/**2** สามารถเร่งปฏิกิริยา ATRP ของ MMA ได้ดีทั้งในสารละลาย MMA และ 50% โดยปริมาตรของ โทลูอีน:MMA ในขณะที่สารประกอบ CuBr/**5** สามารถเร่งปฏิกิริยา ATRP ได้ปานกลางในสภาวะเร่งปฏิกิริยาเดียวกัน การศึกษาทางจลน์ศาสตร์ แสดงให้เห็นว่าตัวเร่งปฏิกิริยา CuBr/**1** และ CuBr/**5** ให้พล็อตเส้นตรงสำหรับกราฟระหว่าง $\ln[M]_o/[M]_t$ กับ เวลา โดยมีความชันของกราฟ (k_{obs}) เท่ากับ 5.0 x 10^{-3} นาที$^{-1}$, 2.7 x 10^{-4} นาที$^{-1}$ ตามลำดับ ผลการทดลองยังแสดงให้เห็นว่าประสิทธิภาพในการเร่งปฏิกิริยา ATRP ของสารประกอบเชิงซ้อน CuBr/**L** จากมากไปน้อย คือ **2** > **1** > **5** นอกจากนี้ยังพบว่าสภาวะการเร่งปฏิกิริยาในสารละลายมีขั้วอย่างเช่น 2-butanone หรือการเติม 40% ของ $CuBr_2$ เมื่อเทียบกับ CuBr เพิ่มเข้าไปในระบบ ทำให้พอลิเมอร์ที่ได้มีค่า PDI (M_w/M_n) ที่ต่ำลง

คำหลัก: คลิ๊ก, ATRP, การเร่งปฏิกิริยา

Abstract

Project Code: MRG5180070

Project Title:

Investigator: Preeyanuch Sangtrirutnugul, Purmpoon Maisopa, Atchariya Sunsin, and Vichai Reutrakul

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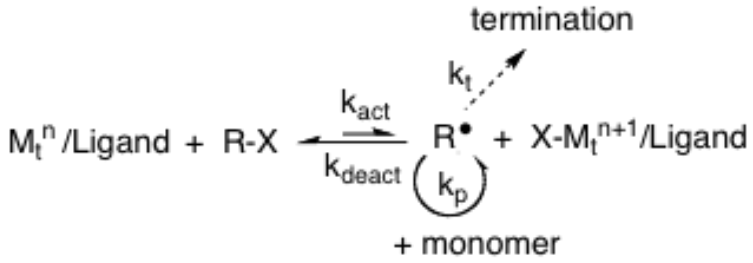
Project Period: 16 May 2008 – 15 June 2010 (2 ปี)

A series of *tris*(R-methyltriazolylmethyl)amines [R = C_6H_5 (**1**), $SiMe_3$ (**2**), 4-FC_6H_4 (**3**), 4-$MeOC_6H_4$ (**4**), Fc (**5**)] were successfully prepared and employed as ligand supports for catalytic ATRP of MMA. At 90 ^{o}C, CuBr/**1** and CuBr/**2** exhibited good catalytic activities both in bulk and solution polymerizations while CuBr/**5** showed a moderate activity. Kinetic studies of CuBr/**1** and CuBr/**5** catalysts revealed a pseudo first-order linear plot of $\ln[M]_o/[M]_t$ versus time with k_{obs} = 5.0 x 10^{-3} min^{-1}, 2.7 x 10^{-4} min^{-1}, respectively. Polymerizations of methylmethacrylate (MMA) showed that, under the same reaction conditions, the catalyst activities followed the trend: **2** > **1** > **5**. Additionally, polymerization conditions in polar solvent 2-butanone or with additional 40% $CuBr_2$ with respect to CuBr led to polymers with narrower polymer polydispersities.

