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Supporting Information

Photothermally-Driven Cobalt Catalyzed Atom Transfer Radical Copolymerisation Enables Isocyanide Copolymer Synthesis

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Experimental

Materials

Vitamin B₁₂ (hydrate) (Cayman Chemicals, >95%) was modified according to literature procedure.¹ Methyl acrylate (MA; Sigma-Aldrich, 99%) was dried over calcium hydride, distilled under vacuum, and degassed via freeze-pump-thaw before transferring to the glovebox. Ethyl 2-bromopropionate (EBP; Oakwood, 99%) was dried over molecular sieves and degassed before transferring to glovebox. Tetrabutylammonium bromide (TBABr; TCI, 98%), was recrystallized in methanol and dried in vacuo before transferring to glovebox. Phenylbis(2,4,6-trimethylbenzoyl) phosphine oxide (BAPO photoinitiator; TCI, 96%), anhydrous *N*, *N*-dimethylformamide (DMF; Sigma-Aldrich, 99.8%), 2-morpholinoethyl isocyanide (MEI; Sigma-Aldrich, 98%), and *p*-toluenesulfonylmethyl isocyanide (TOSMIC; Oakwood, 98.5%) were used as received in the glove box. Zinc dust (Sigma Aldrich, -325 mesh) was rinsed with 10% hydrochloric acid, washed with water, methanol, and acetone, dried in vacuo, and transferred to the glovebox.

Instrumentation

Agilent 1260 Infinity II Isocratic Pump, with 1260 Infinity II Refractive Index detector using two SDV linear M, 8×300 mm, 3 µm columns with one SDV, 8×50 mm, 3 µm, guard column, was used for Molecular weight (M_n) and dispersity (D) of copolymers. Tetrahydrofuran with 250 ppm of BHT (THF; Sigma-Aldrich, >99.0%) used as the eluent at a flow rate of 1 ml/min at 35 °C. The GPC system was calibrated using narrow polystyrene standards.

Nuclear magnetic resonance (NMR) spectra obtained on a Bruker 400 MHz or 500 MHz at room temperature using *d*-chloroform (CDCl₃) as the solvent.

The UV-Vis measurements obtained from Agilent Cary 60 UV-Vis spectrometer. UV-Vis solutions were prepared in a glovebox and measured in sealed quartz cuvettes with screw caps.

LED were purchased from aspectLED and adhered inside a glass dish.

Relative light intensity was measured using a Thorlabs' C-Series Pyroelectric Energy Sensor. Temperature of photoreactor was measured by using the temperature probe on the hot plate and a thermometer.

Light Setup



Figure S1. Picture of reaction setup, vials are 2.5 in away from the LEDs.



Figure S2. Modification of vitamin B_{12} to the hydrophobic derivative. Synthesis of the heptamethyl ester cobyrinate was performed following the literature reports (Gryko *et al.*, *J. Am. Chem. Soc.*, **2020**, *142*, 5355–5361; https://doi.org/10.1021/jacs.0c00245).

Bulk reduction of HME-Cob



Figure S3. Scheme for the reduction of HME-Cob via zinc/NH₄Cl in DMF.

In the glovebox, HME-Cob (102 mg, 0.088 mmol, 1 equiv.), Zn (2.7 mg, 0.041 mmol, 0.5 equiv.), and NH₄Cl (4.5 mg, 0.059 mmol, 0.67 equiv.) were stirred in 3 mL of DMF. The stock solution of the reduced cobalt complex, HME-Cob (Co^{II}), was stored in the glovebox freezer at -20 °C.

General procedure for MA: Isocyanide (180:20) copolymerisation under photothermal activation



Figure S4. General reaction scheme.

Stock solutions of TBABr (0.055 M) and EBP (0.55 M) were prepared fresh in DMF. In the glovebox, a one-dram vial was charged with a stir bar and DMF (278 μ L), HME-Cob (Co^{II}) (0.028 M, 50 μ L of the stock solution, 0.05 equiv.), MA (0.446 mL, 4.95 mmol, 180 equiv.), TBABr (0.055 M, 50 μ L in the stock solution, 0.10 equiv.), EBP (0.55 M, 50 μ L stock solution, 1 equiv.) and isocyanide (0.55 mmol, 20 equiv.), were added to the reaction vial. The vials were brought out of the glovebox after sealing with septa cap. The reaction was irradiated in an LED dish photoreactor placed in an ice bath with airflow, to maintain temperature of photoreactor 25 – 30 °C. For conversion, aliquots via N₂ purged syringe were taken periodically to monitor the monomer conversion and the molecular weight of the copolymer using ¹H NMR and GPC analysis, respectively. For copolymerisations using BAPO, a stock solution of 0.055 M in DMF was made in the glovebox and covered with foil. The solution of BAPO was added to the reaction vial via a nitrogen purged syringe before light irradiation.

Mechanism of polymerization

ATRP Mechanism





Figure S5. Mechanism of ATRP copolymerization with methyl acrylate (top), and isocyanide addition to growing chain end (middle). Potential side reactions with isocyanides such as β -scission and 1,5 HAT shown (bottom).

