

Preventing Alkyne-Alkyne (i.e., Glaser) Coupling Associated with the ATRP Synthesis of Alkyne-Functional Polymers/Macromonomers and for Alkynes under Click (i.e., CuAAC) Reaction Conditions

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Experimental Section

Materials. The monomers used in this study, including styrene (St, Sigma, $\geq 99\%$), deuterated styrene (St-D₈, Polymer Source, 98%) and *tert*-butyl acrylate (*t*BA, Aldrich, 98%) were passed through basic alumina columns prior to ATRP to remove inhibitors. The following chemicals were purchased from Aldrich and used as received: propargyl 2-bromoisobutyrate (PgBiB, $\geq 97\%$), ethyl α -bromoisobutyrate (EBiB, 98%), N,N,N',N',N'' pentamethyldiethylenetriamine (PMDETA, 99%), 4,4'-Dinonyl-2,2'-bipyridine (dNbpy, 97%), 4,4'-Di-*tert*-butyl-2,2'-dipyridyl (dBbpy, 98%), 1,1,4,7,10,10-Hexamethyltriethylenetetramine (HMTETA, 97%), Tris[2-(dimethylamino)ethyl]amine (Me₆TREN, 97%), copper(I) bromide (CuBr, 99.999%), copper(II) bromide (CuBr₂, 99.999%), anisole ($\geq 99.0\%$), N,N-dimethylformamide (DMF, 99.8%), ethyl acetate (EtOAc, 99.9%), tin(II) 2-ethylhexanoate (Sn(EH)₂, 92.5-100.0%), (+)-Sodium L-ascorbate ($\geq 98\%$), and chloroform-d (99.96%). Tetrahydrofuran (THF, 99.9%) and methanol ($\geq 99.8\%$) were purchased from Fisher Scientific.

Polymerization Procedures. Monomers, solvents (if necessary), ligands, and initiators were added to a dry, clean Schlenk flask equipped with a magnetic stirrer and deoxygenated by three freeze-pump-thaw cycles. The flask was backfilled with nitrogen and CuBr was immediately added. After two additional freeze-pump-thaw cycles, the flask was placed in an oil bath held at the desired temperature. The experimental conditions used for ATRP and the resultant molecular weights of the polymers are included in Table S.1 and S.3 for polystyrene (PS) and Table S.2 for poly(*tert*-butyl acrylate) (PtBA).

Kinetics of Glaser coupling for alkyne-terminated polymers at -28°C. Immediately after the synthesis of alkyne end-functional polymer, the ATRP solution was frozen with liquid nitrogen and cold THF was added, if necessary, to reduce viscosity. Next, the sample was thawed in an ice bath of saturated sodium chloride (-21°C) and the solution was transferred into a scintillation vial, placed in a freezer maintained at -28°C. Samples were collected at various time intervals and analyzed by GPC. To purify the polymer, the ATRP solution was passed through a cold neutral alumina column, previously cooled to -20°C. The copper-free solution was precipitated dropwise (5x) in methanol for PS or water/methanol mixture (1:1 vol/vol) for PtBA. The polymer was finally dried *in vacuo* and analyzed by GPC.

Kinetics of Glaser coupling for alkyne-terminated polymers at room temperature. Immediately after synthesis of alkyne-terminated polymer, the flask was placed in a water bath to ensure thermal equilibration with room temperature. The ATRP product was then transferred via a nitrogen-purged syringe to a scintillation vial equipped with a magnetic stirrer set at 600 RPM. Once exposed to air, samples were collected at selected time intervals and quenched by freezing the solution with liquid nitrogen. The samples were thawed and instantly analyzed by GPC. For deuterated α -alkyne, ω -Br-PS, the reaction solution was additionally passed through a cold neutral alumina column and precipitated dropwise in methanol (5x). The sample was finally dried *in vacuo* and analyzed by GPC and ¹H-NMR.

NMR Studies of Glaser coupling between small molecules. PgBiB (0.3mmol), PMDETA (0.3mmol), THF (9mL), and CuBr (0.3mmol) or CuBr₂ (0.3mmol) were added to a scintillation vial equipped with a magnetic stirrer and sonicated for 15 minutes. Sodium L-ascorbate (6mmol) dissolved in 2mL deionized water was added to the vial if required. The vial was subsequently placed on a stir plate set to stir at 600RPM for 24 hours. The samples were finally purified (see supplement) and analyzed by ¹H-NMR.