Keywords: click, ATRP, catalysis

เนื้อหางานวิจัย

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



Scheme 1. The mechanism of transition metal-catalyzed ATRP

Previous studies have shown that a mixture of CuBr and neutral, tetradentate ligands such as *tris*[2-(dimethyl)aminoethyl]amine (Me_6TREN) or 1,4,8,11-tetraaza-tetramethylcyclotetradecane (Me_4CYCLAM) is an effective ATRP catalyst, affording high polymerization activity with narrow polydispersity polymers.[4] Other related nitrogen-based, tetradentate ligands include imidazole[5] and redox-active ferrocene-containing imine functional groups[6] were also investigated as supports in copper-catalyzed ATRP.

The Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) is known to yield the formation of 4-R-1,2,3-triazole (“click”) derivatives.[7] Despite the well-established chemistry of click reactions, examples of click-containing ligands involved in catalysis remain relatively limited.[8,9] In addition, 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 tetradentate *tris*(alkyltriazolylmethyl)amine ligands and investigate their ability as catalyst supports in copper-catalyzed ATRP of methyl methacrylate (MMA).

Objectives

To prepare a series of tetradentate *tris*(alkyl1,2,3-triazolylmethyl)amine ligands and investigate their ability as catalyst supports in copper-catalyzed ATRP of methylmethacrylate (MMA).

Experimental

1. Instruments and Reagents

Manipulations involving air-sensitive reactions were performed using standard Schlenk techniques under an argon atmosphere or in a Braun drybox. Diethyl ether, THF, $CHCl_3$ (Lab Scan), and toluene (Fisher Scientific) for air-free reactions were dried with appropriate drying reagents and distilled under N_2 before use. Hexane is commercial grade and distilled prior to use. De-ionized (DI) water was obtained from Nanopure® Analytical Deionization Water with an electric resistance ≥18.2 MΩ-cm. $CDCl_3$ were purchased from Cambridge Isotopes, stored in 4 Å molecular sieves, and used without further purification.

CuBr (Aldrich), Ascorbic acid (Riedel-de Haën), ferrocene carboxaldehyde, benzyl bromide, oxalyl chloride (Fluka) were used as received. RCH_2Cl (R = 4-FC_6H_4, 4-MeC_6H_4, 4-$OMeC_6H_4$, $SiMe_3$), NaN_3, tripropargyl amine were purchased from Aldrich and used without further purification. The reagents $FcCH_2OH$ [Fc = $(C_5H_5)Fe(C_5H_4)$],[10] 4-$XC_6H_4CH_2N_3$ (X = H, F, OMe),[11] and $Me_3SiCH_2N_3$[12] were prepared following the literature procedures with slight modifications.

^1H (500.1 MHz), $^{13}C\{^1H\}$ (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 while $^{29}Si\{^1H\}$ (99 MHz) NMR spectrum was obtained from the same AV-500 spectrometer featuring a 5 mm proton/broad band probe. Unless otherwise noted, NMR spectra were recorded at room temperature and were referenced to protic impurities in the deuterated solvent for ^1H, solvent peaks for $^{13}C\{^1H\}$, $CFCl_3$ for ^{19}F, or $SiMe_4$ for $^{29}Si\{^1H\}$. Representative DEPT-135 experiments were performed to identify and confirm the $^{13}C\{^1H\}$ signals. All melting points were determined using Staurt SMP3 apparatus and were uncorrected. Elemental analyses were conducted by Chemistry Department, Mahidol University. Electrospray mass spectra (ESMS) were collected on a Bruker Data Analysis Esquire-LC mass spectrometer, ESI mode.

2. Ligands Preparation and Characterizations

2.1 General synthesis of RCH_2N_3 (R = C_6H_5, 4-FC_6H_4, 4-$OMeC_6H_4$, Fc, $SiMe_3$). **Synthesis of 4-$XC_6H_4CH_2N_3$ (X = H, F, OMe).** The 1:1 mixture of THF:H_2O solution (40 mL) of the corresponding RCH_2Cl (15.0 mmol; except $C_6H_5CH_2N_3$, where $C_6H_5CH_2Br$ was used) and NaN_3 (15.0 mmol) was refluxed at 70 °C for 1 – 3 d. The resulting product was extracted with CH_2Cl_2 (3 x 10 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.

