

Supporting Information

A comparative study on atomically precise Au nanoclusters as catalysts for the aldehyde–alkyne–amine (A^3) coupling reaction: Ligand effects on the nature of the catalysis and efficiency

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Experimental

Figure S1. ^1H NMR spectra for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%) in CD_2Cl_2 .

Figure S2. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%) in CD_2Cl_2 at 21 °C.

Figure S3. ^1H NMR spectra for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%) in CDCl_3 .

Figure S4. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%) in CDCl_3 at 21 °C.

Figure S5. ^1H NMR spectra (CDCl_3 , aromatic region) for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%), neat, 21 °C, for the first 12 h.

Figure S6. Plot of $\ln(1-\text{Conv.})$ vs time for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%), neat, 21 °C.

Figure S7. UV-Vis spectrum of the recovered catalyst in DCM, from the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%) under neat conditions at 21 °C for 60 h.

Figure S8. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₃** (0.03 mol%), neat, 21 °C.

Figure S9. ^1H NMR spectra (CDCl_3 , aromatic region): (Top) For the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%), neat, 21 °C, for the first 12 h. Enlarged to show the resonances for the catalyst. (Bottom) An authentic sample of **Au₁₃**.

Figure S10. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₃** (0.5 mol%) and (*p*-tolyl)₃SbAuCl (6.5 mol%), neat, 21 °C.

Figure S11. ^1H NMR spectra (CDCl_3 , aromatic region) for the A^3 coupling reaction catalyzed by **Au₂₅** (0.5 mol%), neat, 21 °C, for the first 40 h.

Figure S12. ^1H NMR spectrum (CD_2Cl_2 , aromatic region): (Top) An authentic sample of $[\text{Au}_{11}(\text{PPh}_3)_7\text{Cl}_3]$ (**Au₁₁'**), prepared according to the literature method. (Bottom) Catalyst recovered from the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, 21 °C (bottom).

Figure S13. ^1H NMR spectra (CDCl_3 , aromatic region): (Top) A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, 21 °C. (Bottom) Recovered catalyst.

Figure S14. UV-Vis spectrum of the crude for the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, 21 °C, at 348 h (71% conversion).

Figure S15. UV-Vis spectrum (DCM) of the recovered catalyst from the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, 21 °C at 348 h (71% conversion).

Figure S16. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%) and Ph_3PAuCl (1.5 mol%), neat, 21 °C.

Figure S17. ^1H NMR spectra (CDCl_3 , aromatic region): (Top) For the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, 50 °C (for the first 12 h) or 21 °C (for the rest). (Bottom) Authentic sample of **Au₁₁**.

Figure S18. UV-Vis spectrum of the crude for the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat conditions, at 50 °C (for the first 12 h) and 21 °C (for another 244 h).

Figure S19. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, at 50 °C (for the first 12 h) and 21 °C (for the rest).

Figure S20. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₂₅** (0.03 mol%), neat, 50 °C.

Figure S21. Plot of conversion vs time for the A^3 coupling reaction catalyzed by **Au₁₃** (0.03 mol%), neat, 50 °C.

Experimental

All solvents and reagents including benzaldehyde, phenylacetylene, and piperidine were commercially available and used as received. $[\text{Au}_{13}\{\text{Sb}(p\text{-tolyl})_3\}_8\text{Cl}_4][\text{Cl}]$ (**Au13**),¹ $[\text{Au}_{11}(\text{PPh}_3)_8\text{Cl}_2][\text{Cl}]$ (**Au11**)² and $[\text{Au}_{25}(\text{SC}_2\text{H}_4\text{Ph})_{18}][\text{TOA}]$ (**Au25**)³ were prepared according to literature methods. UV-Vis absorption spectra were recorded on a Shimadzu UV-1800 Spectrophotometer. NMR spectra were recorded on a JEOL ECA400 SL NMR spectrometer at room temperature. The ¹H NMR chemical shifts were referenced to the residual proton resonance and the chemical shifts (δ) are given in ppm. TGA measurement was performed on TGA-Q500 thermogravimetric analyzer at a heating rate of 10 °C/min under N₂ purge (60 ml/min).

A³ coupling reaction: In a typical procedure, benzaldehyde (106 mg, 1.0 mmol), piperidine (102 mg, 1.2 mmol) and phenylacetylene (133 mg, 1.3 mmol) were mixed in a 10 ml of Pyrex tube containing suitable amount of catalyst under ambient conditions. After additions of catalyst and reagents, (dark) orange or (dark) red oil mixture was obtained and then the tube was capped tightly and the mixture was stirred at room temperature (21 °C) or 50 °C. Suitable amount of oil crude was directly drawn into a NMR tube or a cuvette for subsequent ¹H NMR or UV-Vis absorption experiments, after certain reaction time. When the reactions were carried out in solvents, 1.0 ml of the solvent needed was directly added into the tube under ambient conditions before capping and stirring.

Determination of the conversion rate of benzaldehyde by ¹H NMR spectrum: Two singlet resonances at $\delta = 10.0$ ppm and 4.81 ppm are ascribed to the hydrogens in benzaldehyde ($\text{HC}=\text{O}$) and product propargylamine ($\text{R}_1\text{R}_2\text{R}_3\text{CH}$), respectively. Since there is essentially no more side reaction found in the ¹H NMR spectrum of the crude, the relative integral ratios of those two resonances were used to determine the conversion of benzaldehyde.

Product separation: When the reaction was completed, the mixture was washed with ethyl ether (3 x 5 mL) and filtered. The compounds were concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 20:1) to afford the desired propargylamines as a pale yellow oily liquid. ¹H NMR (CDCl_3): δ 1.40-1.67 (m, 6H), δ 2.56-2.59 (t, 4H), δ 4.81 (s, 1H), δ 7.26-7.37 (m, 6H), δ 7.52-7.55 (m, 2H), δ 7.63-7.71 (m, 2H).

¹ Y.-Z. Li, R. Ganguly, K. Y. Hong, Y. Li, M. E. Tessensohn, R. Webster, W. K. Leong, *Chem. Sci.* 2018, **9**, 8723-8730.

² L. C. McKenzie, T. O. Zaikova, J. E. Hutchison, *J. Am. Chem. Soc.* 2014, **136**, 13426-13435.

³ M. Zhu, E. Lanni, N. Garg, M. E. Bier, R. Jin, *J. Am. Chem. Soc.* 2008, **130**, 1138-1139.

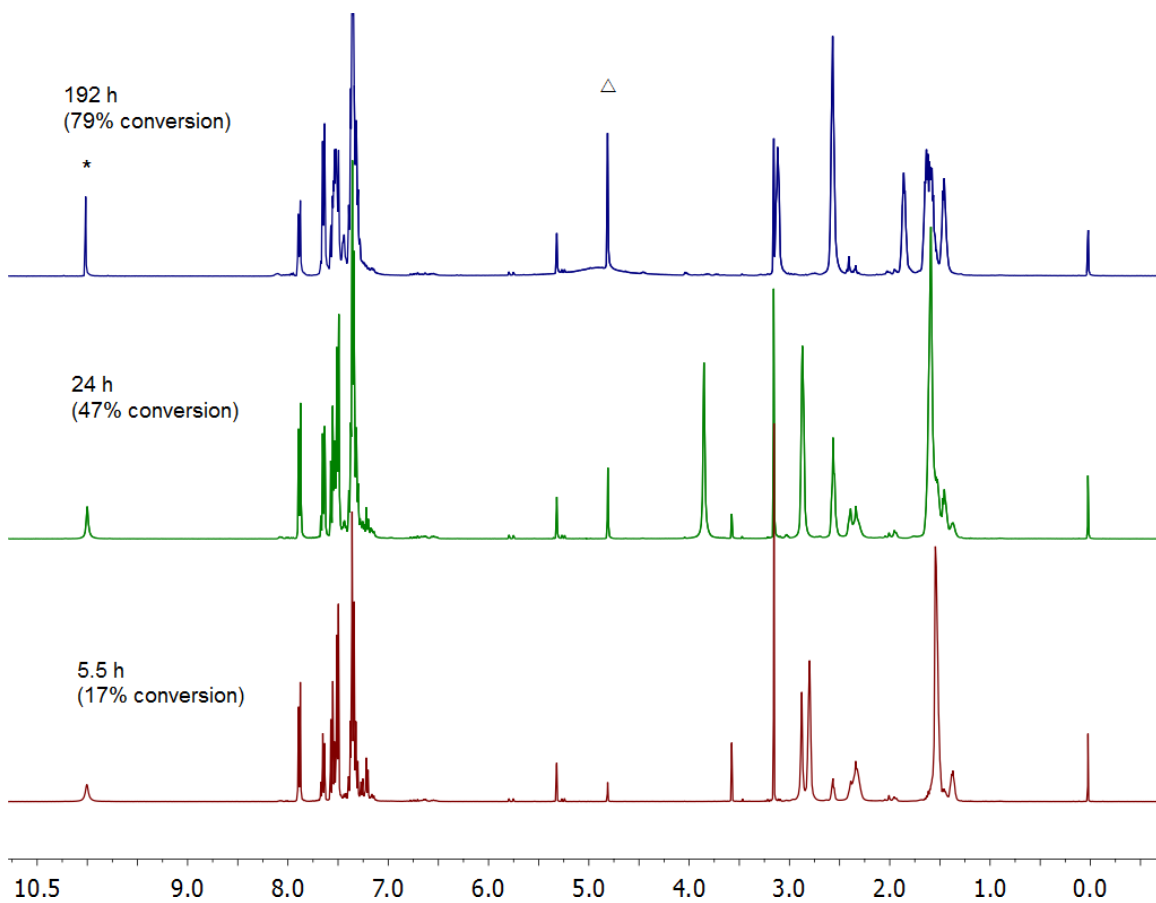


Figure S1. ¹H NMR spectra for the A³ coupling reaction catalyzed by Au₁₃ (0.5 mol%) in CD₂Cl₂.