Effect of ATRP ligands on Glaser coupling. The synthesis of α -alkyne, ω -Br-PS was performed with various nitrogen-based ligands as described in Table S.3. After polymerization, the kinetic studies of the Glaser coupling of alkyne end-functional polymers were performed at room temperature following the procedure presented earlier.

Effect of the Reducing Agents on the Glaser Coupling post-ATRP. Immediately after ATRP of styrene using PgBiB initiator and CuBr/PMDETA, the solution was frozen with liquid nitrogen. The sample was thawed in an ice bath of saturated sodium chloride (-21°C) and the solution was transferred via a nitrogen purged syringe to 0.97M Sn(EH)₂ (6.8 mmol, 20 equiv. to CuBr) in degassed toluene. The solution was then stirred in a water bath to ensure thermal equilibration with room temperature. The sample was then exposed to air and analyzed by GPC at various time intervals.

Synthesis and Kinetic Studies of α -alkyne, ω -Br-PS via Activator ReGenerated by Electron Transfer (ARGET) ATRP. Styrene (10mL, 87mmol), Me₆TREN (12 μ L, 4.5×10^{-2} mmol), PgBiB (92mg, 0.45mmol), and CuBr₂ (1mg, 0.45×10^{-2} mmol) were added to a scintillation vial equipped with a magnetic stirrer and capped with a rubber septum. The solution was frozen with liquid nitrogen and Sn(EH)₂ (15 μ L, 4.6×10^{-2} mmol) was added. The vial was placed in an ice bath with a constant stirring rate for 2 hours. The solution was sonicated additionally for 15 minutes and later placed in an oil bath held constant at 90°C. The samples were taken at different time intervals and analyzed by GPC.

After 2.5 hours of polymerization (Mn=3050, PDI=1.22), the sample was placed in a water bath to allow thermal equilibrium with room temperature. The vial was then opened to air and samples were collected and analyzed by GPC at different time intervals. To purify the polymer, the solution was passed through a neutral alumina column and precipitated dropwise (5x) in excess methanol. The polymer was finally dried *in vacuo*.

Instrumentation. Molecular weight distributions were measured using a Shimadzu LC-10AT gel permeation chromatography (GPC), equipped with a ResiPore guard column, two ResiPore GPC columns, and three detectors: ultraviolet light (UV, 254 nm), refractive index (RI), and static light scattering. Polystyrene standards in the range of $M_p=162\text{--}483,400$ g/mol were used for calibration. Proton nuclear magnetic resonance ($^1\text{H-NMR}$) spectra were recorded on a Bruker 400MHz spectrometer in CDCl_3 with chemical shifts expressed relative to the tetramethylsilane standard ($\delta=0.00$). The X-ray photoelectron spectroscopy (XPS) spectra were recorded on a PHI 5500 XPS equipped with Al/Mg standard X-ray source running at 15kV, a hemispherical electron energy analyzer, and a multichannel detector. High-resolution spectra were acquired with a step size in the range of 0.025-0.2 eV/Step, a pass energy of 23.5 eV, and a takeoff angle of 50° . Cu concentrations of ATRP reaction solutions were measured using Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) (ACTIVA-M, HORIBA Scientific) and calibrated using Copper standards in the range of 0.1-10.0 PPM.

Study of Cu oxidation state

After the synthesis of α -alkyne, ω -Br-PS ($M_n=2980$ g $\cdot\text{mol}^{-1}$, PDI=1.10), 3mL of the ATRP mixture was transferred via a nitrogen purged syringe into an argon purged 20mL scintillation vial equipped with a clean (1×1 cm 2) silicon wafer and capped with a rubber septum. The remaining ATRP solution was exposed to air for 24 hours and afterward transferred into a scintillation vial equipped with a clean silicon wafer. For the Cu(II) standard, a solution of $\text{CuBr}_2/\text{dNbpy}$ (1:2 mol/mol) in styrene was used. Argon was bubbled and later blown into the vials for 5 days until the solution was completely dry. The Cu oxidation states of the dried films were then analyzed via X-ray photoelectron spectroscopy (XPS).

