Electronic Supplementary Information for:

Copper-catalyzed tandem A³-coupling – isomerization – hydrolysis reactions of aldehydes and terminal alkynes leading to chalcones

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Table of Contents

1. General Information
2. General Procedure of Tandem Reactions
3. Control Experiments
4. Copies for ¹H NMR and ¹³C NMR spectra
1. General Information

All chemicals were purchased from Adamas Reagent Ltd, energy chemical company, J&K Scientific Ltd, Alfa Aesa chemical company, etc. Unless otherwise noted, materials obtained from commercial suppliers were directly used without further purification. NMR spectra were recorded on BRUKER Avence III 500MHz spectrometers. Chemical shifts were reported in parts per million (ppm) down field from TMS with the solvent resonance as the internal standard. Coupling constants \( J \) were reported in Hz and referred to apparent peak multiplications. Qualitative analyses of the products were carried out on a SHIMADZU GCMS-QP2010 gas chromatograph mass spectrometer. The yield of the product \( 3\text{aa} \) was based on GC analysis on an Agilent 7890B GC system by using dodecane as the internal standard.

2. General Procedure of the Tandem Reactions

\[
\begin{align*}
\text{CHO} + \text{R}^1\text{R}^2\text{R}^3 + \text{CuSO}_4, (20 \text{ mol\%}) & \rightarrow \text{R}^1\text{R}^2\text{R}^3 \\
\text{pyridine (2 equiv)} & \rightarrow \text{DMSO} \text{ N}_2, 130 \degree \text{C, 12 h} & \rightarrow \text{R}^1\text{R}^2\text{R}^3
\end{align*}
\]

To a 25 mL schlenk tube was added anhydrous CuSO\(_4\) (16.0 mg, 0.1 mmol). Then, aldehyde \( 1 \) (52 \( \mu \)L, 0.5 mmol), terminal alkyne \( 2 \) (75 \( \mu \)L, 0.75 mmol), piperidine (74 \( \mu \)L, 0.75 mmol), pyridine (75 \( \mu \)L, 1 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 \degree \text{C} for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate for three times. The organic phases were combined, dried by anhydrous NaSO\(_4\) and concentrated under vacuum. The residue was purified by chromatography on silica gel with ethyl acetate/petroleumether to give corresponding product \( 3 \).

\((E)-\text{chalcone}\) (CAS Registry Number 94-41-7)

\[
\text{O} \quad \text{CHO} \quad \text{R}^1\text{R}^2\text{R}^3
\]

This product \( 3\text{aa} \) was synthesized from the reaction of benzaldehyde \( 1\text{a} \) and phenylacetylene.
(2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a yellow crystal (73 mg, 70% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.44-7.47 (m, 3H), 7.52-7.58 (m, 3H), 7.60-7.63 (m, 1H), 7.67-7.69 (m, 2H), 7.84 (d, $J$ = 15.5 Hz, 1H), 8.04-8.07 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 122.1, 128.5, 128.5, 128.6, 129.0, 132.8, 134.9, 138.2, 144.9, 190.6. GC-MS: calcd for C$_{13}$H$_{12}$O (M$^+$): m/z = 208, found: 208; Melting Point: 52-57°C.

(E)-1-(4-bromophenyl)-3-phenylprop-2-en-1-one (CAS Registry Number 2403-27-2)

This product (3ba) was synthesized from the reaction of 4-bromobenzaldehyde (1b) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 100/1 v/v) afforded the desired product as a yellow crystal (94 mg, 66% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.42-7.44 (m, 3H), 7.48 (d, $J$ = 15.5 Hz, 1H), 7.64-7.66 (m, 4H), 7.82 (d, $J$ = 15.5 Hz, 1H), 7.88-7.90 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 121.5, 127.9, 128.5, 129.0, 130.0, 130.8, 131.9, 134.7, 136.9, 145.4, 189.4. GC-MS: calcd for C$_{13}$H$_{11}$OBr (M$^+$): m/z = 286; 288, found:; Melting Point: 96-98 °C.

(E)-1-(3-bromophenyl)-3-phenylprop-2-en-1-one (CAS Registry Number 22966-26-3)

This product (3ca) was synthesized from the reaction of 3-bromobenzaldehyde (1c) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 100/1 v/v) afforded the desired product as a yellow crystal (mg, % yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.38-7.48 (m, 5H), 7.65-7.67 (m, 2H), 7.70-7.72 (m, 1H), 7.83 (d, $J$ = 15.5 Hz, 1H), 7.93-7.95 (m, 1H), 8.14-8.15 (m, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 121.4, 123.0, 127.0, 128.6, 129.0, 130.2, 130.9, 131.5, 134.6, 135.6, 140.0, 145.7, 189.1. GC-MS: calcd for C$_{15}$H$_{11}$OBr (M$^+$): m/z = 286; 288, found:; Melting Point: 92-95 °C (Lit.: °C).
(E)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (CAS Registry Number 956-02-5)

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}}
\end{align*}
\]

This product (3da) was synthesized from the reaction of 4-chlorobenzaldehyde (1d) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (80 mg, 66% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.42-4.35 (m, 3H), 7.47-7.50 (m, 3H), 7.64-7.66 (m, 2H), 7.82 (d, $J$ = 15.5 Hz, 1H), 7.96-7.98 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 121.5, 128.5, 128.9, 129.0, 130.7, 134.7, 136.5, 139.2, 145.3, 189.2. GC-MS: calcd for C$_{15}$H$_{11}$OCl (M$^+$): $m/z$ = 242, found: 242; Melting Point: 93-96 °C.