Note: Resonance at 10.0 ppm (*) and 4.81 ppm (Δ) are assigned to benzaldehyde (HC=O) and propargylamine, respectively. Their relative integration ratios were used to determine the conversion of benzaldehyde. Since there are no other side reactions observed, the conversion of benzaldehyde was also used to compute reaction yield.

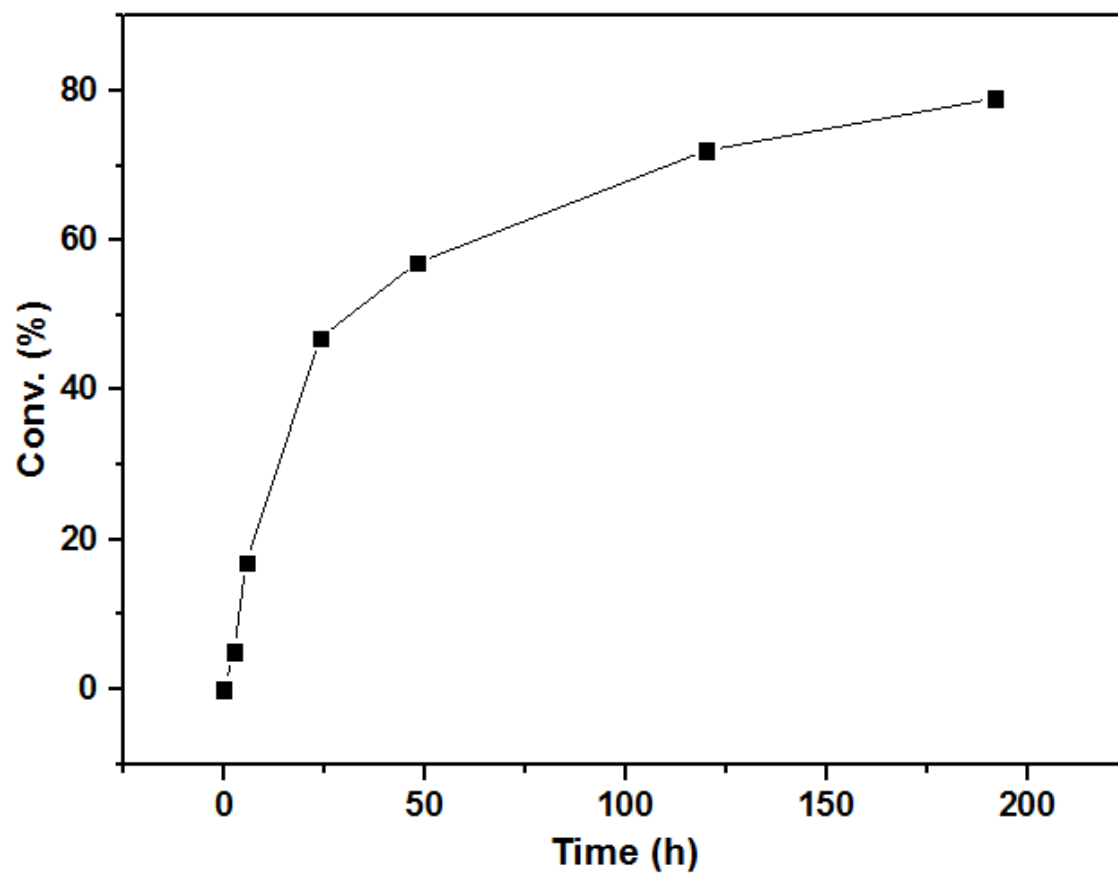


Figure S2. Plot of conversion vs time for the A³ coupling reaction catalyzed by Au₁₃ (0.5 mol%) in CD₂Cl₂ at 21 °C.

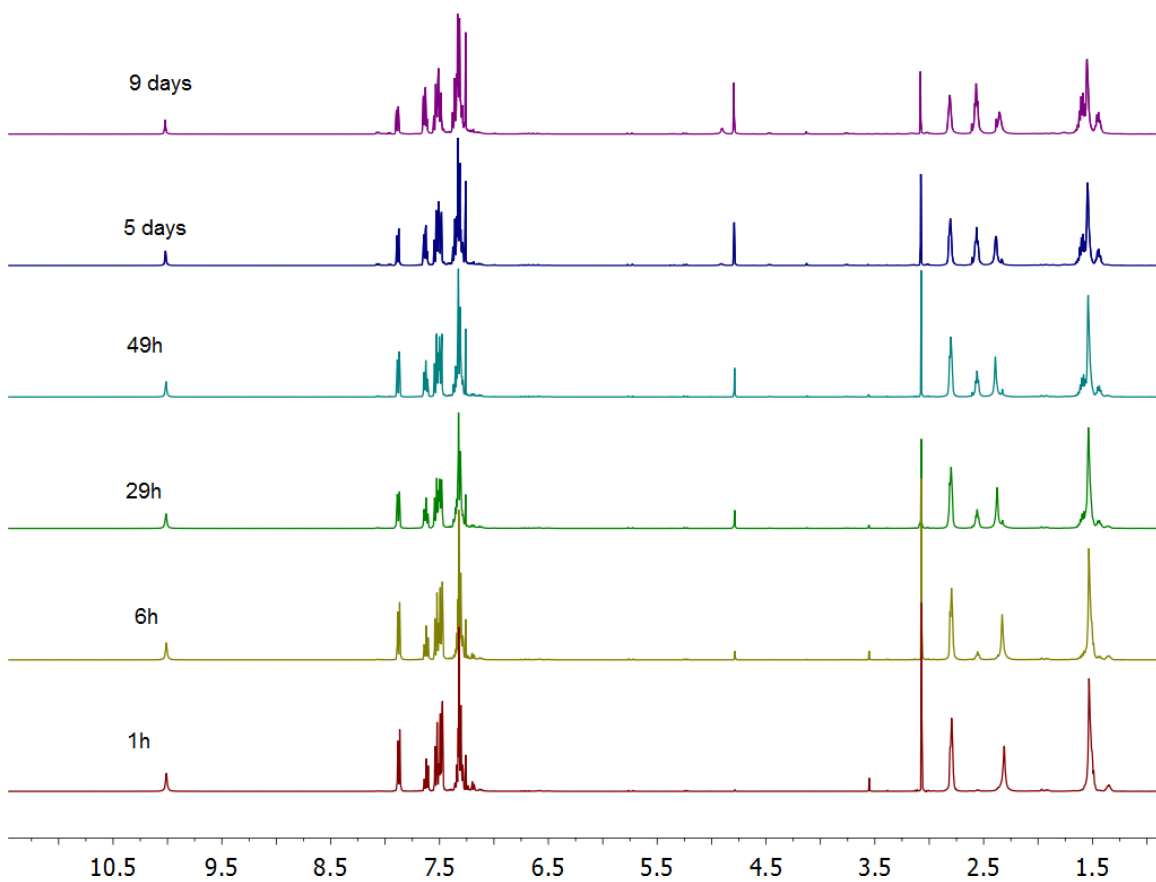


Figure S3. ¹H NMR spectra for the A³ coupling reaction catalyzed by Au₁₃ (0.5 mol%) in CDCl₃.

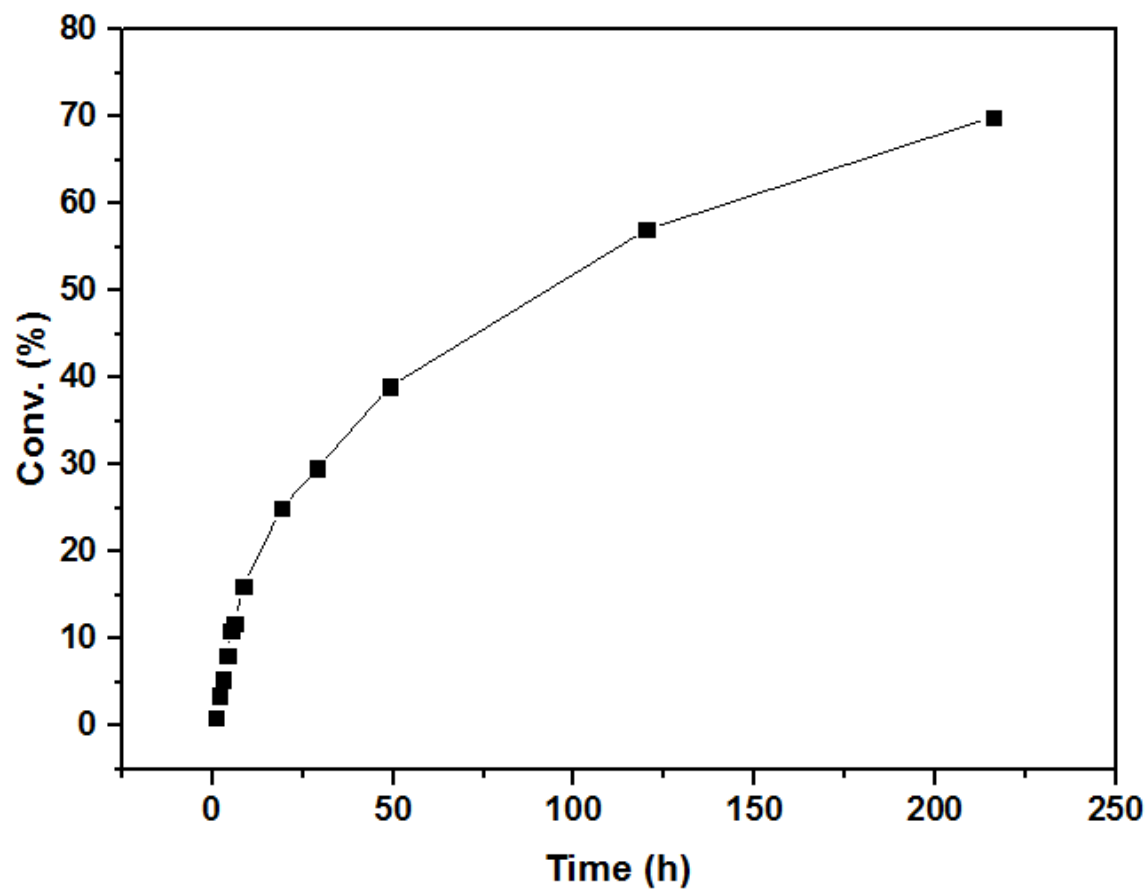


Figure S4. Plot of conversion vs time for the A³ coupling reaction catalyzed by Au₁₃ (0.5 mol%) in CDCl₃ at 21 °C.