$C_6H_5CH_2N_3$. Reaction time = 1 d. A colorless oil was obtained in 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48–7.37 (*m*, 5H, C_6H_5), 4.37 (*s*, 2H, CH_2). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 136.3, 129.6, 129.1, 129.0 (aryl carbons), 55.5 (CH_2).

4-$FC_6H_4CH_2N_3$. Reaction time = 1 d. A pale yellow oil was obtained in 91% yield (approximately or more than 95% pure). ^{1}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). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 163.5 (d, J_{CF} = 245 Hz), 132.1, 130.8 (d, J_{CF} = 8 Hz), 116.6 (d, J_{CF} = 22 Hz) (aryl carbons), 54.8 (CH_2). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ –114.

4-$MeOC_6H_4CH_2N_3$. Reaction time = 3 d. The ^{1}H NMR spectrum of the crude reaction mixture revealed 70% of 4-$MeOC_6H_4CH_2N_3$ and 30% of the remaining alkyl chloride 4-$MeOC_6H_4CH_2Cl$. The resulting pale yellow oil was used in the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (*d*, J_{HH} = 8.7 Hz, 2H, C_6H_4), 6.92 (*d*, J_{HH} = 8.7 Hz, 2H, C_6H_4), 4.24 (*s*, 2H, CH_2), 3.79 (*s*, 3H, OCH_3). $^{13}C\{^1H\}$ 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 $Me_3SiCH_2N_3$.[12] Reaction time = 12 h. A colorless oil was obtained from distillation under vacuum in 78% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.74 (*s*, 2H, CH_2), 0.10 (*s*, 9H, CH_3).

Synthesis of $FcCH_2N_3$. The preparation procedure was modified from that reported in the literature.[13] 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 x 20 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 based on ^{1}H NMR spectroscopy and was immediately used in the next step without further purification. ^{1}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}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 82.9, 69.5, 69.4, 69.3 (Cp carbons), 51.6 (CH_2).

2.2 General Synthesis of *tris*(R-methyltriazolylmethyl)amines [R = C_6H_5 (**1**), $SiMe_3$ (**2**), 4-FC_6H_4 (**3**), 4-$MeOC_6H_4$ (**4**), Fc (**5**)]. Compounds **1** – **5** were synthesized following the previously reported preparations of **1**.[8a] To a 1:1 mixture of CH_2Cl_2:H_2O (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 $CuSO_4$•$5H_2O$ (100 μL), respectively. The reaction mixture was stirred at room temperature for 2 – 5 d, after which 20 mL of water was added. The product was extracted using CH_2Cl_2 (3 x 20 mL) and the organic extracts were dried over anhydrous Na_2SO_4. Vacuum evaporation afforded a crude solid product.

***Tris*(trimethylsilylmethyltriazolylmethyl)amine (2).** Reaction time = 2 d. Crystallization from diethyl ether and *n*-pentane provided **2** as an off-white solid in 39% yield (0.264 g, 0.409 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.9 (*br s*, 3H, C*H*=), 3.93 (*br s*, 6H, NCH_2), 3.72 (*s*, 6H, CH_2Si), 0.16 (*s*, 9H, CH_3). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 143.5, 124.4 (triazole carbons), 46.9 (CH_2), 41.8 (CH_2), −2.6 (CH_3). ^{29}Si{^{1}H} NMR (99 MHz, $CDCl_3$): δ 2.34. ESIMS (*m/z*): calcd. 518.29 (found: 519.30). Anal. Calcd for $C_{21}H_{42}N_{10}Si_3$: C, 48.61; H, 8.16; N, 26.99. Found: C, 48.27; H, 8.10; N, 27.12. m.p. = 117 − 118 °C.

***Tris*(4-fluorobenzyltriazolylmethyl)amine (3).** Reaction time = 4 d, Crystallization from $CHCl_3$ and diethyl ether at *ca.* 4 °C provided **3** as a light brown solid in 91% yield (0.719 g, 1.23 mmol). ^{1}H NMR (500 MHz, $CDCl_3$, 253 K): δ 7.74 (*br s*, 3H, C*H*=), 7.24 (*br s*, 6H, C_6H_4), 7.03–7.00 (*br s*, 6H, C_6H_4), 5.45 (*br s*, 6H, $CH_2C_6H_4$), 3.68 (*br s*, 6H, NCH_2). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 253 K): δ 163.4 (*d*, J_{CF} = 246 Hz), 144.4, 131.2, 130.8 (*d*, J_{CF} = 6 Hz), 125.0, 116.9 (*d*, J_{CF} = 22 Hz) (aryl and triazole carbons), 54.2 (CH_2), 47.1 (CH_2). ^{19}F NMR (376.5 MHz, $CDCl_3$,): δ –113. ESIMS (*m/z*): calcd. 584.24 (found: 585.24). Anal. Calcd for $C_{30}H_{27}F_3N_{10}$: 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 (4).** Reaction time = 3.5 d, Washing the crude product with approximately 50 mL of diethyl ether afforded analytically pure **4** as a white solid in 89% yield (0.745 g, 1.20

mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (*br s*, 3H, C*H*=), 7.20 (*d*, J_{HH} = 8.6 Hz, 6H, C_6H_4), 6.86 (*d*, J_{HH} = 8.6 Hz, 6H, C_6H_4), 5.42 (*s*, 6H, $CH_2C_6H_4$), 3.79 (*s*, 9H, OCH_3), 3.66 (*br s*, 6H, NCH_2). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 160.8, 145.2, 130.5, 127.7, 124.5, 115.4 (aryl and triazole carbons), 56.3 (OCH_3) , 54.6 (CH_2), 48.1 (CH_2). ESIMS (*m/z*): calcd. 620.30 (found: 621.30). Anal. Calcd for $C_{33}H_{36}N_{10}O_3$: C, 63.86; H, 5.85; N, 22.57. Found: C, 63.52; H, 5.81; N, 22.20. m.p. = 135 – 139 ^{o}C.

***Tris*(ferrocenylmethyltriazolylmethyl)amine (5).** Reaction time = 5 d, Crystallization from $CHCl_3$ and diethyl ether at *ca.* 4 ^{o}C provided **5** as a yellow solid in 90% yield (1.04 g, 1.22 mmol). ^{1}H NMR (500 MHz, $CDCl_3$, 253 K): δ 7.66 (*br s*, 3H, C*H*=), 5.26 (*br s*, 6H, $CH_2C_5H_4$), 4.28 (*br s*, 6H, C_5H_4), 4.17 (*br s*, 21H, C_5H_4 and C_5H_5), 3.60 (*br s*, 6H, NCH_2). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$, 253 K): δ 144.1, 124.2, 81.4, 70.0, 69.9, 69.7 (aryl, Cp, and triazole carbons), 50.8 (CH_2), 47.4 (CH_2). ESIMS (*m/z*): calcd. 854.16 (found: 854.17). Anal. Calcd for $C_{42}H_{42}Fe_3N_{10}$: C, 59.04; H, 4.95; N, 16.39. Found: C, 58.98; H, 5.00; N, 16.25. m.p. = 105 – 108 ^{o}C.

3. Copper-Catalyzed ATRP of Methylmethacrylate (MMA)

Bulk Polymerization. Under Ar, the tripodal ligands **1** – **5** (0.930 mmol) and CuBr (0.930 mmol) were added to a dried Schlenk flask equipped with a magnetic stir bar. 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 – 15 min at room temperature, before preheating the mixture at 90 ^{o}C for 10 min. Then, EtBrIB (1.86 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, a toluene (2 mL) or a 2-butanone (2 mL) solution of MMA (0.930 mmol) was added.