Degree of copolymerisation (DP) for Copolymers Made with TOSMIC



Figure S6. Target DP copolymerisation with methyl acrylate and *p*-toluenesulfonylmethyl isocyanide with а ratio of 9:1 for all entries. Copolymerisation conditions: [MA]/[Isocyanide]/[HME]/[EBP]/[TBABr]/[BAPO] = MA/TOSMIC/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~ 0.2 W) with air-cooling for 2 h. Monomer conversion from ¹H NMR in CDCl₃. Conversions used to calculate theoretical molecular weight $(M_{n,th})$ and theoretical TOSMIC incorporation (TOSMIC_{th}). $M_{n,th} = (DP_{MA} * MW_{MA} * Conv._{MA}) +$

(DP_{TOSMIC} * MW_{TOSMIC} * Conv._{TOSMIC}) + MW_{EBP}. MEI_{th} = (DP_{MEI} * Conv._{TOSMIC}) / ((DP_{TOSMIC} * Conv._{TOSMIC}) + (DP_{MA} * Conv._{MA})) Experimental molecular weights (M_{n,exp}.) obtained via gel permeation chromatography (GPC). Initiator efficiency (I_{eff}) = $M_{n,th}$ / $M_{n,exp}$. ¹H NMR of precipitated samples used for TOSMIC % incorporation TOSMIC_{exp}).





Figure S7. Target DP copolymerisation with methyl acrylate and 2-morpholinoethyl isocyanide with a ratio of 9:1 for all entries. Copolymerization conditions: [MA]/[MEI]/[HME]/[EBP]/[TBABr]/[BAPO] = MA/MEI/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h. Monomer conversion from ¹H NMR in CDCl₃. Conversions used to calculate theoretical molecular weight ($M_{n,th}$) and theoretical MEI incorporation (MEI_{th}). $M_{n,th} = (DP_{MA} * MW_{MA} * Conv._{MA}) + (DP_{MEI} * MW_{MEI} * Conv._{MEI}) + MW_{EBP}$. MEI_{th} = (DP_MEI * Conv._MEI) / ((DP_MEI * Conv._MEI) + (DP_MA * Conv._MA)) Experimental molecular weights ($M_{n,exp}$.) obtained via gel permeation chromatography (GPC). Initiator efficiency (I_{eff}) = $M_{n,th}/M_{n,exp}$. ¹H NMR of precipitated samples used to for MEI % incorporation (MEI_{exp}).



Figure S8. Addition of tetrabutylammonium bromide for control over copolymerisation. Copolymerization conditions: [MA]/[Isocyanide]/[HME]/[EBP]/[**TBABr**]/[BAPO] = 180/20/0.05/1/X/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h. Monomer conversion from ¹H NMR in CDCl₃. Conversions used to calculate theoretical molecular weight ($M_{n,th}$) and theoretical MEI incorporation (MEI_{th}). M_{n,th} = (DP_{MA} * MW_{MA} * Conv._{MA}) + (DP_{MEI} * MW_{MEI} * Conv._{MEI}) + MW_{EBP}. MEI_{th} = (DP_{MEI} * Conv._{MEI}) / ((DP_{MEI} * Conv._{MEI}) + (DP_{MA} * Conv._{MA})) Experimental molecular weights ($M_{n,exp}$.) obtained via gel permeation chromatography (GPC). Initiator efficiency (I_{eff}) = $M_{n,th} / M_{n,exp}$. ¹H NMR of precipitated samples used to for MEI % incorporation (MEI_{exp}).

Copolymerization Controls Without BAPO



Figure S9. Controls of copolymerization without photoinitator, BAPO. Copolymerisation conditions: [MA]/[Isocyanide]/[HME]/[EBP]/[TBABr] = 180/20/0.05/1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h. Conversions used to calculate theoretical molecular weight ($M_{n,th}$) and theoretical MEI incorporation (MEI_{th}). M_{n,th} = (DP_{MA} * MW_{MA} * Conv._{MA}) + (DP_{MEI} * MW_{MEI} * Conv._{MEI}) + MW_{EBP}. MEI_{th} = (DP_{MEI} * Conv._{MEI}) / ((DP_{MEI} * Conv._{MEI}) + (DP_{MA} * Conv._{MA})) Experimental molecular weights ($M_{n,exp}$.) obtained via gel permeation chromatography (GPC). Initiator efficiency (I_{eff}) = $M_{n,th}/M_{n,exp}$. ¹H NMR of precipitated samples used to for MEI % incorporation (MEI_{exp}).