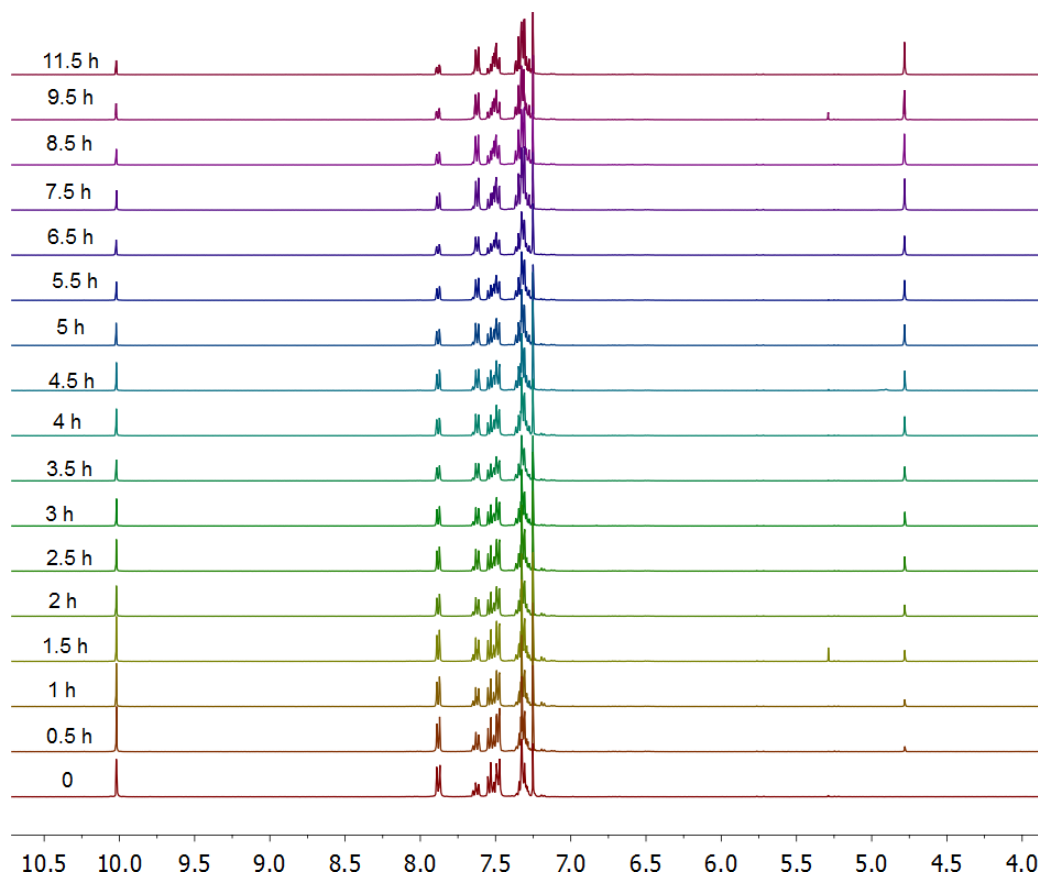


Figure S5. ¹H NMR spectra (CDCl₃, aromatic region) for the A³ coupling reaction catalyzed by Au₁₃ (0.5 mol%), neat, 21 °C, for the first 12 h.

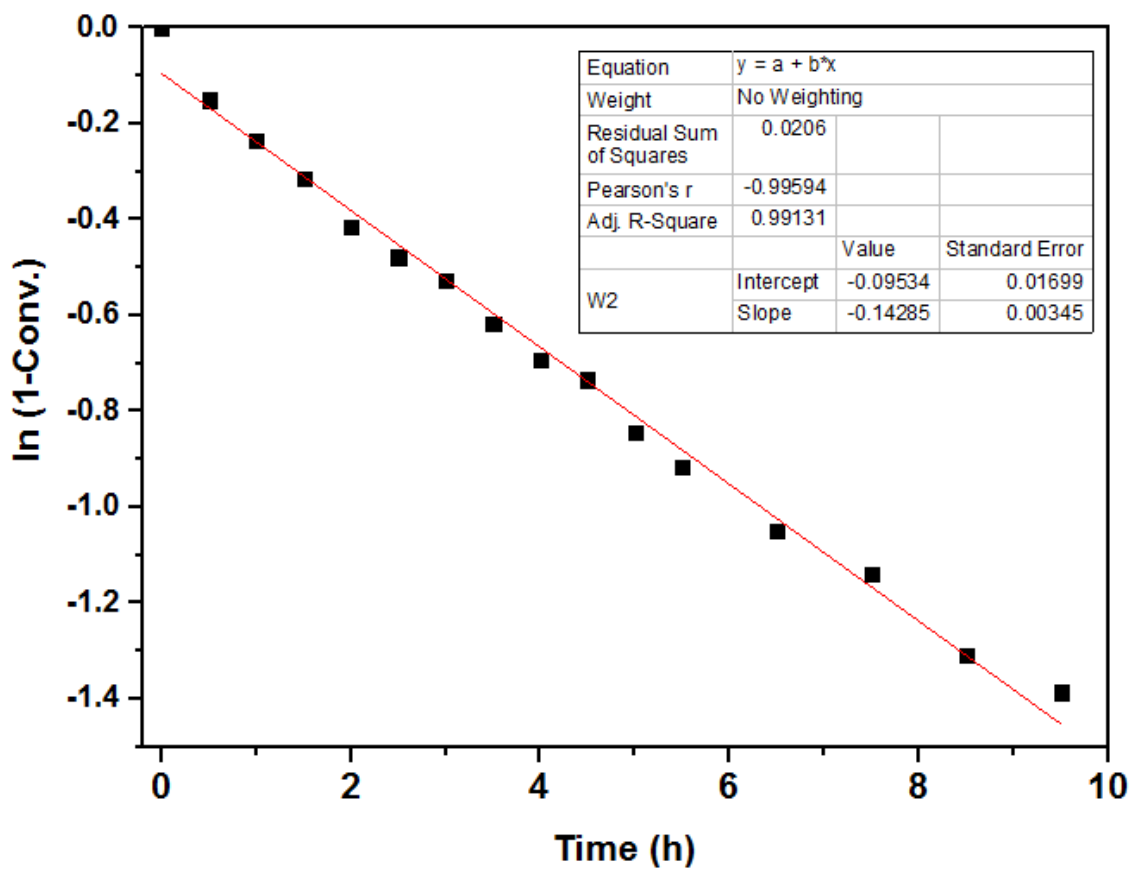


Figure S6. Plot of $\ln(1-\text{Conv.})$ vs time for the A^3 coupling reaction catalyzed by **Au13** (0.5 mol%), neat, 21 °C.

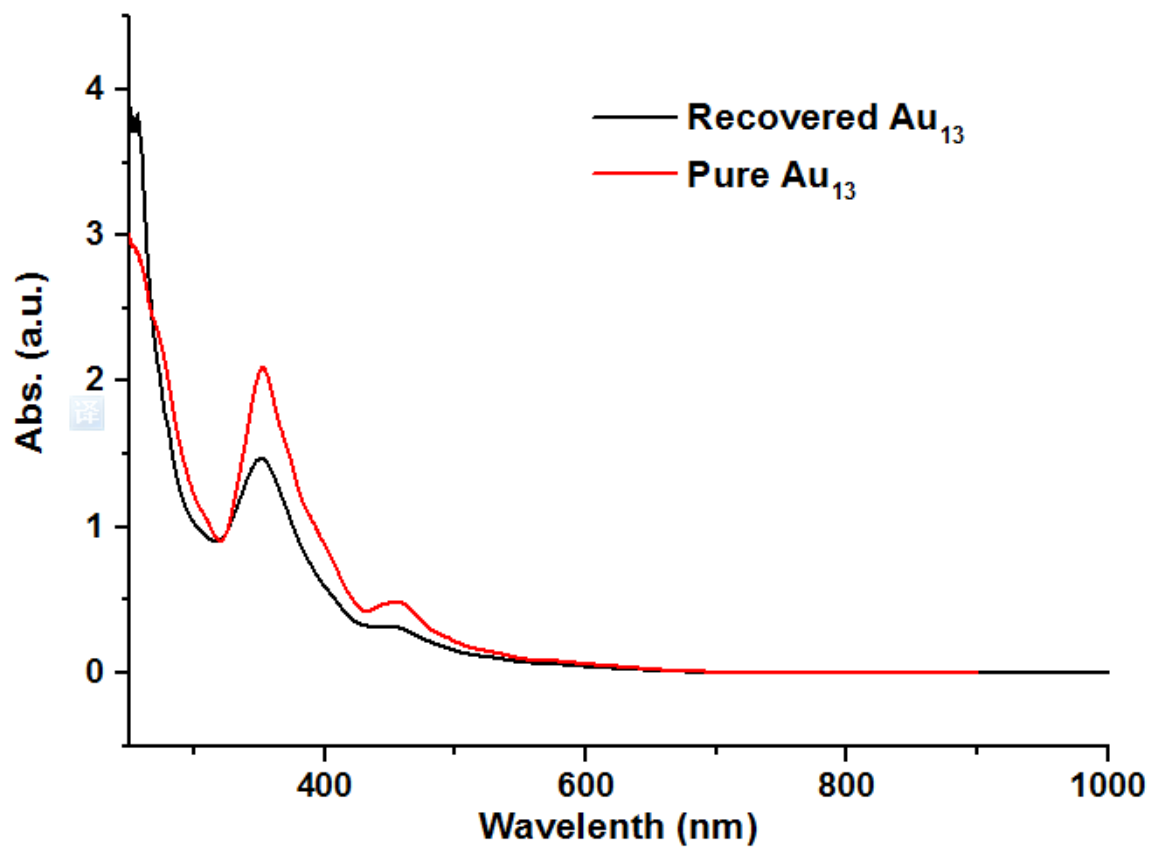


Figure S7. UV-Vis spectrum of the recovered catalyst in DCM, from the A³ coupling reaction catalyzed by Au₁₃ (0.5 mol%) under neat conditions at 21 °C for 60 h.