Copper solubility studies

After the synthesis of α -alkyne, ω -Br-PS ($M_n=3170$ g $\cdot\text{mol}^{-1}$, PDI=1.09), the mixture was transferred to an open scintillation vial placed either in room temperature or in a freezer maintained at -28°C . After 24 hours, the samples were centrifuged and filtered to remove precipitates and afterward dried using rotary evaporator. 20mL of 2M nitric acid was then added to dissolve the precipitant. The solution was finally diluted and the copper contents analyzed via ICP-OES.

Purification of small alkyne molecules for $^1\text{H-NMR}$ Studies

The procedure to purify the products following the incubation of PgBiB with $\text{CuBr}_2/\text{PMDETA}$ and Sodium L-ascorbate was as followed. The volatile fraction was first removed by rotary evaporation. The crude product was then dissolved in EtOAc and washed with deionized water (5x). The organic layer was decanted, dried using anhydrous sodium sulfate, and passed through a neutral alumina column to remove trace copper. The solvent was filtered and removed *in vacuo*.

For the reaction mixture with no reducing agent added, the solution was first passed through a neutral alumina column to remove the copper catalyst and the solvent was subsequently removed by rotary evaporation. The crude product was then dissolved in EtOAc and washed with deionized water (5x) to remove PMDETA. The organic layer was decanted, dried with anhydrous sodium sulfate, and the solvent was removed *in vacuo*. The products were finally extracted and characterized with $^1\text{H-NMR}$.

Polymerization Conditions

Table S.1. Experimental Conditions for the ATRP of Styrene

Polymer	Styrene (mmol)	Ligand (mmol)	Initiator (mmol)	CuBr (mmol)	Reaction Temperature (°C)	Reaction Time (min)	M _n (kg·mol ⁻¹); PDI
Br-PS	43.5	1.10 ^c	0.55 ^a	0.55	110	70	2.84; 1.11
Br-PS	152.2	1.10 ^c	0.55 ^a	0.55	110	301	10.90; 1.06
α-alkyne,ω-Br-PS	78.3	0.68 ^c	0.34 ^b	0.34	110	63	3.2±0.4; 1.09
α-alkyne,ω-Br-PS	255.3	0.68 ^c	0.34 ^b	0.34	110	210	10.50; 1.09
α-alkyne,ω-Br-PS (deuterated)	78.3	0.68 ^c	0.34 ^b	0.34	110	63	3.09; 1.12
α-alkyne,ω-Br-PS	78.3	0.34 ^d	0.34 ^b	0.34	90	70	4.4; 1.10

The following initiators were used: ^aEBiB Initiator; ^bPgBiB. ATRP ligands: dNbpy^c; PMDETA^d

Table S.2. Experimental Conditions for the ATRP of *tert*-butyl acrylate

Polymer	<i>t</i> -butyl acrylate (mmol)	PMDETA (mmol)	PgBiB (mmol)	CuBr (mmol)	DMF (mL)	Reaction Temperature (°C)	Reaction Time (min)	M _n (kg·mol ⁻¹); PDI
α-alkyne,ω-Br-PtBA	50	0.2	0.2	0.2	5	60	25	11.30; 1.19

Table S.3. Experimental Conditions for the ATRP of Styrene and for the studies of ATRP ligands on Glaser Coupling

Polymer	Styrene (mmol)	Ligand (mmol)	PgBiB (mmol)	CuBr (mmol)	Reaction Temperature (°C)	Reaction Time (min)	M _n (kg·mol ⁻¹); PDI
α-alkyne,ω-Br-PS	78.3	0.34 ^a	0.34	0.34	90	105	3.39; 1.11
α-alkyne,ω-Br-PS	78.3	0.34 ^b	0.34	0.34	80	240	3.30; 1.17
α-alkyne,ω-Br-PS	78.3	0.68 ^c	0.34	0.34	70	70	2.68; 1.10
α-alkyne,ω-Br-PS	78.3	0.68 ^d	0.34	0.34	110	63	2.93; 1.09