Feed Ratio Screen MA:MEI



Figure S10. Data for varying the ratio between MA and MEI. Copolymerisation conditions: [MA]/[MEI]/[HME]/[EBP]/[TBABr]/[BAPO] = MA/MEI/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h. Conversions used to calculate theoretical molecular weight ($M_{n,th}$) and theoretical MEI incorporation (MEI_{th}). $M_{n,th} =$ (DP_{MA} * MW_{MA} * Conv._{MA}) + (DP_{MEI} * MW_{MEI} * Conv._{MEI}) + MW_{EBP}. MEI_{th} = (DP_{MEI} * Conv._{MEI}) / ((DP_{MEI} * Conv._{MEI}) + (DP_{MA} * Conv._{MA})) Experimental molecular weights ($M_{n,exp}$.) obtained via gel permeation chromatography (GPC). Initiator efficiency (I_{eff}) = $M_{n,th}/M_{n,exp}$. ¹H NMR of precipitated samples used to for MEI % incorporation (MEI_{exp}).



Figure S11. Monitoring conversion of copolymerisation. Copolymerisation conditions: MA]/[Isocyanide]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20I/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h. Aliquots for each time point were taken via N₂ purged syringe. Conversions used to calculate theoretical molecular weight ($M_{n,th}$) and theoretical MEI incorporation (MEI_{th}). M_{n,th} = (DP_{MA} * MW_{MA} * Conv._{MA}) + (DP_{MEI} * MW_{MEI} * Conv._{MEI}) + MW_{EBP}. MEI_{th} = (DP_{MEI} * Conv._{MEI}) / ((DP_{MEI} * Conv._{MEI}) + (DP_{MA} * Conv._{MA})) Experimental molecular weights (M_{n,exp}.) obtained via gel permeation chromatography (GPC). Initiator efficiency (I_{eff}) = $M_{n,th}/M_{n,exp}$. ¹H NMR of precipitated samples used to for MEI % incorporation (MEI_{exp}).

Longer Periods of Temporal Control



Figure S12. Temporal control for a 180:20 (MA:MEI) cocopolymerisation, long period of reaction without light after short cycles of on/off light irradiation. **A**) Full graph showing conversion of both MA and MEI. **B**) Zoom in version of graph to show MEI conversion. **C**) Data table for each time point. Copolymerisation conditions: Reaction conditions using 0.028 mmol of EBP: [MA]/[Isocyanide]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h. Aliquots for each on/off cycle were taken in a N₂ purged syringe for crude NMR and GPC analysis.

Insitu Chain Extension



Figure S13. Results for copolymerization with MA and MEI after 3 h. Results after addition of MA for insitu chain extension. Reaction conditions with HME-Cob (Co^{II}) using 0.028 mmol of EBP: $[MA]/[MEI]/[HME-Cob (Co^{II})]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/1/0.1/0.1$ in 50 vol % DMF for 3 h then addition of 400 equivalents of MA and left to stir for 4 h. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling.

Copolymerisation via Cu-catalysed ATRP



Figure S14. General scheme of copolymerisation using CuBr/PMDETA or HME with results of with copolymerisation. Reaction conditions CuBr using 0.028 mmol of EBP: [MA]/[Isocyanide]/[CuBr]/[PMDETA]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/0.06/1/0.1/0.1 in 50 vol % DMF. Reaction conditions using with HME using 0.028 mmol of EBP: [MA]/[Isocyanide]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~ 0.2 W) with air-cooling for 2 h.





Figure S15. Precipitated ¹H NMR for copolymer made with a 9:1 ratio of MA to MEI. Standard copolymerisation conditions: [MA]/[MEI]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/1/0.1/1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h.



Figure S16. Precipitated ¹H NMR for copolymer made with a 9:1 ratio of MA to MEI. Standard copolymerisation conditions: [MA]/[TOS]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/1/0.1/1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h.



Figure S17. Precipitated ¹H NMR for copolymer made with a 9:1 ratio of MA to MEI without the use of photoinitator, BAPO. Standard copolymerisation conditions: [MA]/[MEI]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20/0.05/1/0.1/0 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h.



Figure S18. Precipitated ¹H NMR for copolymer made with a 9:1 ratio of MA to MEI without the use of photoinitator, BAPO and without additional TBABr. Standard copolymerisation conditions: [MA]/[MEI]/[HME]/[EBP]/[TBABr]/[BAPO] = 180/20/0/1/0/0 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h.



Figure S19. ¹H NMR spectra of isolated macroinitiator. Copolymerisation conditions: MA]/[Isocyanide]/[HME]/[EBP]/[TBABr]/[BAPO] = 45/5/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h.



Figure S20. ¹H NMR of precipitated chain extended polymer with *tert*-butyl acrylate. Copolymerisation conditions using 0.029 mmol macroinitiator: [tBA]/[pMA-r-MEI]/[HME]/[TBABr]/[BAPO] = 150/1/0.05/1/0.1/0.1 in 50 vol % DMF. Reactions were prepared in the glovebox and brought out of the glovebox to react under white LEDs (relative intensity ~0.2 W) with air-cooling for 2 h.



Figure S21. Zoom of ¹H NMR spectra showing chain ends of parent polymer (top) and chain extended polymer (bottom).

Reference

1 M. Ociepa, A. J. Wierzba, J. Turkowska and D. Gryko, J. Am. Chem. Soc., 2020, 142, 5355–5361.