

Electronic Supplementary Information for:

Transesterification of functional methacrylate monomers during alcoholic copper-catalyzed atom transfer radical polymerization: Formation of compositional and architectural side products

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Materials

Triply-distilled 2-hydroxyethyl methacrylate (HEMA) was kindly donated by Cognis UK Ltd., 2-methacryloyloxyethyl phosphorylcholine, 2,2'-bipyridyl (bipy), N,N,N',N',N''-pentamethyldiethylenetriamine (PMDETA), copper (I) chloride, ethylene glycol (EG), ethylene glycol dimethacrylate (EGDMA), methyl methacrylate (MMA), and oligo(ethylene glycol) methyl ether methacrylate ($M_n=300$) (OEGMA) were all purchased from Sigma-Aldrich. Methanol- d_4 (99.8 % deuteration degree) was purchased from VWR International (Merck), ethanol- d_6 (99.5 % deuteration degree) and isopropanol- d_8 (99.5 % deuteration degree) were purchased from Sigma-Aldrich. All materials were used as received.

Instruments

NMR All ^1H NMR spectra except HEMA kinetics experiments were recorded in methanol- d_4 using a Bruker AV-400 spectrometer operating at 400 MHz. The spectra were referenced to the solvent signal with respect to TMS at δ 3.34 ppm. Kinetics experiments were carried out in methanol- d_4 , ethanol- d_6 , or isopropanol- d_8 using a Bruker AV-500 spectrometer operating at 500 MHz.

Experimental

Kinetics experiments were carried out *in situ* under ATRP conditions at room temperature. To prepare these reactions, HEMA (0.932 g, 7.16 mmol) was degassed with nitrogen for 30 min while simultaneously degassing 2 mL methanol- d_4 /ethanol- d_6 /isopropanol- d_8 with nitrogen gas for 30 min. Cu(I)Cl (23.3 mg, 0.235 mmol) and bipy (92.6 mg, 0.592 mmol) were added to the degassed solvent, turning the solution dark brown. The brown solvent/catalyst solution was added to degassed HEMA and 0.7 mL was transferred to an NMR tube and the first spectra taken immediately on a Bruker AV-500 instrument. Subsequent spectra were taken every 30 min up to 24 hours. To prevent spinning side bands, the samples were not spun and each spectra consisted of a single scan to reduce errors associated with passing time.

The kinetics experiment of MPC was carried out by degassing MPC (529 mg, 1.79 mmol) and 0.5 mL methanol- d_4 with nitrogen gas for 30 min. Cu(I)Cl (5.9 mg, 0.060 mmol) and bipy (23.3 mg, 0.149 mmol) were added to the degassed solution. Aliquots of 0.02 mL were taken at 0, 3, 6, 9, 12 and 24 h and diluted in 0.6 mL methanol- d_4 in NMR tubes. ^1H NMR spectra were measured using a Bruker AV-400 instrument.

Reference spectra of the initial HEMA monomer, EG, MMA, EGDMA, OEGMA monomer, and MPC monomer were measured in methanol- d_4 using a Bruker AV-400 instrument. Spectra were also measured in the presence of Cu(I)Cl and bipy. For HEMA, EG, EGDMA

and OEGMA, monomer or by-product (3.56 mmol) and 1 mL methanol-d₄ was degassed with nitrogen for 30 min. Cu(I)Cl (11.8 mg, 0.119 mmol) and bipy (46.3 mg, 0.296 mmol) were added to the degassed solution and stirred for 24 h. At 0 h and 24 h, an aliquot of 0.02 mL was taken from the solution and diluted with 0.6 mL methanol-d₄ in an NMR tube. The diluted sample was scanned with a Bruker AV-400 instrument operating at 400 MHz.

To investigate using an alternative catalyst system, 2 mL methanol-d₄ and HEMA (0.932 g, 7.16 mmol) were degassed separately with nitrogen for 30 min. PMDETA (41.32 mg, 0.238 mmol) was added to the degassed solvent before adding Cu(I)Cl (23.6 mg, 0.238 mmol). The degassed HEMA was added to the solvent/catalyst solution and stirred for 24 hr. Aliquots of 0.02 mL were taken after 0 h and 24 h and diluted in 0.7 mL methanol-d₄ in NMR tubes. ¹H NMR spectra were taken on a Bruker AV-400 instrument operating at 400 MHz.