The following ligands were used: ^aPMDETA, ^bHMTETA, ^cdBbpy, and ^ddNbpy

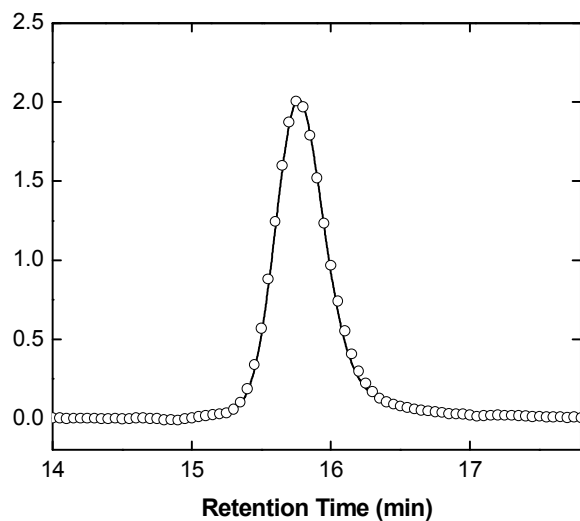


Figure S.1. Superimposed GPC chromatograms of bromine-functional polystyrene with average number molecular weights of $10900 \text{ g}\cdot\text{mol}^{-1}$, $\text{PDI}=1.06$ taken immediately after ATRP reaction (solid line) and 18 hours after stirring in air (open circle, plotted for every 30th data points) at room temperature.

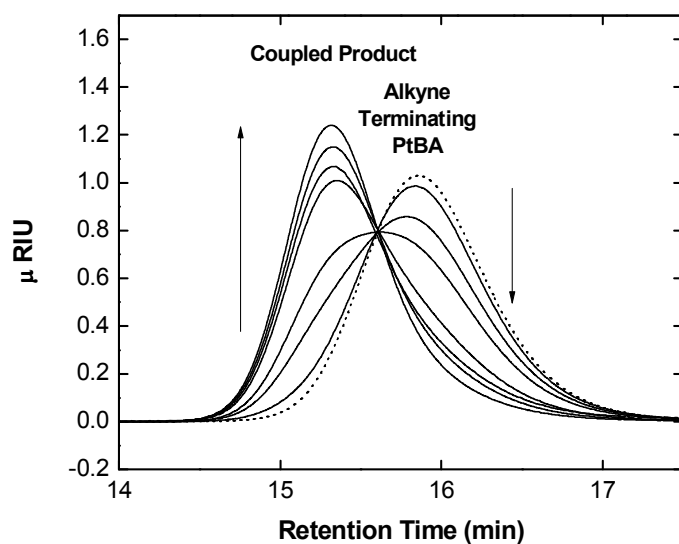


Figure S.2. GPC signals of α -alkyne, ω -Br-PtBA ($11300 \text{ g}\cdot\text{mol}^{-1}$, $\text{PDI}=1.19$) taken as a function of time after exposing the solution to air at room temperature