Addition of 40% $CuBr_2$. In solution polymerization (toluene or 2-butanone solvent), an additional 40% $CuBr_2$ (0.372 mmol) was added.

4. 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-μm 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 ^{o}C and at a flow rate of 1.0 mL/min.

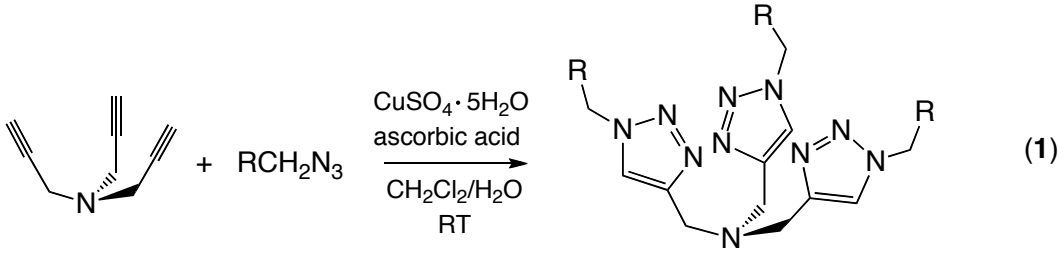
5. Kinetic Experiments

To obtain the kinetic data, the polymerization was carried out in 50% v/v toluene:MMA under the same reaction conditions as described in 2.3 (Solution). After each desired interval, an approximately 0.5 mL of the reaction mixture was collected and its ^{1}H NMR spectrum in $CDCl_3$ was taken to determine a percentage yield.

Results and Discussion

1. Synthesis and Characterization of Tripodal "Click" Ligands

A series of tetradentate ligands featuring 4-*R*-1,2,3-triazole substituents were synthesized following the previously reported literature preparations for *tris*(benzyltriazolylmethyl)amine (TBTA, **1**)[8a] with minor modifications. Reactions of tripropagylamine with freshly prepared RCH_2N_3 in a 1:1 mixture of CH_2Cl_2 and H_2O catalyzed by sodium ascorbate and $CuSO_4{\cdot}5H_2O$ at room temperature afforded the corresponding 1,2,3-triazole products **2** – **5**. (eq 1) Compounds **1** – **5** were purified by crystallizations from a mixture of CH_2Cl_2 and diethyl ether affording the desired 1,2,3-triazole products with percentage yields ranging from 39% – 91%. The ^{1}H NMR spectra of **1** – **5** in $CDCl_3$ contain two characteric broad resonances at approximately δ 7.6 and δ 3.6 corresponding to C*H*=C (of the triazole ring) and NCH_2, respectively.



R = C_6H_5 (**1**), $SiMe_3$ (**2**), 4-F-C_6H_4 (**3**),
4-$MeOC_6H_4$ (**4**), Fc (**5**)

2. ATRP Catalytic Activity of CuBr/L (L = 1 – 5)

Atom Transfer Radical Polymerizations (ATRP) catalyzed by CuBr/**1** – **5** systems were conducted under Ar at 90 ^{o}C, with ethyl-2-bromoisobuthyrate (EBrIB) as an initiator. Polymerization data of CuBr/**1**, **2**, and **5** were shown in Table 1. It appeared that these copper complexes were active ATRP catalysts affording moderate to high polymer yields. Interestingly, CuBr containing tripodal ligands with a *para*-substituent at the benzyl group (**3** , **4**) exhibited no catalytic activity toward polymerization after 3 d in neat MMA, under the same polymerization conditions. We speculate that, for ligands **3** and **4**, the heteroatoms (*i.e.*, F and O) present in the 1,2,3-triazole moieties might involve in the coordination of copper and, as a result, inhibited the polymerization activity.[14]