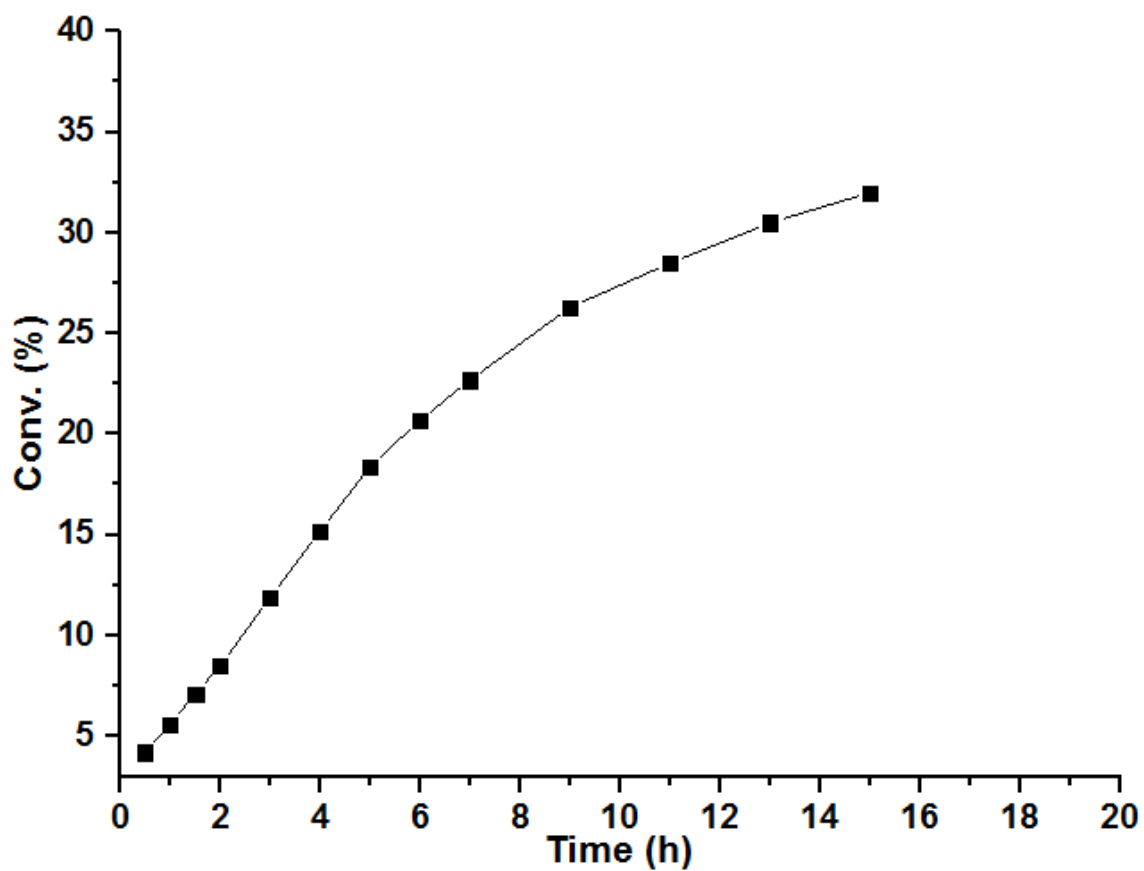


Figure S8. Plot of Conversion vs time for the A³ coupling reaction catalyzed by Au₁₃ (0.03 mol%), neat, 21 °C.

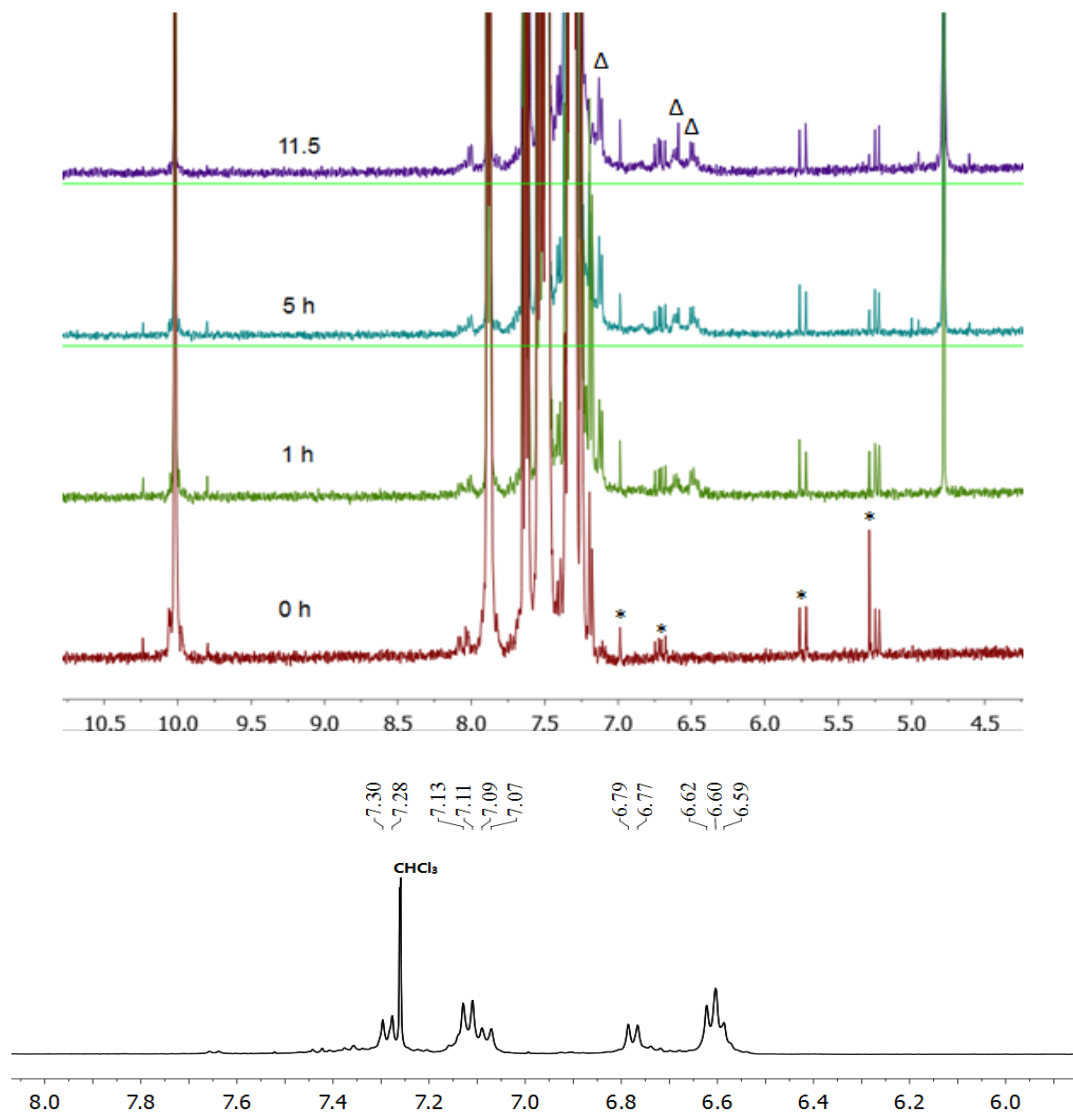


Figure S9. ^1H NMR spectra (CDCl_3 , aromatic region): (Top) For the A^3 coupling reaction catalyzed by Au_{13} (0.5 mol%), neat, 21 $^\circ\text{C}$, for the first 12 h. Enlarged to show the resonances for the catalyst. (Bottom) An authentic sample of Au_{13} .

Note: Peaks labelled with * are impurities. Peaks centred at 6.48, 6.59 and 7.10 ppm (labelled with Δ) ascribable to a “less intact” Au_{13} cluster with one or more ligands dissociated or replaced; these do not change in intensity, pattern and position within 12 h when conversion reached *ca.* 79%, suggesting that the real catalytically active species is most probably the “less intact” Au_{13} cluster, rather than its further decomposition products.

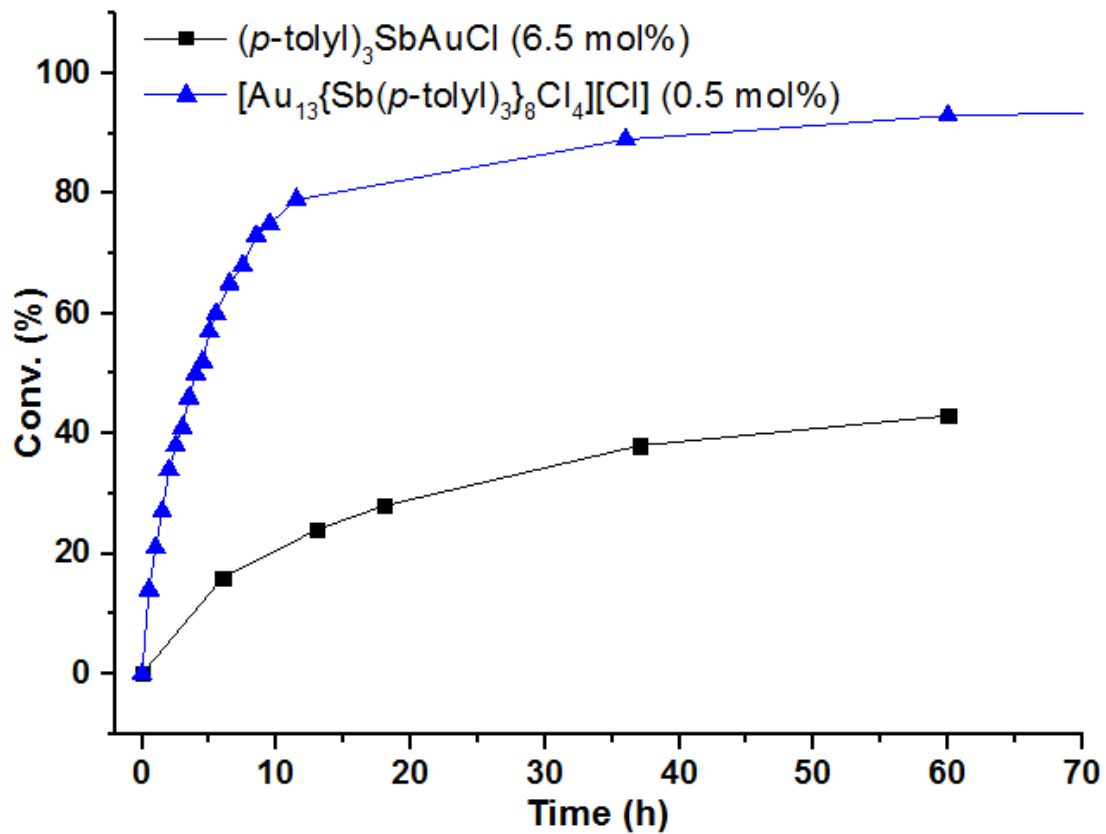


Figure S10. Plot of conversion vs time for the A^3 coupling reaction catalyzed by Au_{13} (0.5 mol%) and $(\textit{p}\text{-tolyl})_3\text{SbAuCl}$ (6.5 mol%), neat, 21 °C.

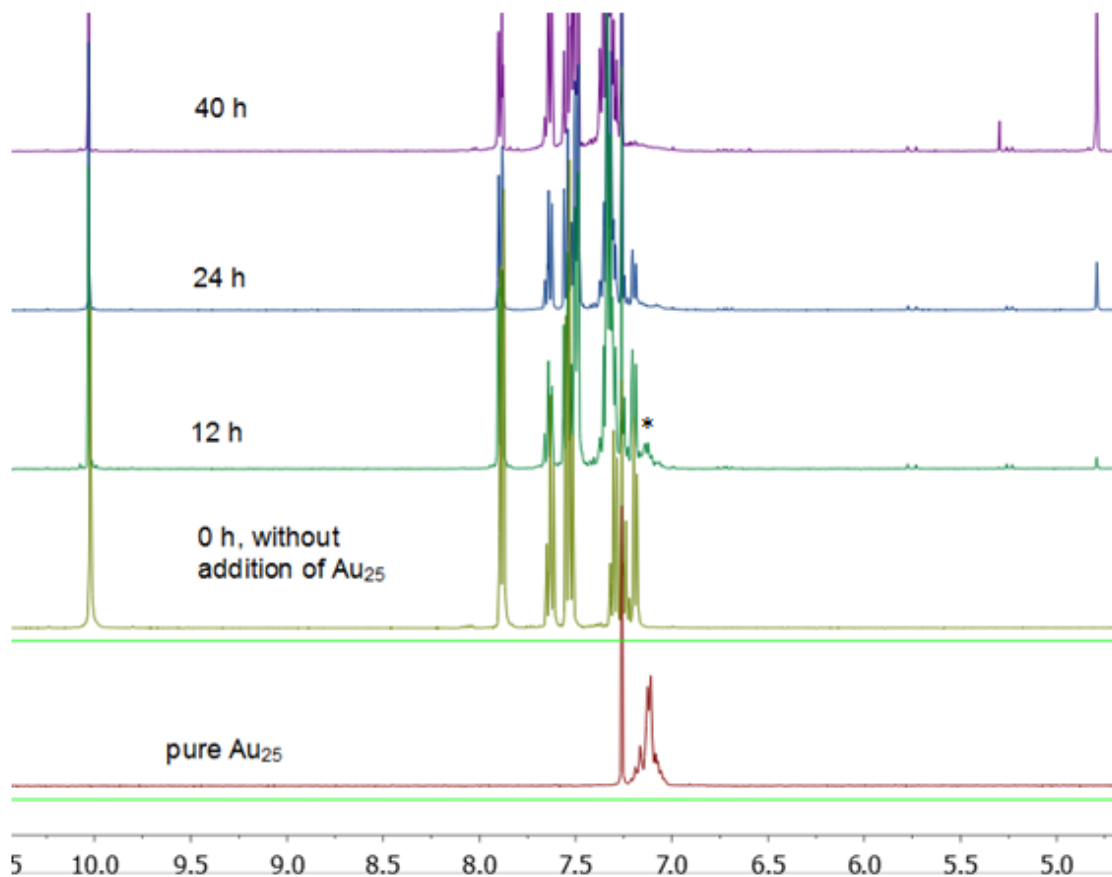


Figure S11. ^1H NMR spectra (CDCl_3 , aromatic region) for the A^3 coupling reaction catalyzed by Au_{25} (0.5 mol%), neat, 21°C , for the first 40 h.

Note: Bottom spectrum is of pure Au_{25} for comparison. Resonances ascribable to the catalyst (*) observable after 12h (4% conversion). The peaks gradually disappeared over time, accompanied by large increase in conversion to 58% after 40 h, indicating that the catalytically active species may be the decomposition products of Au_{25} .

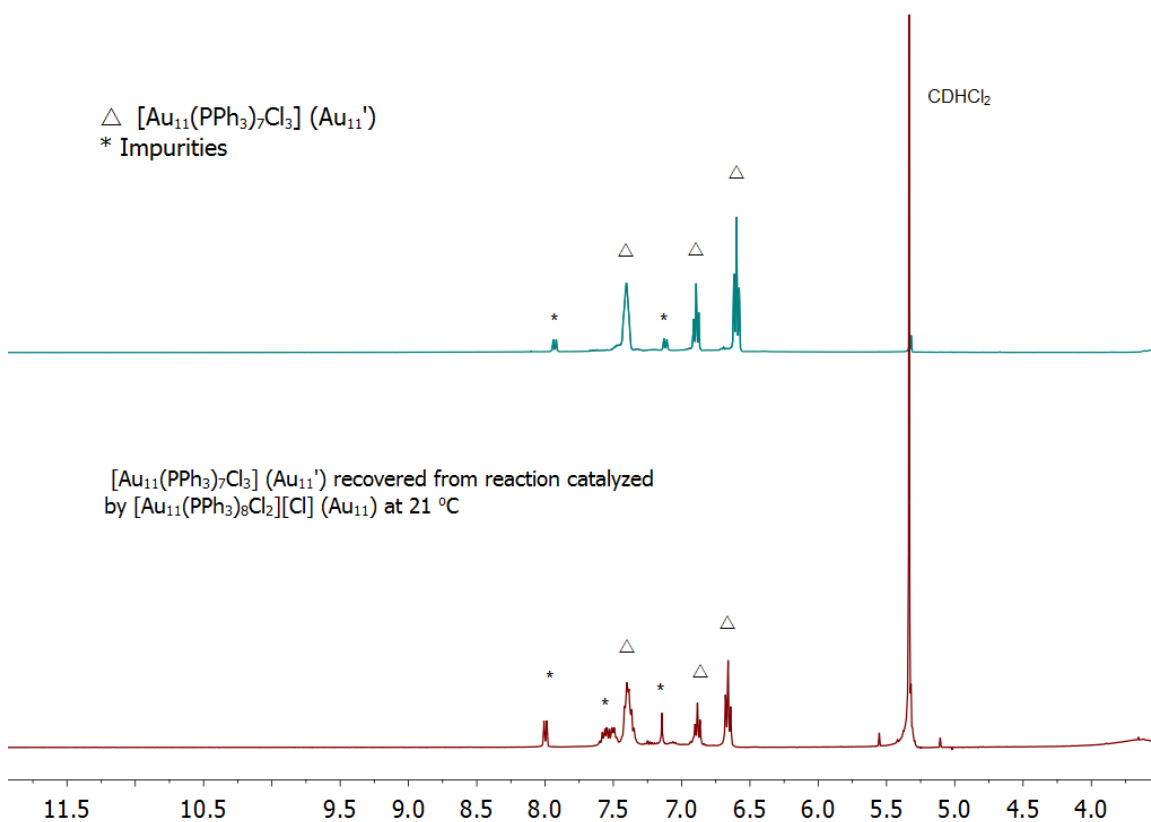


Figure S12. ^1H NMR spectrum (CD_2Cl_2 , aromatic region): (Top) An authentic sample of $[\text{Au}_{11}(\text{PPh}_3)_7\text{Cl}_3]$ (Au_{11}'), prepared according to the literature method.⁴ (Bottom) Catalyst recovered from the A^3 coupling reaction catalyzed by Au_{11} (0.5 mol%), neat, 21 °C (bottom).

Note: Spectrum of the recovered catalyst contains the same resonances as those of authentic Au_{11}' , indicating that the recovered catalyst contains mainly Au_{11}' .