Investigation of the effect of temperature was carried out by degassing separately 2 mL methanol-d₄ and HEMA (0.932 g, 7.16 mmol) with nitrogen for 30 min. The methanol was heated to and maintained at 50 °C in an oil bath. Cu(I)Cl (23.3 mg, 0.235 mmol) and bipy (92.6 mg, 0.592 mmol) were added to the degassed solvent, turning the solution dark brown. The degassed HEMA was added to the solvent/catalyst solution and stirred for 24 hr. Aliquots of 0.02 mL were taken after 0, 1, 3, 6 and 24 h and diluted in 0.7 mL methanol-d₄ in NMR tubes. ¹H NMR spectra were taken on a Bruker AV-400 instrument operating at 400 MHz.

The effect of catalyst concentration on MMA formation was carried out by degassing separately two batches of 2 mL methanol-d₄ and HEMA (0.932 g, 7.16 mmol) with nitrogen for 30 min. Cu(I)Cl (11.7 mg, 0.118 mmol or 0.2mg, 0.002 mmol) and bipy (46.3 mg, 0.296 mmol or 0.9 mg, 0.006 mmol) were added to the degassed solvent, turning the solution dark brown. The degassed HEMA was added to the solvent/catalyst solution and stirred for 24 hr. Aliquots of 0.02 mL were taken after 0, 1, 3, 6 and 24 h and diluted in 0.7 mL methanol-d₄ in NMR tubes. ¹H NMR spectra were taken on a Bruker AV-400 instrument operating at 400 MHz.

Kinetics of transesterification of HEMA in alternative alcoholic solvents

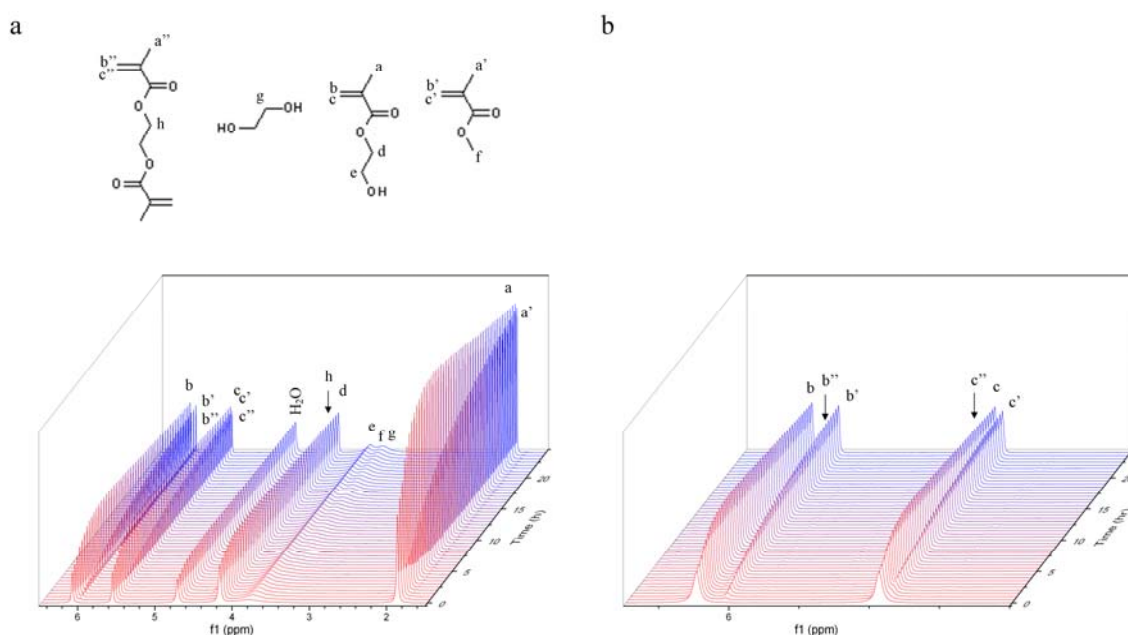


Figure S1 – (a) ^1H NMR kinetics plots of HEMA transesterification in methanol- d_4 (b) Vinyl region of the ^1H NMR spectra showing the splitting of the vinyl proton peaks to form MMA from HEMA by transesterification with methanol. Note the peak corresponding to EGDMA (b'') at δ 6.11 ppm which becomes obscured behind the MMA peak (b') at δ 6.09 ppm after 6 h.