Table 1. ATRP of MMA with CuBr/**L** (**L** = **1**, **2**, **5**)

Entry	Ligand (L)	time (h)	% yield	M_n (theo)	M_n (GPC)	M_w/M_n
1	**1**[a]	0.5	88	9,006	24,498	4.23
2	**1**[b]	3	52	5,401	58,691	2.70
3	**1**[c]	3	68	7,003	14,674	1.81
4	**2**[a]	0.3	94	9606	15,073	1.73
5	**2**[b]	3	77	7904	12,586	1.67
6	**2**[c]	3	8	996	6,795	1.24
7	**5**[a]	17	69	7,103	31,557	3.74
8	**5**[b]	18	52	5,401	12,423	1.49
9	**5**[c]	18	32	3399	5,863	1.36

Polymerization conditions: Molar ratio of MMA:CuBr:L:initiator = 100:0.5:0.5:1, 90 ^{o}C, initiator = ethyl-2-bromoisobuthyrate (EBrIB)
[a] neat MMA. [b] 50% v/v toluene:MMA. [c] 50% v/v 2-butanone:MMA.

At 0.5 mol% CuBr/**1** and CuBr/**2** in neat MMA, *p*MMA was isolated in 88% and 94% yields after 30 min (entries 1 and 4), while CuBr/**5** catalyst exhibited lower activity and required longer reaction time (17 h) to afford 69% isolated yield (entry 7). When a 1:1 v/v solution of toluene:MMA was used as a solvent under similar reaction conditions, CuBr/**1**, CuBr/**2**, and CuBr/**5** afforded *p*MMA in 52% (3 h), 77% (3 h), and 52% (18 h) yields (entries 2, 5, 8). Despite good catalytic activity, ATRP of MMA catalyzed by CuBr/**L** were not well-controlled and resulted in polymers with high polydispersities. In general, lower activities and M_w/M_n values were obtained when the polymerizations were conducted in a 1:1 v/v toluene:MMA as compared to those resulted from bulk polymerizations. This is due to the direct rate dependence on monomer concentrations, as evidenced by linear

kinetic plots of $\ln[M]_o/[M]_t$ versus time for CuBr/**L**. At 90 °C in a 1:1 v/v toluene:MMA, CuBr/**L** catalysts provided linear kinetic plots with k_{obs} = 5.0 x 10^{-3} min^{-1}, 2.7 x 10^{-4} min^{-1} for CuBr/**1** and CuBr/**5**, respectively (Figure 1). These kinetic data indicate pseudo-first-order rate dependence on monomer concentration and a constant radical concentration during the course of polymerization.

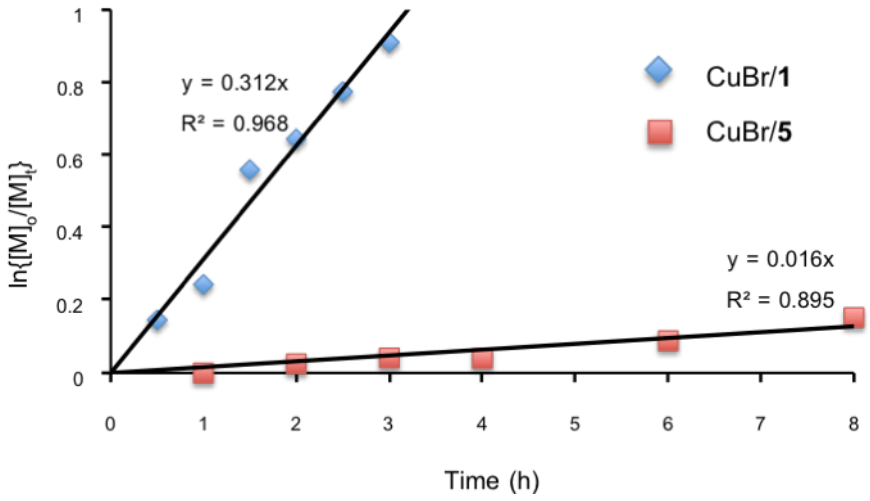


Figure 1. Kinetic plots for polymerizations of MMA by CuBr/**1** and CuBr/**5**. Polymerization conditions: molar ratio of MMA:CuBr:L:initiator = 100:0.5:0.5:1, MMA:toluene = 1:1 (v/v), 90 °C, initiator = ethyl-2-bromoisobuthyrate (EBrIB)