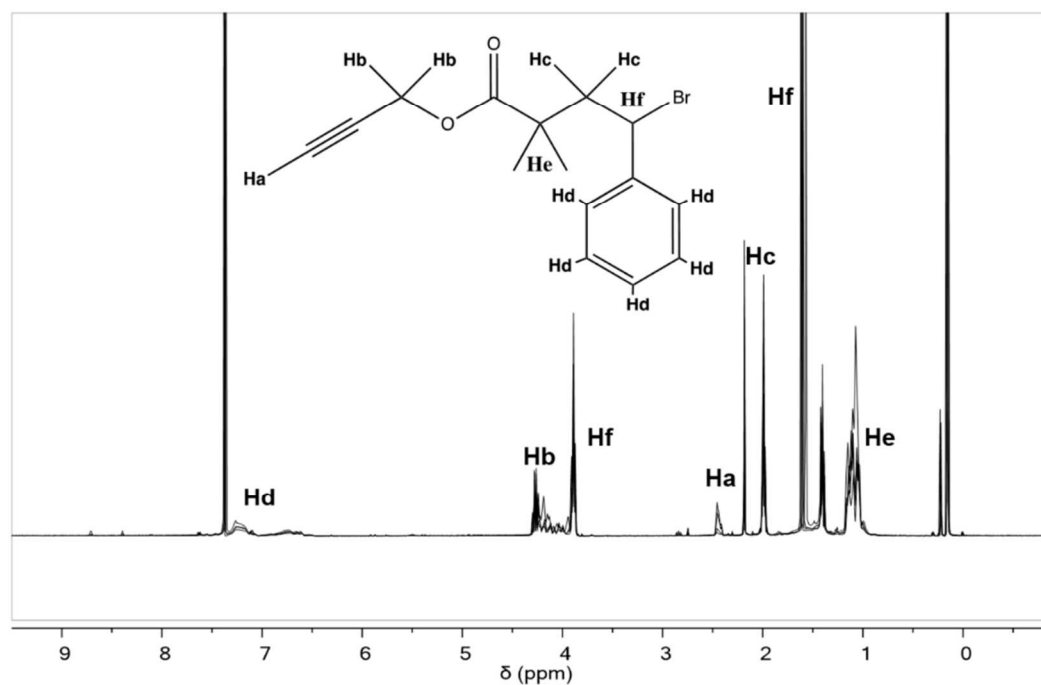


Figure S.3. Superimposed 1H NMR (400MHz) spectra recorded in $CDCl_3$ of deuterated α -alkyne, ω -Br-PS (Mn=3090, PDI=1.12) at varying exposure time to air at room temperature.

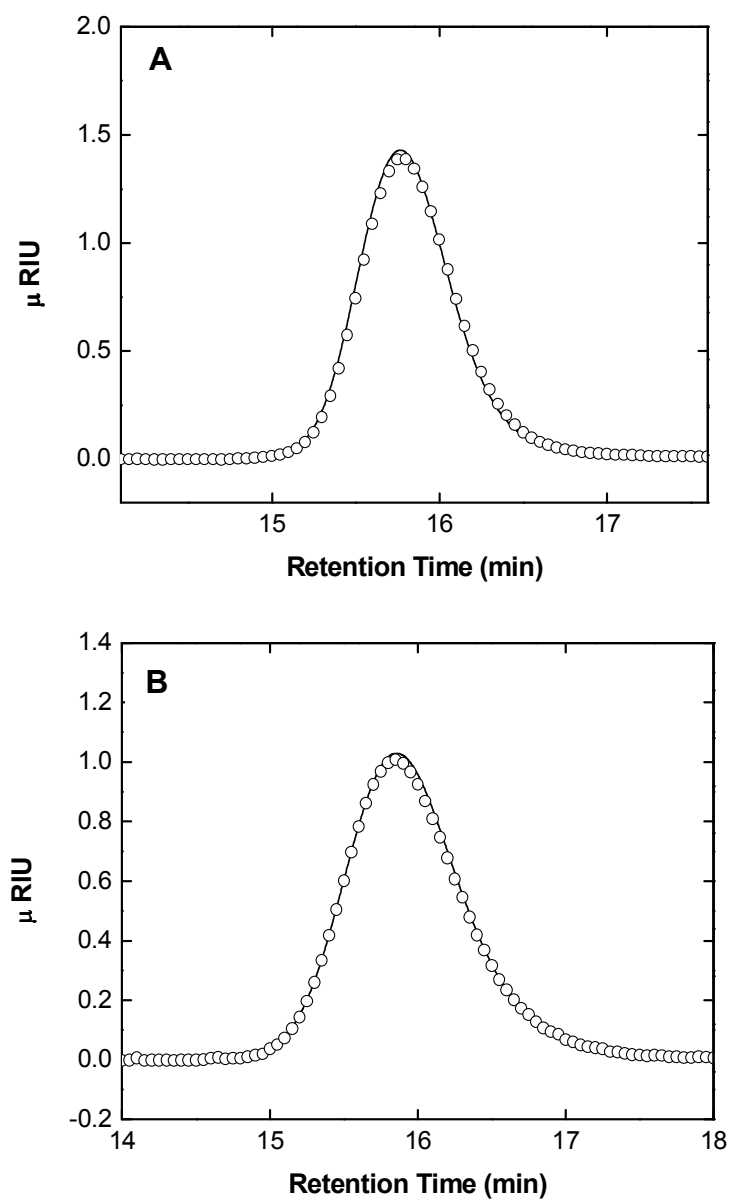


Figure S.4. GPC chromatograms taken immediately after ATRP (solid line) and 16 hours after exposure to air followed by copper removal at -28°C (open circle, potted for every 30th data points) for (A) α -alkyne, ω -Br-PS (10500 g·mol⁻¹, PDI=1.09); and (B) α -alkyne, ω -Br-PtBA (11300 g·mol⁻¹, PDI=1.19). The superimposed signals indicate that at low temperature, polymer coupling is eliminated.