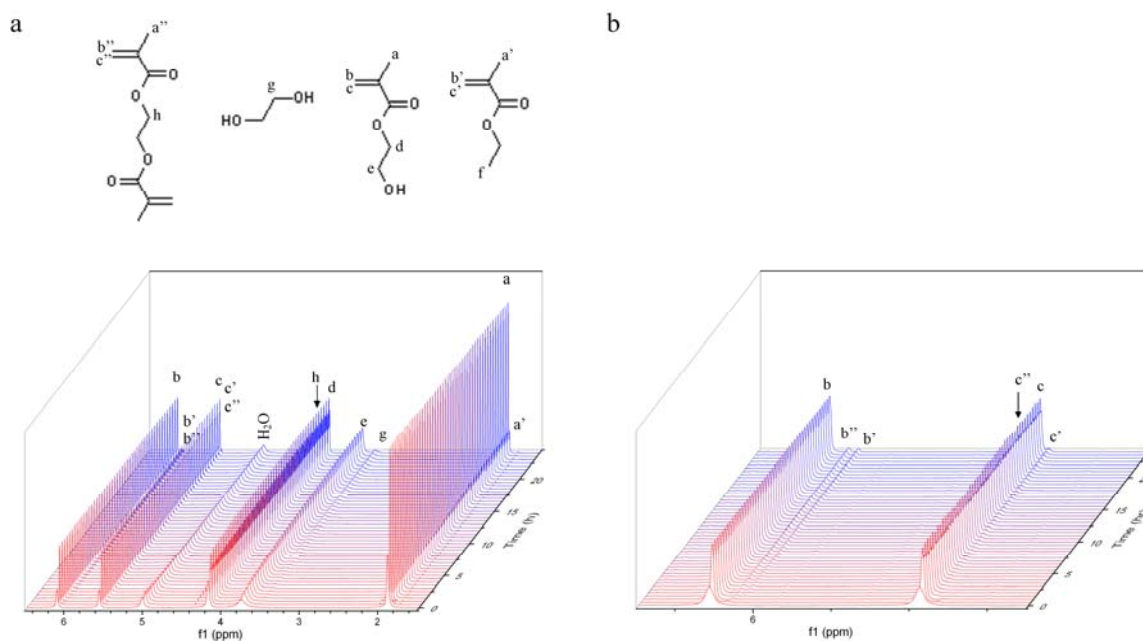


Figure S2 – (a) ^1H NMR kinetics plot of HEMA transesterification in ethanol- d_6 (b) Vinyl region of the ^1H NMR spectra showing the progressive splitting of the two vinyl protons as the ethyl methacrylate (b' and c' at δ 6.04 ppm and 5.56 ppm) and EGDMA (b'' and c'' at δ 6.07 ppm and 5.59 ppm) are formed from HEMA.

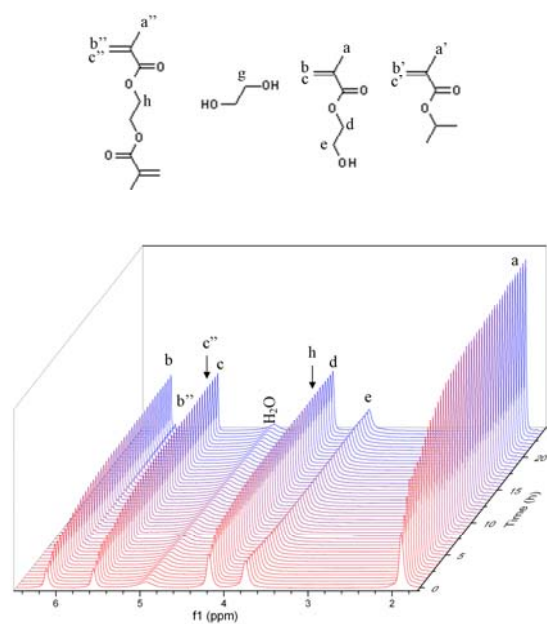


Figure S3 – ^1H NMR kinetics plot of HEMA transesterification in isopropanol- d_8 .