Interestingly, M_n values of polymers obtained from CuBr/**1** catalyst are substantially higher than those from other catalysts (entries 1, 2). It is possible that a significant degree of radical termination reactions may be involved during the polymerization process.[15] In an attempt to improve the solubility of $CuBr_2$/**L** and consequently reduce polydispersities of the resulting polymer, 2-butanone (50% v/v 2-butanone:MMA) was added to the reaction mixture. Entries 3, 6, and 9 show lower M_w/M_n values compared to those obtained from 50% v/v toluene:MMA solvent. This observed trend suggests that, as expected, polar solvent 2-butanone may allow higher concentration of $CuBr_2$/**L** species in the system which accelerates the deactivating step (k_{deact}). Thus, a radical concentration and a radical-radical coupling process are expected to decrease, leading to polymers with lower M_n values.

3. Effect of Added $CuBr_2$ on Polydispersity Values

Similar to the use of more polar solvent, addition of 40% $CuBr_2$ with respect to CuBr was aimed at increasing the concentration of Cu^{2+} species, speeding up the rate of the deactivating step (large k_{deact}), and consequently lowering the concentration of active radicals, which allowed an improvement in polymer

polydispersities. Thus, polymerization experiments were carried out both in toluene and 2-butanone solutions (Table 2). The data showed that addition of 40% $CuBr_2$ generally afforded polymers with lower percentage yields and relatively narrower polymer PDI values in the range of 1.36 – 2.14. For example, the M_w/M_n values of 1.67 (77%) and 1.47 (56%) were obtained for *p*MMA generated from the CuBr/**2** catalyst in the absence of $CuBr_2$ and with 40% $CuBr_2$ added, respectively. In comparison to toluene, more polar solvent 2-butanone was expected to increase the solubility of $CuBr_2$/**L** resulting in lower polymerization rates and PDI values. Consistent with this assumption, 2-butanone solvent afforded *p*MMA with narrower polydispersities at lower percentage yields (Table 2). In fact, when the supporting ligand is TBTA-TMS (**2**), the polymerization conditions with 40% $CuBr_2$ in 2-butanone at 90 ^{o}C resulted in a trace amount of *p*MMA after 3 h (entry 4).

Table 2. ATRP of MMA with 40% $CuBr_2$

Entry	Ligand (L)	time (h)	% yield	M_n (theo)	M_n (GPC)	M_w/M_n
1	**1**[a]	3	64	6603	41,503	2.00
2	**1**[b]	3	71	7304	30,496	2.14
3	**2**[a]	3	56	5802	6,474	1.47
4	**2**[b]	3	trace	N/A	N/A	N/A
5	**5**[a]	18	31	3299	9,641	1.59
6	**5**[b]	18	31	3299	4,835	1.36

Polymerization conditions: Molar ratio of MMA:CuBr:L:initiator = 100:0.5:0.5:1, 90 ^{o}C, initiator = ethyl-2-bromoisobuthyrate (EBrIB)

[a] 50% v/v toluene:MMA. [b] 50% v/v 2-butanone:MMA.

It should be noted that when CuBr/**5** was the catalyst, the M_w/M_n value was slightly larger with added 40% $CuBr_2$ (1.59) compared to that with no additional $CuBr_2$ (1.49). From the ATRP experiment with 40% $CuBr_2$ in toluene (entry 5, Table 2), we observed the appearance of fine precipitates which were believed to be the insoluble complex $CuBr_2$/**5**. As a result, a discrepancy in the M_w/M_n trend might be attributed to the insolubility of $CuBr_2$/**5** species.