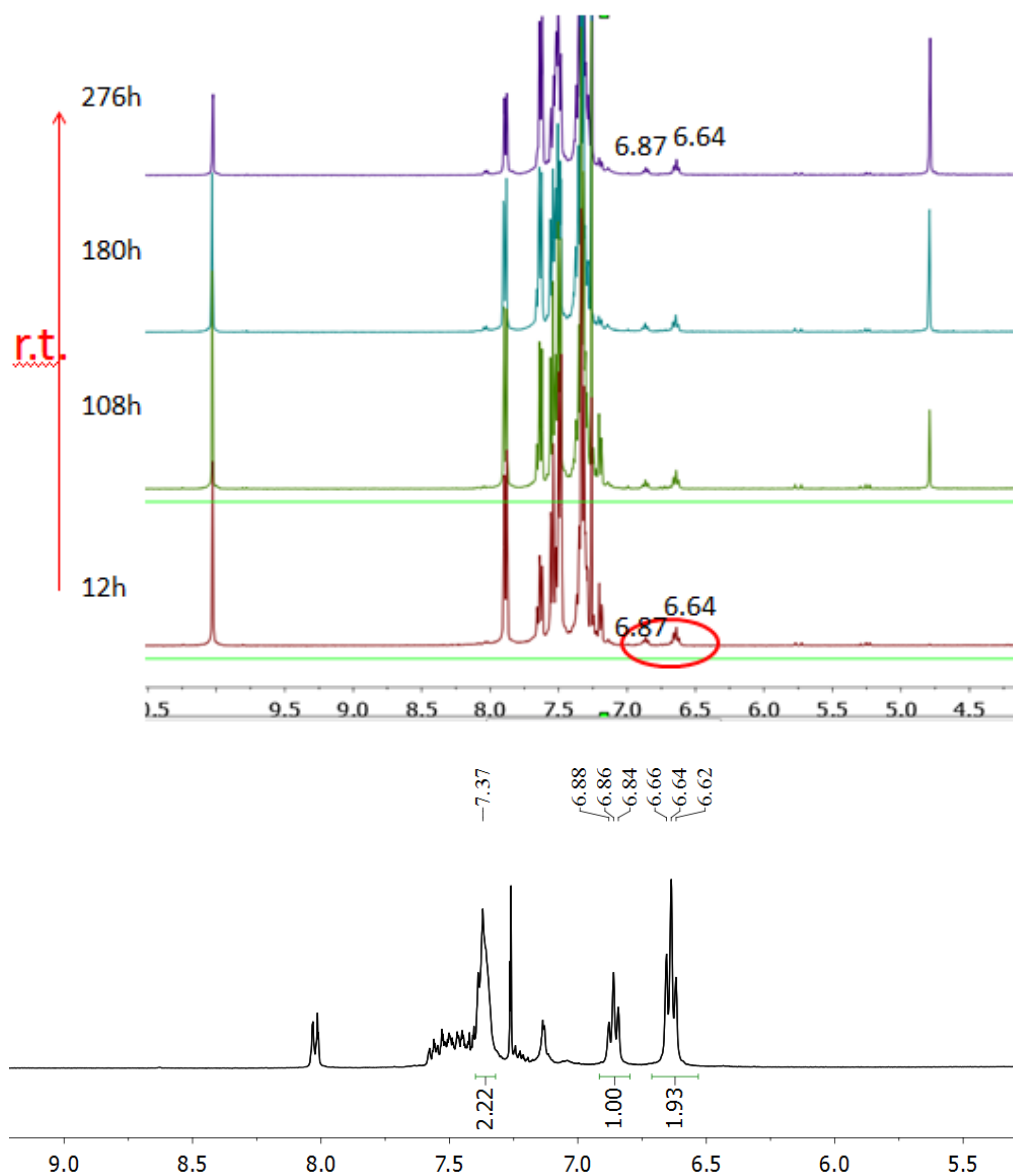


Figure S13. ¹H NMR spectra (CDCl₃, aromatic region): (Top) A³ coupling reaction catalyzed by **Au₁₁** (0.5 mol%), neat, 21 °C. (Bottom) Recovered catalyst.

Note: Two peaks (circled) present in the spectra determined to be **Au₁₁'**, which is poorly soluble in the reaction mixture and thus precipitated out. No other catalyst-related peak was observed, possibly due to too low concentrations. This may account for the very long induction period, assuming that the catalytically active species is from the decomposition of **Au₁₁** or **Au₁₁'**.

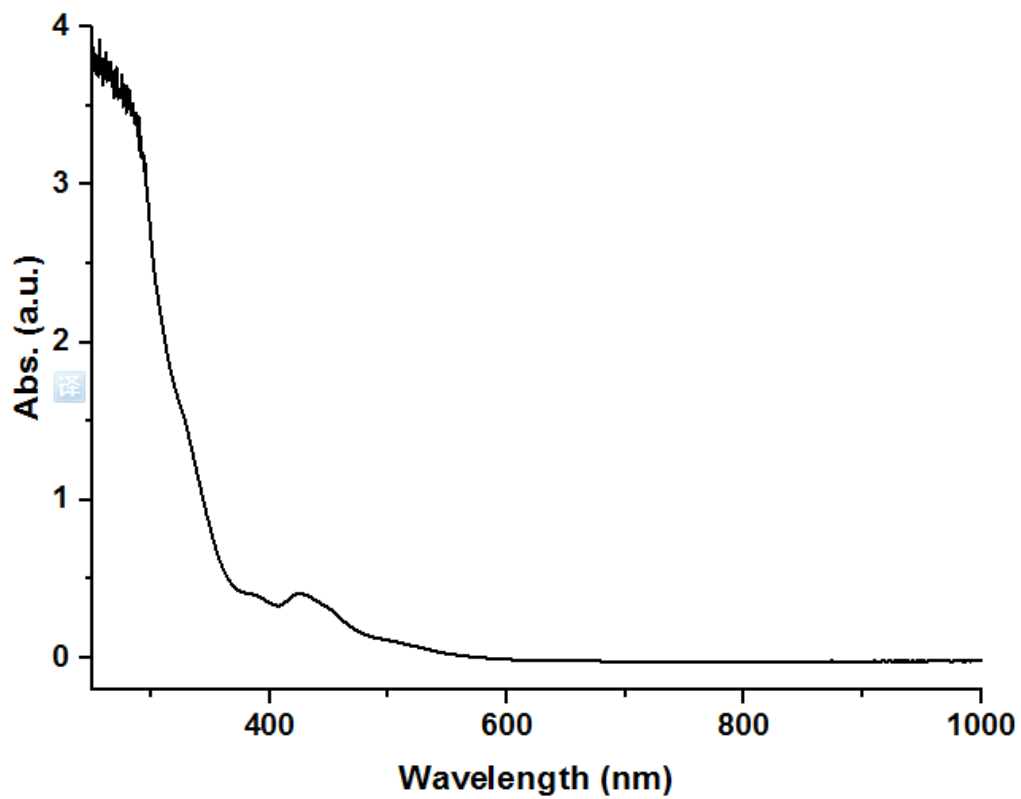


Figure S14. UV-Vis spectrum of the crude for the A³ coupling reaction catalyzed by Au₁₁ (0.5 mol%), neat, 21 °C, at 348 h (71% conversion).

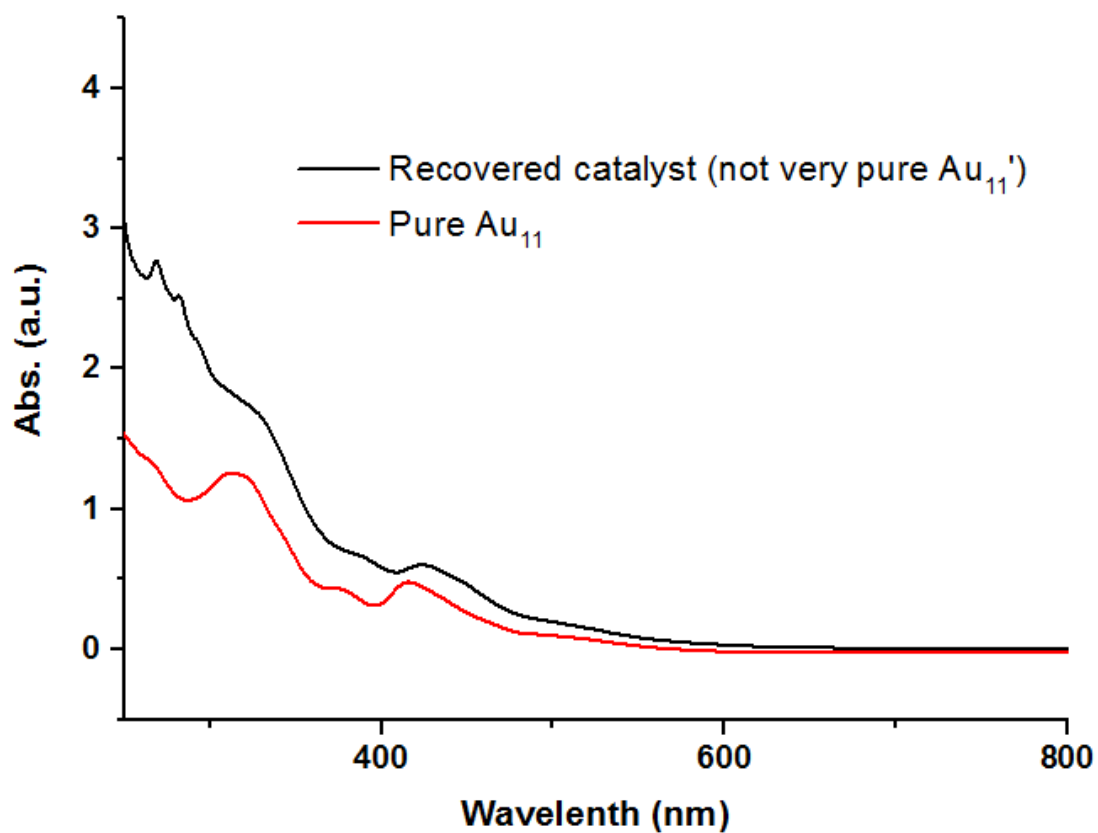


Figure S15. UV-Vis spectrum (DCM) of the recovered catalyst from the A³ coupling reaction catalyzed by Au₁₁ (0.5 mol%), neat, 21 °C at 348 h (71% conversion).