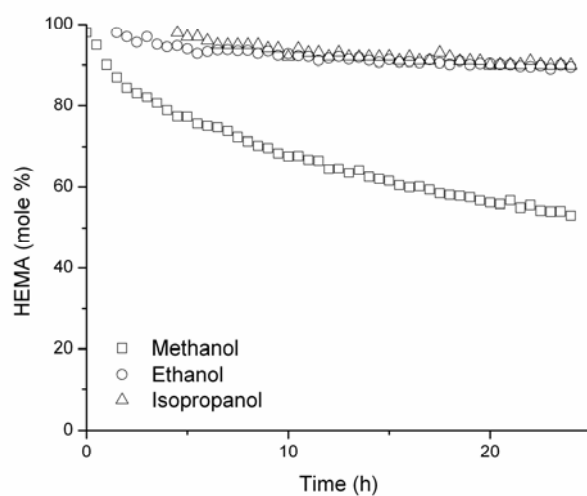


Figure S4 – Kinetics of HEMA transformation under standard, normalized, copper/bipy-catalyzed ATRP conditions in the presence methanol- d_4 , ethanol- d_6 and isopropanol- d_8 .

Reference Spectra – MMA, EGDMA, EG

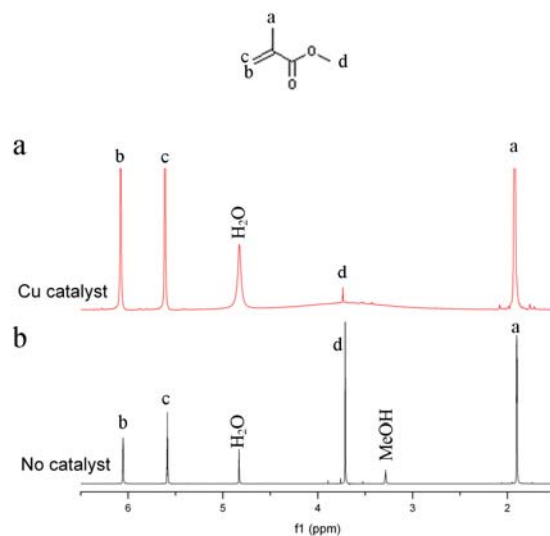


Figure S5 – ^1H NMR reference spectra of MMA in methanol- d_4 in the presence and absence of Cu(I)Cl/bipy catalyst. When the catalyst is present a broadening of peak d is observed suggesting evidence of monomer-catalyst complexation.

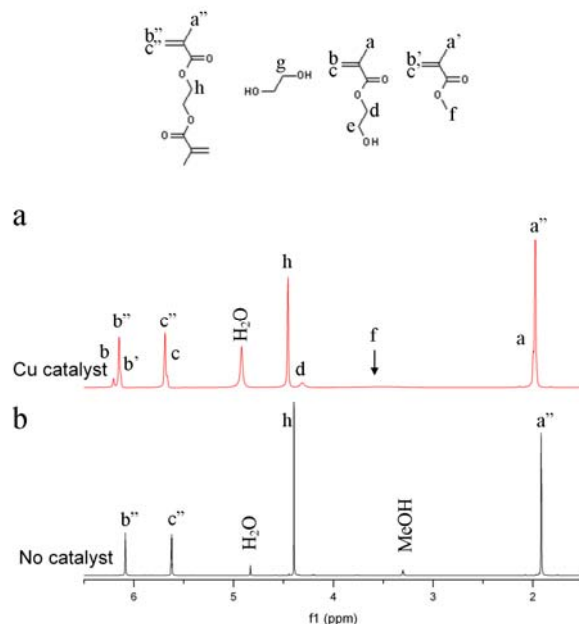


Figure S6 – Reference ^1H NMR spectra of EGDMA in methanol- d_4 in the presence and absence of Cu(I)Cl/bipy catalyst. Note some transesterification of EGDMA to HEMA can be observed in the catalyst-containing sample by the splitting of vinyl peaks b and c at δ 6.13 ppm and 5.67 ppm and the development of a peak at δ 4.29 ppm.

