CuO@Fe$_2$O$_3$ catalyzed C1-alkynylation of tetrahydroisoquinolines (THIQs) via A3 coupling and its decarboxylative strategies

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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 2θ range of 10–70° with Cu Kα 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@Fe$_2$O$_3$ MNPs

Figure S2: PXRD of (a) fresh; (b) recycled CuO@Fe$_2$O$_3$ MNPs

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

\[
\begin{align*}
\text{FW} & \quad 133.19\text{g/mol} \quad 120.15\text{g/mol} \quad 102.13\text{g/mol} \quad 337.45\text{g/mol} \\
\text{Weight} & \quad 0.146g \quad 0.132g \quad 0.102g \quad 0.303g
\end{align*}
\]
**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

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 ÷ Σ(MW of stoichiometric reactants) × 100

AE = (337.45 ÷ 380) × 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.

\[
AE = \frac{\text{MW of product}}{\Sigma (\text{MW of stoichiometric reactants})} \times 100
\]

\[
AE = \frac{337.45}{424} \times 100
\]

\[
AE = 80\%
\]

**Spectral data of known compounds:**

2-(4-Methylbenzyl)-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline (4a):

Yellow liquid. IR (\(\bar{\nu}_{\text{max}}/\text{cm}^{-1}\) CHCl\(_3\)): 2922, 2855, 1725, 1608, 1567, 1490, 1490, 1448, 1328, 1216, 1026, 749, 693, 662. \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta = 7.48-7.46\) (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, \(J = 13.7\) 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). \(^13\)C NMR (CDCl\(_3\), 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 C\(_{25}\)H\(_{24}\)N [M+H]: Calc. 338.1909 found 338.1894.

2-Benzyl-1-phenylethynyl-1,2,3,4-tetrahydroisoquinoline (4b):

Yellow liquid. IR (\(\bar{\nu}_{\text{max}}/\text{cm}^{-1}\) CHCl\(_3\)): 3060, 2924, 2855, 2266, 1728, 1605.32, 1566, 1490, 1449, 1327, 1216, 1081, 1029, 998, 930, 838, 753, 698, 662. \(^1\)H NMR (CDCl\(_3\), 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, \(J = 13.7\) Hz, 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): Yellow liquid. 

\[
\text{IR} \quad (\theta_{\text{max}}/\text{cm}^{-1} \text{ CHCl}_3) : 3060, 2956, 2902, 1709, 1642, 1602, 1568, 1510, 1446, 1324, 1228, 1160, 1099, 1023, 840, 757, 694. \]
\[
\text{H NMR (CDCl}_3, 400 \text{ MHz}) \delta = 7.49-7.39 (m, 4H), 7.30-7.25 (m, 4H), 7.21-7.10 (m, 3H), 7.01 (t, J = 8.3 \text{ Hz}, 2H), 4.75 (s, 1H), 3.89 (d, J = 13.7 \text{ Hz}, 1H), 3.09-2.97 (m, 2H), 2.86-2.75 (m, 2H) ppm.
\]

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

\[
\text{H NMR (CDCl}_3, 400 \text{ MHz}) \delta = 7.45-7.43 (m, 2H), 7.38 (d, J = 8.3 \text{ Hz}, 2H), 7.29-7.25 (m, 4H), 7.18-7.10 (m, 3H), 6.88 (d, J = 8.3 \text{ Hz}, 2H), 4.76 (s, 1H), 3.88 (d, J = 12.9 \text{ Hz}, 1H), 3.84 (d, J = 12.9 \text{ Hz}, 1H), 3.80 (s, 3H), 3.09-2.97 (m, 2H), 2.87-2.76 (m, 2H) ppm.
\]

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

\[
\text{IR} \quad (\theta_{\text{max}}/\text{cm}^{-1} \text{ CHCl}_3): 2923, 2853, 1706, 1644, 1597, 1485, 1448, 1408, 1310, 1227, 1164, 1108, 1070, 1011, 831, 750, 712, 650. \]
\[
\text{H NMR (CDCl}_3, 400 \text{ MHz}) \delta = 7.46-7.39 (m, 4H), 7.33 (d, J = 7.6 \text{ Hz}, 2H), 7.29-7.27 (m, 3H), 7.24-7.23 (m, 1H), 7.13-7.08 (m, 3H), 4.75 (s, 1H), 3.88 (d, J = 13.7 \text{ Hz}, 1H), 3.84 (d, J = 12.9 \text{ Hz}, 1H), 3.09-2.97 (m, 2H), 2.83-2.75 (m, 2H) ppm.
\]

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

\[
\text{H NMR (CDCl}_3, 400 \text{ MHz}) \delta = 7.69 (d, J = 7.6 \text{ Hz}, 1H), 7.64 (d, J = 7.6 \text{ 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 ($\nu_{\text{max}}$/cm$^{-1}$, CHCl$_3$): 2924, 2857.99, 1735, 1608, 1565, 1514, 1455, 1329, 1213, 1047, 813, 748, 666. $^1$H NMR (CDCl$_3$, 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; $^{13}$C NMR (CDCl$_3$, 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 C$_{25}$H$_{32}$N [M+H]$^+$: 346.2535, found 346.2526.

$^1$H and $^{13}$C NMR Spectra of all compounds
References:
