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CuO@Fe₂O₃ catalyzed C1-alkynylation of tetrahydroisoquinolines (THIQs) *via* A3 coupling and its decarboxylative strategies

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1	General Remarks	Pg. S2-S2
2	Experimental procedure for preparation of CuO@Fe ₂ O ₃	Pg. S2-S2
3	PXRD and TEM of fresh and recycled CuO@Fe ₂ O ₃	Pg. S3-S3
4	Calculation of E-factor and AE of (4a)	Pg. S3-S5
5	Spectral data for known compounds	Pg. S5-S7
6	¹ H and ¹³ C NMR Spectra of all compounds	Pg. S7- S24
7	References	Pg S24-S24

General Remarks:

In the analysis of catalytic activities, all reagents and substrates were purchased from Merk, Alfa Aesar, Aldrich and used as such. The X-ray diffraction (XRD) patterns of fresh and recycled CuO@Fe₂O₃ catalysts were recorded on Rigaku Rotaflex spectrometer at 20 range of 10–70° with Cu K α radiation. Transmission electron microscopy (TEM), SAED micrographs were obtained on a Joel JEM 2010 transmission electron microscope. The samples were supported on carbon-coated copper grids for the experiment. The ¹H NMR and ¹³C NMR spectra were recorded on Jeol Spectrospin spectrometer at 400 MHz and 100 MHz respectively using TMS as an internal standard. The chemical shift values are recorded on δ scale and the coupling constants (*J*) are in Hz. IR spectra were recorded using Perkin-Elmer and Bruker FT-IR in the range of 4000–100 cm⁻¹ and only characteristic frequencies are expressed.

Typical procedure for the synthesis of the CuO@Fe₂O₃ MNPs:

The CuO@Fe₂O₃ MNPs were synthesised by following reported method by our group.¹ Typically, 10 mL of a 0.2 M FeCl₃ aqueous solution (2 mmol, 0.324 g) and 10 mL of a 2.0 M aqueous urea solution (20 mmol, 1.2 g) were mixed in 10 mL of ethylene glycol. To this mixture, 10 mL of a 0.2 M CuCl₂ aqueous solution (2 mmol, 0.27 g), glucose (10 mol%) and 5 mL of 20.6 M (40%) aqueous NH₃ were mixed successively and sonicated for 15 min to form a homogeneous mixture. The resulting mixture was transferred into a 100 mL Teflon-lined stainless-steel autoclave and heated at 180 °C for 8 h. The autoclave was allowed to cool naturally to room temperature. The resulting solid nanoparticles were washed several times with water followed by a final wash with acetone and recovered using an external magnetic field. The obtained MNPs were collected and dried in an oven at 90 °C for 6 h.



Figure S1: TEM image of (a) fresh; (b) recycled CuO@Fe₂O₃ MNPs



Figure S2: PXRD of (a) fresh; (b) recycled CuO@Fe₂O₃ MNPs

Calculation of E-factor and Atom economy of compound (4a):



E factor: The E-factor calculates the actual amount of waste produced in the chemical process, which actually compares the mass of product to the mass of waste produced with ideal value as zero.

E-factor = [total mass of raw materials minus the total mass of product]/ mass of product

E-factor = (0.146 + 0.132 + 0.102 - 0.303)/0.303

E-factor = (0.380 - 0.303)/0.303

E-factor = 0.25

Atom economy (AE): The ideal value of AE is 100% (all atoms from the starting materials reside in the product). AE determine the efficiency of a chemical reaction with regard to how many atoms from the starting materials reside within the product.

AE = MW of product $\div \Sigma$ (MW of stoichiometric reactants) $\times 100$

 $AE = (337.45 \div 380) \times 100$

AE = 89%



E factor: The E-factor calculates the actual amount of waste produced in the chemical process, which actually compares the mass of product to the mass of waste produced with ideal value as zero.

E-factor = [total mass of raw materials minus the total mass of product]/ mass of product E-factor = (0.146 + 0.132 + 0.146 - 0.310)/(0.310) (for decarboxylative reaction)

E-factor = (0.424 - 0.296)/0.296

E-factor = 0.37

Atom economy (AE): The ideal value of AE is 100% (all atoms from the starting materials reside in the product). AE determine the efficiency of a chemical reaction with regard to how many atoms from the starting materials reside within the product.

AE = MW of product $\div \Sigma$ (MW of stoichiometric reactants) $\times 100$

 $AE = (337.45 \div 424) \times 100$

Spectral data of known compounds:

2-(4-Methylbenzyl)-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline $(4a)^2$: Yellow liquid. **Me** IR (ϑ_{max} /cm⁻¹ CHCl₃): 2922, 2855, 1725, 1608, 1567, 1490, 1490, 1448, 1328, 1216, 1026, 749, 693, 662. ¹H NMR (CDCl₃, 400 MHz) δ = 7.48-7.46 (m, 2H), 7.38 (d, J = 7.6 Hz, 2H), 7.31-7.26 (m, 4H), 7.19-7.13 (m, 5H), 4.81 (s, 1H), 3.94 (d, J = 12.9 Hz, 1H), 3.89 (d, J = 13.7 Hz, 1H), 3.13-3.00 (m, 2H), 2.87-2.78 (m, 2H), 2.37 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz) $\delta = 136.74$, 135.47, 135.13, 134.05, 131.75, 129.23, 128.97, 128.17, 127.98, 127.77,

126.86, 125.86, 125.76, 123.23, 87.51, 86.80, 59.24, 54.22, 45.66, 28.18, 21.12 ppm. HRMS for C₂₅H₂₄N [M+H]⁺: Calc. 338.1909 found 338.1894.