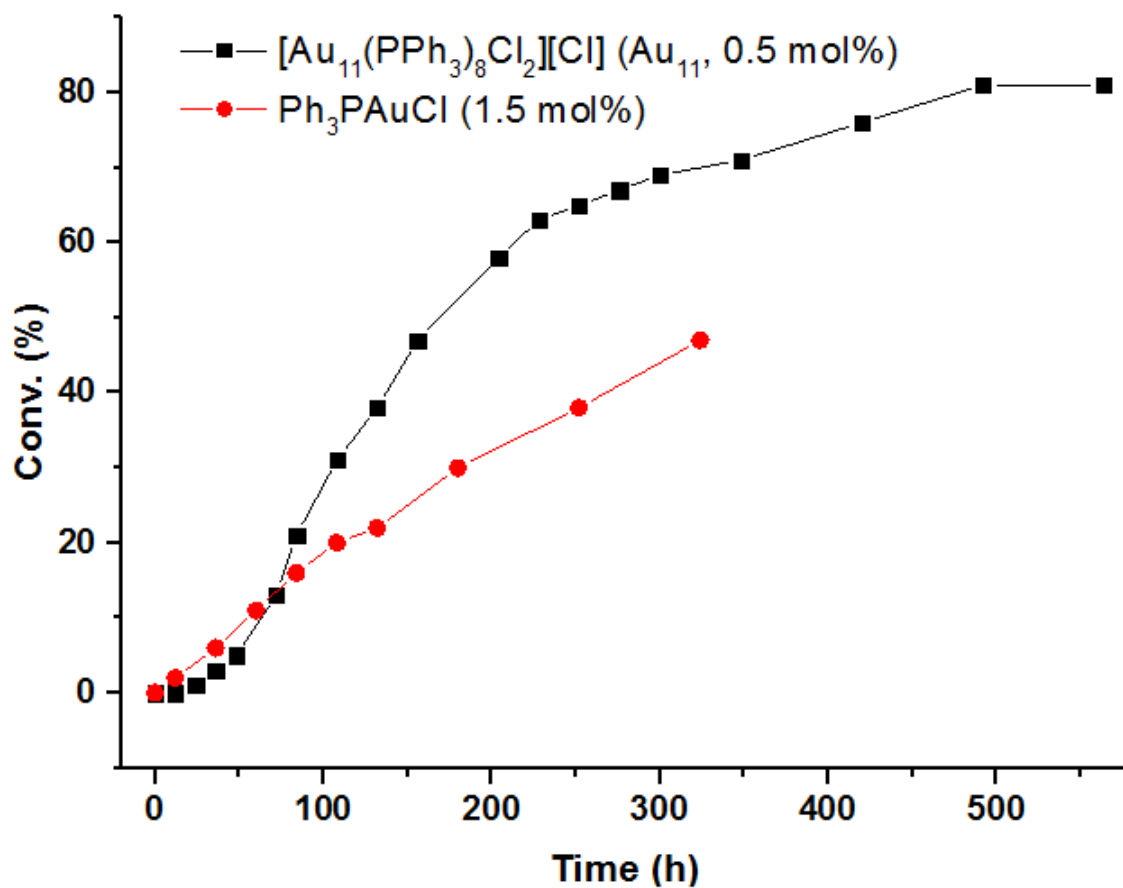


Figure S16. Plot of conversion vs time for the A^3 coupling reaction catalyzed by Au_{11} (0.5 mol%) and Ph_3PAuCl (1.5 mol%), neat, 21 °C.

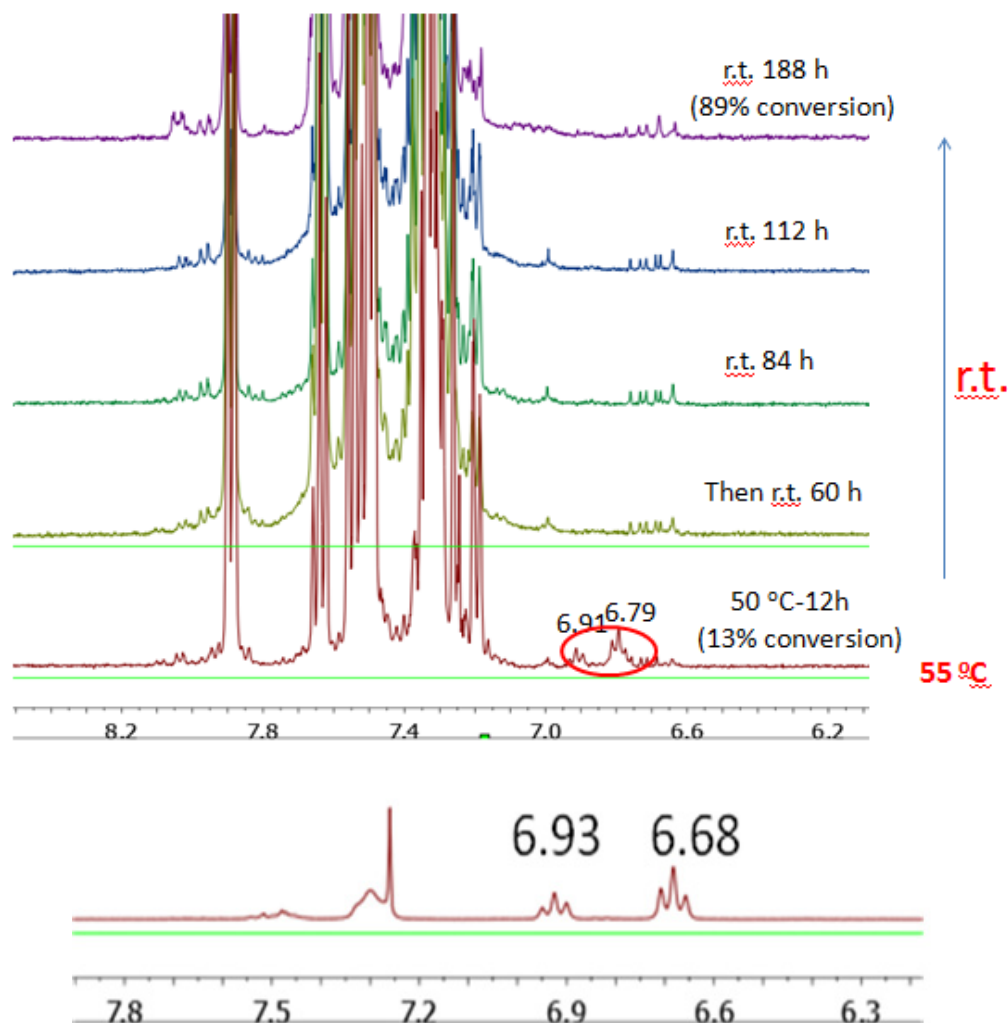


Figure S17. ^1H NMR spectra (CDCl_3 , aromatic region): (Top) For the A^3 coupling reaction catalyzed by Au_{11} (0.5 mol%), neat, 50 °C (for the first 12 h) or 21 °C (for the rest). (Bottom) Authentic sample of Au_{11} .

Note: After heating at 50 °C for 12 h, the Au_{11} converted to an unknown species with resonances at 6.79 and 6.91 ppm, probably from the initially formed Au_{11} '. This newly-formed species is soluble in the reaction mixture and gradually disappeared over the course of the reaction at room temperature, while conversion increased from 13% to 89%, indicating that this may be the catalytically active species.

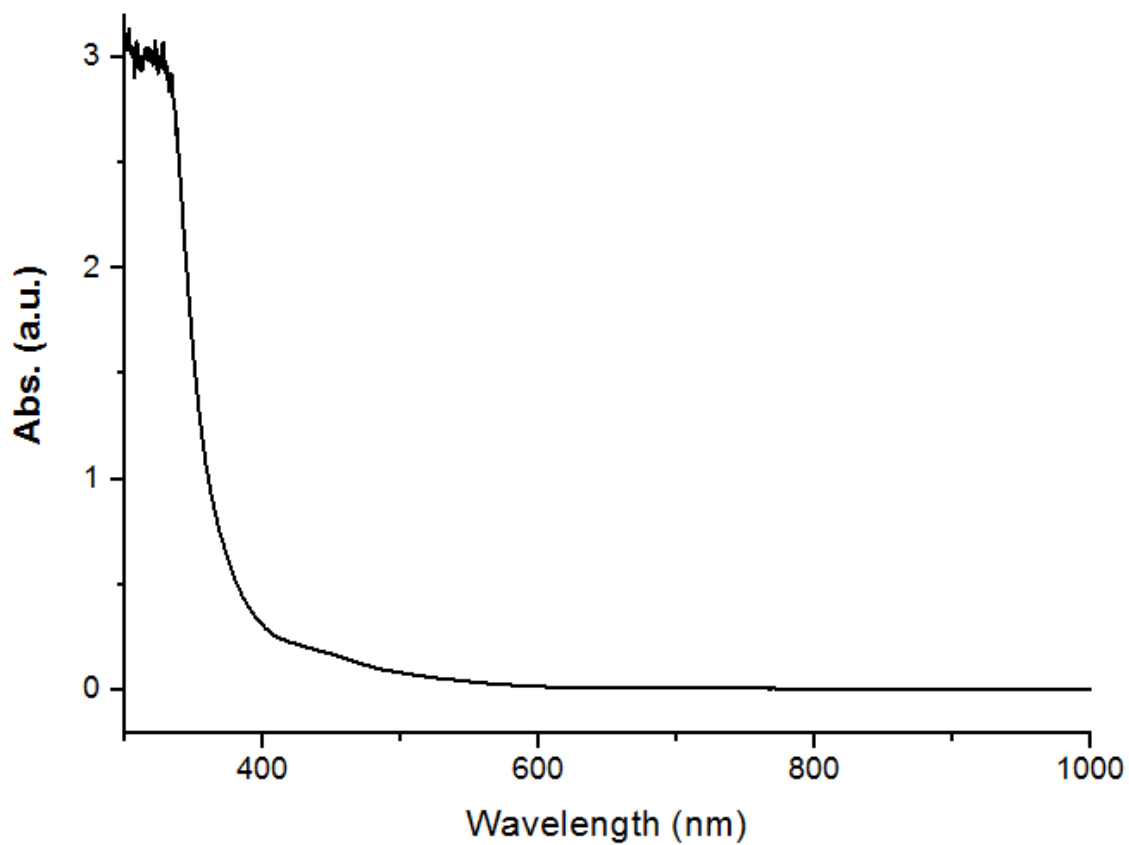


Figure S18. UV-Vis spectrum of the crude for the A³ coupling reaction catalyzed by Au₁₁ (0.5 mol%), neat conditions, at 50 °C (for the first 12 h) and 21 °C (for another 244 h).