4. Effect of Ligands on ATRP

The polymerization data suggest that substituents on 1,2,3-triazole groups have a significant effect on polymerization rates. Previous studies have shown that more electron-donating ligands generally lead to more basic ligand donors and subsequently more active ATRP catalysts.[14a,16] For example, CuBr/Me_6TREN catalyzed

the ATRP of methyl acrylate at a much faster rate than CuBr/TREN affording polymers with narrower polydispersity.[16b]

According to Hammet's substituent constant, σ, electron-donating ability decreases from Fc > $SiMe_3$ > C_6H_5.[17] Our catalytic studies, however, revealed the observed polymerization rate constants (k_{obs}) followed the order of **2** ($SiMe_3$) > **1** (C_6H_5) > **5** (Fc). Although ATRP activities of the catalyst containing the silyl and phenyl groups were consistent with the electron-donating trend, it is surprising that the strongest electron-releasing ligand **5** resulted in the least active copper catalyst. To account for this, we reasoned that steric hindrance imposed by ferrocenyl substituents might interfere with the halide abstraction process resulting in lower ATRP activity. However, we cannot rule out the electronic effect caused by the redox active ferrocenyl groups which may affect the redox process at the Cu^+/Cu^{2+} center.

Conclusion

A series of *tris*(R-methyltriazolylmethyl)amines [R = C_6H_5 (**1**), $SiMe_3$ (**2**), 4-FC_6H_4 (**3**), 4-$MeOC_6H_4$ (**4**), Fc (**5**)] were successfully prepared and employed as ligand support for catalytic ATRP. Polymerization activities were good with CuBr/**1** and CuBr/**2** catalysts and moderate with CuBr/**5**, while CuBr/**3** and CuBr/**4** exhibited no ATRP catalytic activity. Apparently, the substituents at the 1,2,3-triazole rings have a dramatic effect on the activity of copper catalysts toward ATRP of MMA. Along the same line with previous studies, the stronger electron-donating groups $SiMe_3$ on the click ligand **2** resulted in better catalytic activities than those from CuBr/**1**. However, the strongest electron-donating ferrocenyl groups in ligand **5** surprisingly produce copper catalyst with low ATRP activity. In addition to large steric hindrance from the ferrocenyl substituents, it is possible that an electronic factor from redox active ferrocene may involve in the redox process at the Cu^+/Cu^{2+} center. As a result, an investigation of electrochemical behaviors of these catalyst systems is currently in progress.

Furthermore, with relatively polar nature of click ligands, more polar 2-butanone has proven to be a better solvent than toluene to afford polymers with lower polydispersity values. Thus, it is of interest to further explore other polar solvents which may lead to a more controlled polymerization of MMA.

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ผลลัพธ์ที่ได้จากโครงการ

(1) ผลวิจัยที่ได้เป็นส่วนหนึ่งของผลงาน thesis นักศึกษาปริญญาโท ภาควิชาเคมี มหาวิทยาลัยมหิดล

(2) การเสนอผลงานวิจัยแบบโปสเตอร์: Copper Complexes Featuring Tripodal “Click” Ligands for Atom Transfer Radical Polymerization, การประชุมนักวิจัยรุ่นใหม่..พบ..เมธีวิจัยอาวุโส สกว. ครั้งที่ 9 ระหว่างวันที่ 15 – 17 ตุลาคม 2552 ณ โรงแรมฮอลิเดย์อินน์ รีสอร์ท รีเจ้นท์บีช ชะอำ จ.เพชรบุรี

(3) ผลงานวิจัยชิ้นนี้กำลังอยู่ในระหว่างการเตรียม manuscript 1 เรื่อง เพื่อส่งตีพิมพ์ในวารสารวิชาการ Applied Catalysis A: General