2-Benzyl-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline $(4b)^2$: Yellow liquid. IR (ϑ_{max} /cm⁻¹CHCl₃) 3060, 2924, 2855, 2266, 1728, 1605.32, 1566, 1490, 1449, 1327, 1216, 1081, 1029, 998, 930, 838, 753, 698, 662. ¹H NMR (CDCl₃, 400 MHz) $\delta = 7.47$ -7.43 (m, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.29-7.24 (m, 5H), 7.17-7.11 (m, 3H), 4.78 (s, 1H), 3.95 (d, J = 13.7 Hz, 1H), 3.90 (d, J = 13.7Hz, 1H), 3.11-2.98 (m, 2H), 2.85-2.76 (m, 2H) ppm.

2-(4-Fluorobenzyl)-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline (4c)²: Yellow liquid.



IR $(\vartheta_{max}/cm^{-1} \text{ CHCl}_3)$: 3060, 2956, 2902, 1709, 1642, 1602, 1568, 1510, 1446, 1324, 1228, 1160, 1099, 1023, 1023, 840, 757, 694. ¹H NMR (CDCl₃, 400 MHz) δ = 7.49-7.39 (m, 4H), 7.30-7.25 (m, 4H), 7.21-7.10 (m, 3H), 7.01 (t, *J* = 8.3 Hz, 2H), 4.75 (s, 1H), 3.89 (d, *J* =

13.7 Hz, 1H), 3.86 (d, J = 13.7 Hz, 1H), 3.09-2.97 (m, 2H), 2.86-2.75 (m, 2H) ppm.

2-(4-Methoxybenzyl)-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline (4d)²: Yellow



liquid. ¹H NMR (CDCl₃, 400 MHz) δ = 7.45-7.43 (m, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.29-7.25 (m, 4H), 7.18-7.10 (m, 3H), 6.88 (d, *J* = 8.3Hz, 2H), 4.76 (s, 1H), 3.88 (d, *J* = 12.9 Hz, 1H), 3.84 (d, *J* = 12.9 Hz, 1H), 3.80 (s, 3H), 3.09-2.97 (m, 2H), 2.87-2.76 (m, 2H) ppm.

2-(4-Bromobenzyl)-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline (4e)² : Yellow liquid.



IR $(\vartheta_{max}/cm^{-1}CHCl_3)$: 2923, 2853, 1706, 1644, 1597, 1485, 1448, 1408, 1310, 1227, 1164, 1108, 1070, 1011, 831, 750, 712, 650. ¹H NMR (CDCl₃, 400 MHz) δ = 7.46-7.39 (m, 4H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.29-7.27 (m, 3H), 7.24-7.23 (m, 1H), 7.13-7.08 (m, 3H), 4.75

(s, 1H), 3.88 (d, *J* = 13.7 Hz, 1H), 3.84 (d, *J* = 12.9 Hz, 1H), 3.09-2.97 (m, 2H), 2.83-2.75 (m, 2H) ppm.

2-(2-Bromobenzyl)-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline (4g)² : Yellow liquid.



¹H NMR (CDCl₃, 400 MHz) δ = 7.69 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.54-7.52 (m, 2H), 7.38-7.32 (m, 5H), 7.26-7.25 (m, 2H), 7.21-

7.16 (m, 2H), 4.97 (s, 1H), 4.15 (d, *J* = 14.5 Hz, 1H), 4.09 (d, *J* = 14.5 Hz, 1H), 3.26-3.08 (m, 2H), 2.94- 2.83 (m, 2H) ppm.

2-(4-Methylbenzyl)-1-octynyl-1,2,3,4-tetrahydroisoquinoline (4m)³ : Yellow liquid. IR (ϑ_{max}/cm^{-1} , CHCl₃): 2924, 2857.99, 1735, 1608, 1565, 1514, 1455, 1329, 1213, 1047, 813, 748, 666. ¹H NMR (CDCl₃, 400 MHz) $\delta =$ 7.32 (d, J = 7.6 Hz, 2H), 7.19-7.07 (m, 6H), 4.53 (s, 1H), 3.84 (d, J =12.9 Hz, 1H), 3.76 (d, J = 12.9 Hz, 1H), 3.00-2.91 (m, 2H), 2.79-2.67 (m, 2H), 2.34 (s, 3H), 2.23 (d, J = 6.9 Hz, 2H), 1.56-1.48 (m, 2H), 1.44-1.37 (m, 2H), 1.33-1.25 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) $\delta = 135.72$, 135.46, 134.52, 132.97, 128.31, 128.04, 128.00, 126.79, 125.75, 124.75, 86.24, 58.25, 53.11, 44.59, 30.45, 28.15, 28.07, 27.70, 21.72, 20.27, 17.98, 13.20 ppm. HRMS (ESI) calcd for C₂₅H₃₂N [M+H]⁺: 346.2535, found 346.2526.

¹H and ¹³C NMR Spectra of all compounds

































S23



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