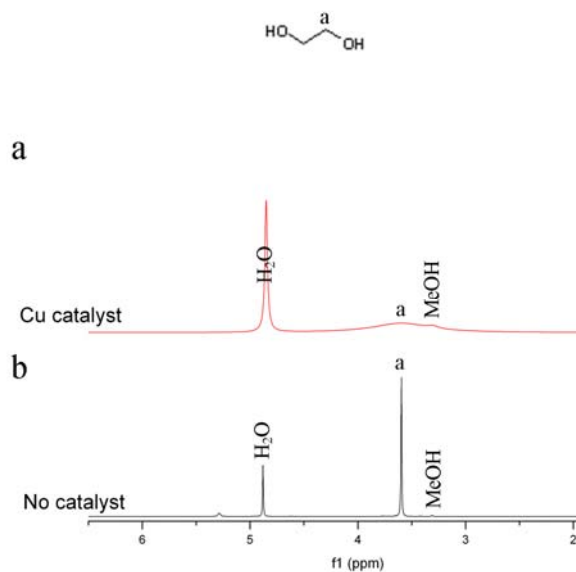


Figure S7 – ^1H NMR reference spectra of ethylene glycol in the presence and absence of Cu(I)Cl/bipy catalyst. Note in the presence of the catalyst, the single peak becomes significantly broadened suggesting coordination to the copper catalyst.

Transesterification of alternative monomers – OEGMA and MPC

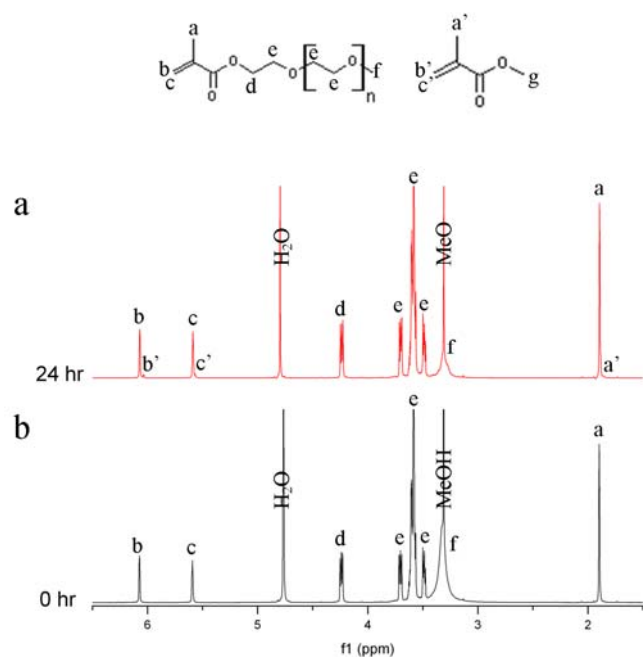


Figure S8 – ^1H NMR spectra showing the transesterification of oligo(ethylene glycol) methyl ether methacrylate ($M_n = 300$) in methanol- d_4 . Splitting of vinyl peaks b and c is observed at the rate of 7 mole % MMA formed after 24 h.

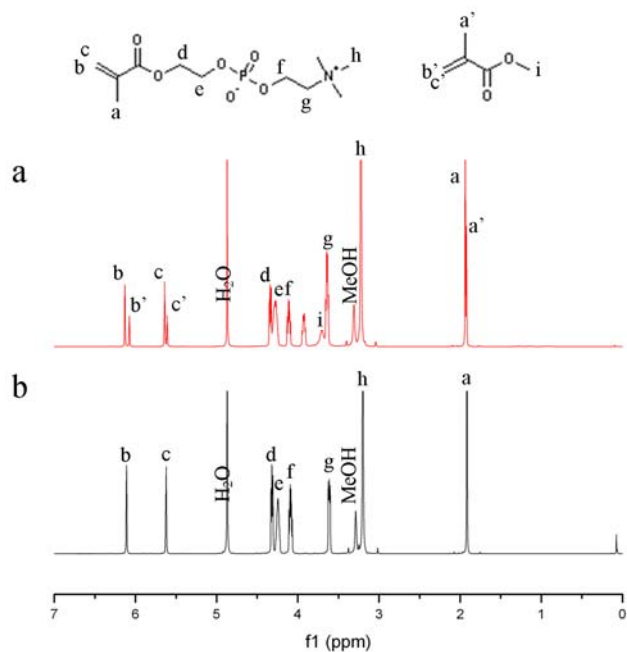


Figure S9 – ^1H NMR spectra of MPC in methanol- d_4 with Cu(I)Cl/bipy catalyst at (a) 24 h and (b) 0 h. The splitting of the vinyl peaks shows formation of 34 mole % MMA after 24 h. Note additional side reactions.