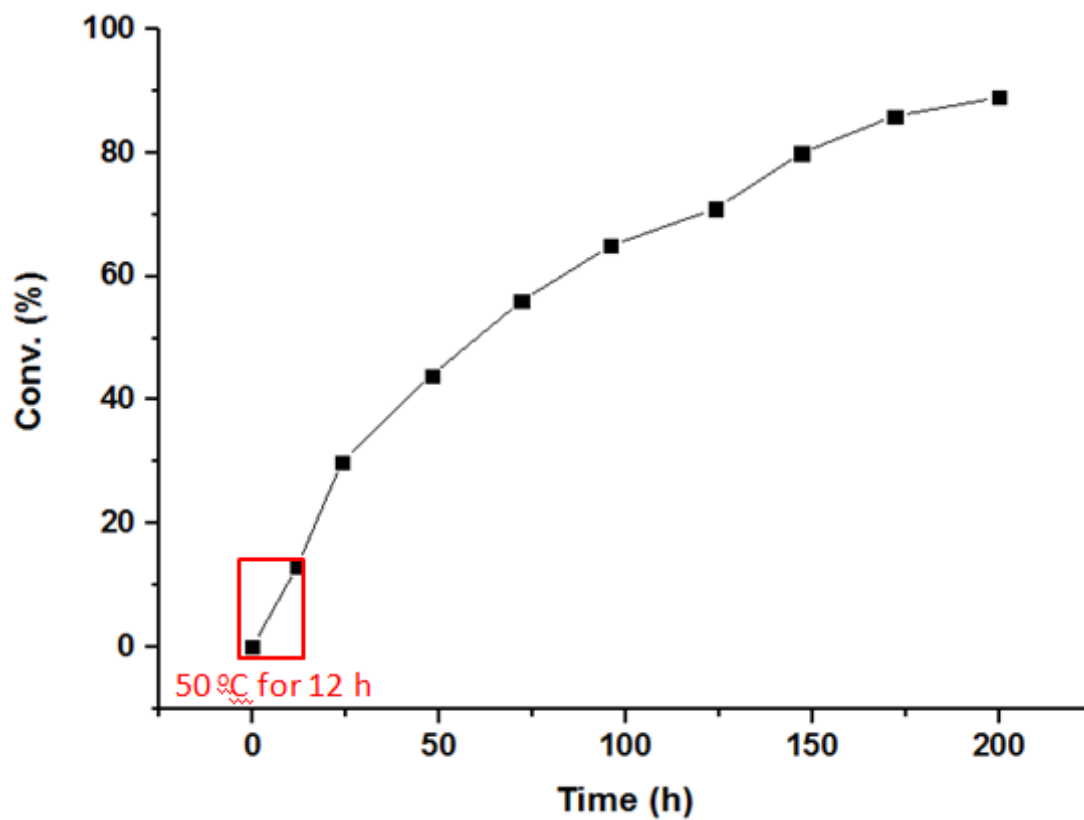


Figure S19. Plot of conversion vs time for the A³ coupling reaction catalyzed by Au₁₁ (0.5 mol%), neat, at 50 °C (for the first 12 h) and 21 °C (for the rest).

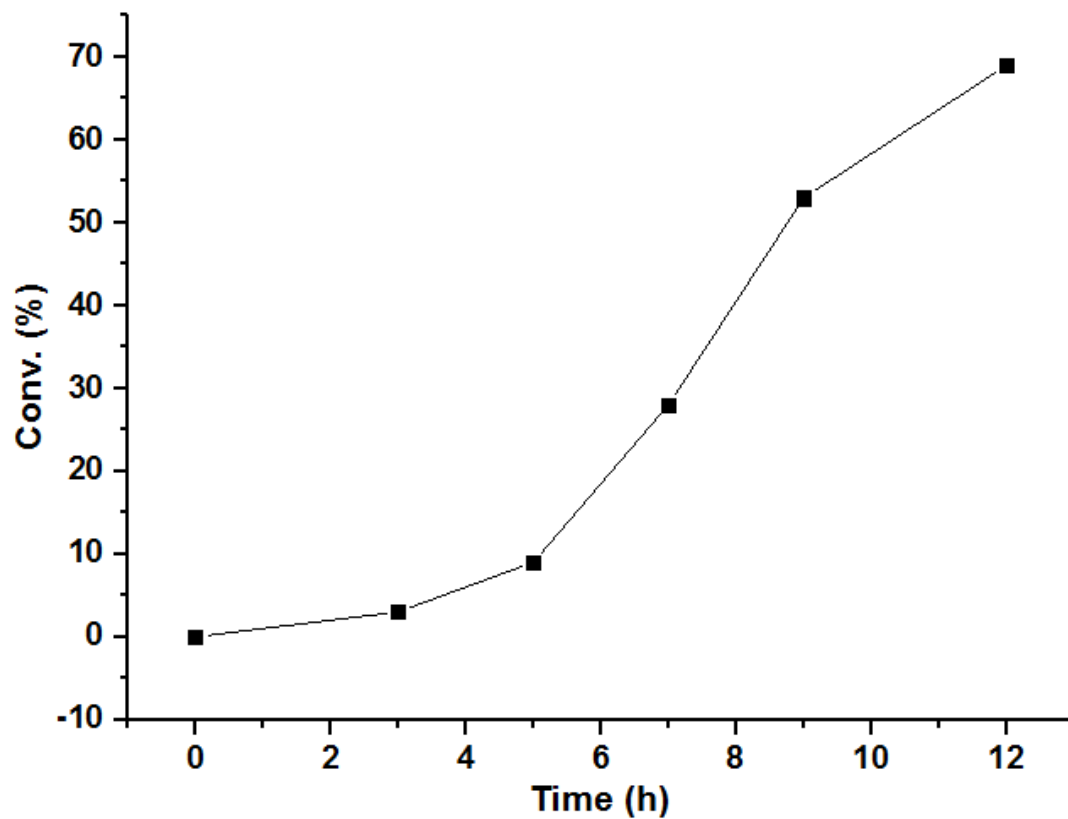


Figure S20. Plot of conversion vs time for the A³ coupling reaction catalyzed by Au₂₅ (0.03 mol%), neat, 50 °C.

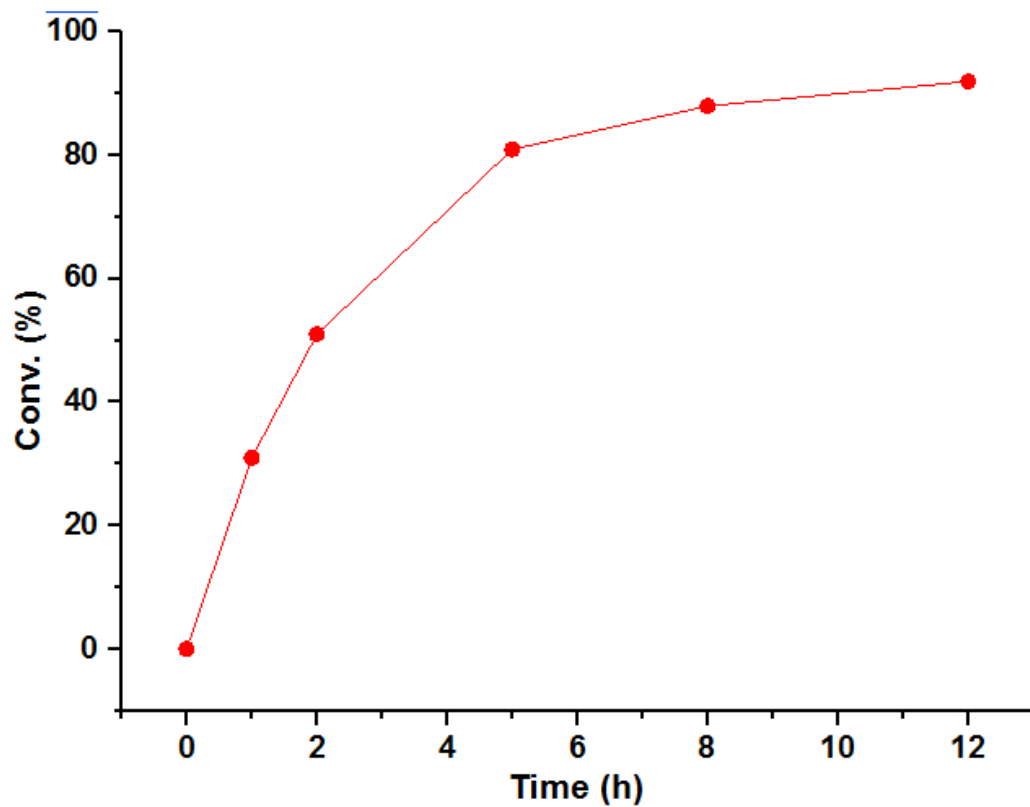


Figure S21. Plot of conversion vs time for the A³ coupling reaction catalyzed by Au₁₃ (0.03 mol%), neat, 50 °C.