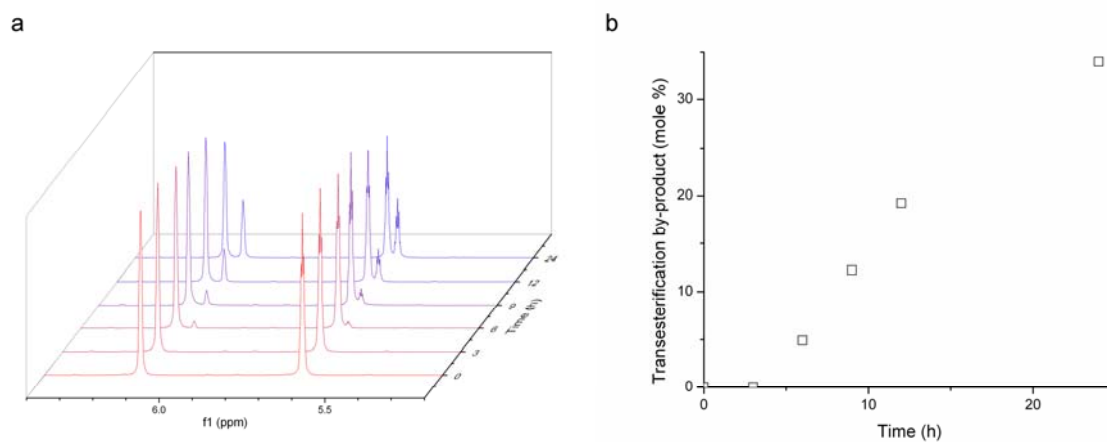


Figure S10 – (a) Vinyl region of ^1H NMR spectra showing MPC transesterification in methanol- d_4 . (b) Kinetics plot of MPC methacrylate side-product up to 24 h in methanol- d_4 as calculated from the relative peak areas in (a).

Transesterification of HEMA – Cu(I)Cl/bipy and Cu(I)Cl/PMDETA catalyst systems

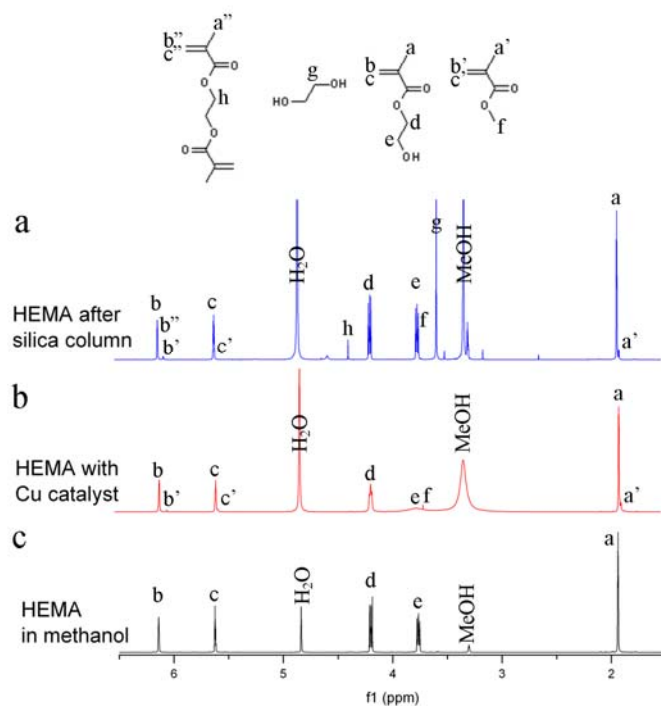


Figure S11 – ^1H NMR spectra of HEMA in methanol- d_4 in the presence and absence of Cu(I)Cl/bipy catalyst. Spectra were recorded within 15 min of adding catalyst, and after removal of the copper catalyst by running the solution through a silica column three times. Broadening of peaks in (b) were observed in the presence of the catalyst which returned to their sharp peaks once the catalyst is removed (a) suggesting catalyst-HEMA coordination.

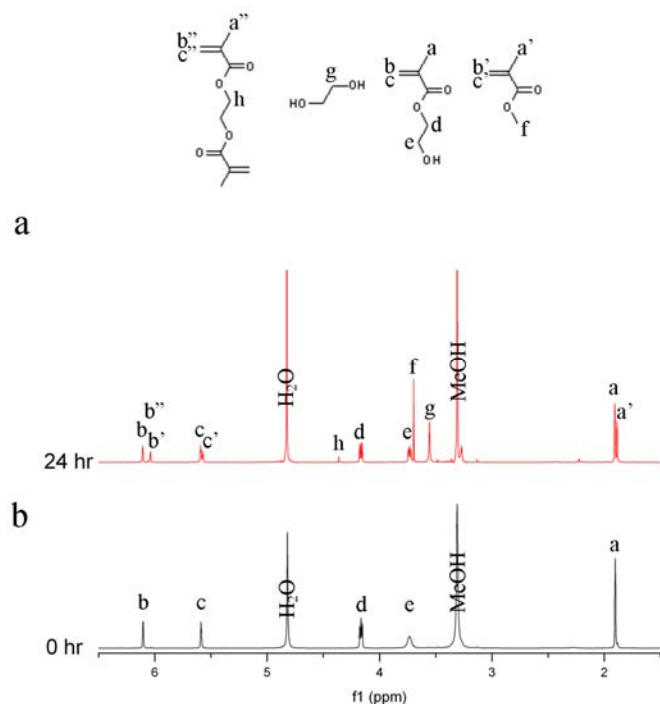


Figure S12 – ^1H NMR spectra of HEMA in methanol- d_4 with alternative Cu(I)Cl/PMDETA catalyst at 0 h and 24 h. Note transesterification is still observed.

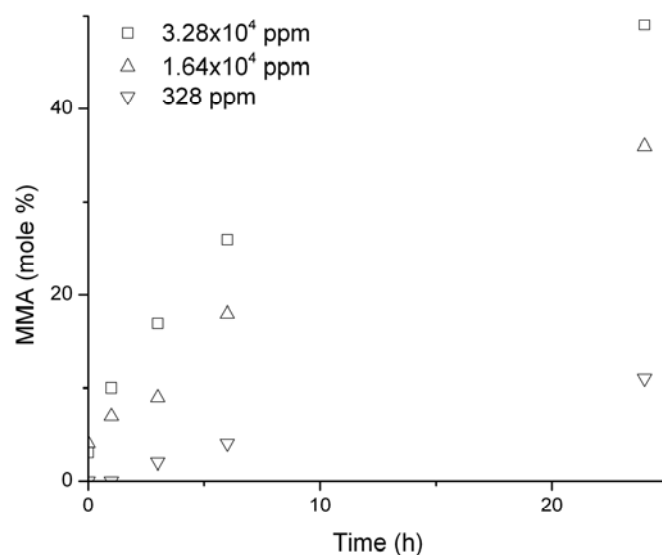


Figure S13 – Kinetics plot of MMA formation in methanol solution with HEMA and different concentrations of Cu(I)Cl/bipy catalyst concentration. A reduction in the rate of transesterification is observed as the copper concentration reduces, suggesting ATRP techniques such as ARGET ATRP may show negligible MMA formation within typical ATRP timescales.

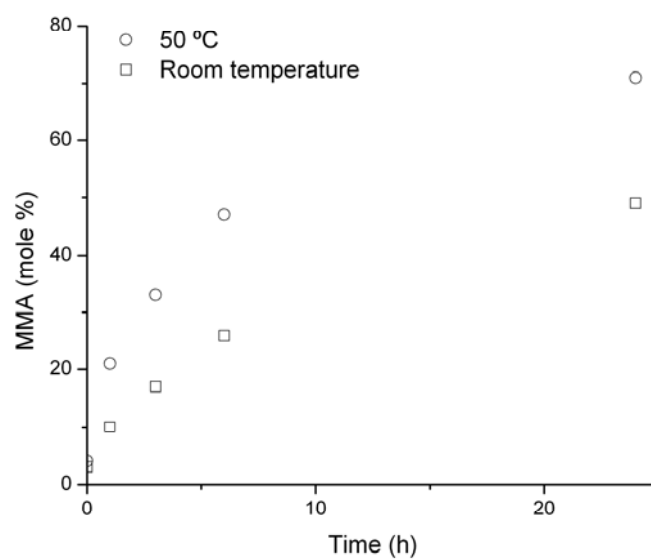


Figure S14 – Kinetics plot of HEMA transesterification at room temperature and at 50 °C showing a substantial increase in MMA formation at elevated temperatures.