(E)-1-(3-chlorophenyl)-3-phenylprop-2-en-1-one (CAS Registry Number 20426-48-6)

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}}
\end{align*}
\]

This product (3ea) was synthesized from the reaction of 3-chlorobenzaldehyde (1e) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (75 mg, 62% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.46-7.51 (m, 5H), 7.58-7.60 (m, 1H), 7.67-7.69 (m, 2H), 7.86 (d, $J$ = 15.5 Hz, 1H), 7.91-7.93 (m, 1H), 8.01 (t, $J$ = 2.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 121.5, 126.6, 128.6, 128.6, 129.0, 130.0, 130.8, 132.7, 134.6, 134.9, 139.8, 145.7, 189.2. GC-MS: calcd for C$_{15}$H$_{11}$OCl (M$^+$): $m/z$ = 242, found: 242; Melting Point: 94-96 °C.

4-cinnamoylbenzonitrile (CAS Registry Number 31083-73-5)

\[
\begin{align*}
\text{NC} & \quad \text{O} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}} \\
\text{\underline{C}} & \quad \text{\underline{C}}
\end{align*}
\]

This product (3fa) was synthesized from the reaction of 4-formylbenzonitrile (1f) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 10/1 v/v) afforded the desired product as a white solid (95 mg, 82% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.42-7.48 (m, 4H), 7.65-7.67 (m, 2H), 7.80-
3-cinnamoylbenzonitrile (CAS Registry Number 72344-12-8)

This product (3ga) was synthesized from the reaction of 3-formylbenzonitrile (1g) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 10/1 v/v) afforded the desired product as a white solid (72 mg, 62% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.44-7.49 (m, 4H), 7.64-7.68 (m, 3H), 7.85-7.88 (m, 2H), 8.23-8.25 (m, 1H), 8.29-8.30 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 113.2, 118.0, 120.8, 129.1, 129.7, 131.2, 132.1, 132.4, 134.4, 135.6, 139.1, 146.6, 188.3. GC-MS: calcd for C$_{16}$H$_{11}$NO (M$^+$): m/z = 233, found: 233; Melting Point: 128-130 °C.

(E)-3-phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (CAS Registry Number 32120-33-5)

This product (3ha) was synthesized from the reaction of 4-(trifluoromethyl)benzaldehyde (1h) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (100 mg, 72% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.43-7.46 (m, 3H), 7.49 (d, $J$ = 15.5 Hz, 1H), 7.65-7.67 (m, 2H), 7.77 (d, $J$ = 8.0 Hz, 2H), 7.83 (d, $J$ = 15.5 Hz, 1H), 8.10 (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 121.6, 123.6 (q, $J_{CF}$ = 267.5 Hz), 125.7, 125.6, 128.6, 128.8, 129.1, 131.0, 134.0 (d, $J$ = 32.5 Hz), 134.5, 141.1, 146.1, 189.7; $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ = -63.0. GC-MS: calcd for C$_{16}$H$_{11}$F$_3$O (M$^+$): m/z = 276, found: 276; Melting Point: 113-116 °C.
This product (3ia) was synthesized from the reaction of 4-acetylbenzaldehyde (1i) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 20/1 v/v) afforded the desired product as a white solid (65 mg, 52% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 2.67 (s, 3H), 7.43-7.45 (m, 3H), 7.51 (d, $J$ = 15.5 Hz, 1H), 7.65-7.67 (m, 2H), 7.83 (d, $J$ = 15.5 Hz, 1H), 8.08 (s, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 26.9, 121.8, 128.5, 128.6, 128.7, 129.1, 130.9, 134.6, 139.9, 141.6, 145.9, 190.0, 197.5. GC-MS: calcd for C$_{17}$H$_{14}$O$_2$ (M$^+$): m/z = 250, found: 250; Melting Point: 116-119 °C.

(E)-1-(3-nitrophenyl)-3-phenylprop-2-en-1-one (CAS Registry Number 16619-21-9)

This product (3ja) was synthesized from the reaction of 3-nitrobenzaldehyde (1j) and phenylacetylene (2a) following the general procedure. Purification via silica gel column chromatography (petroleum ether/EtOAc = 20/1 v/v) afforded the desired product as a white solid (42 mg, 33% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.45-7.48 (m, 3H), 7.53 (d, $J$ = 15.5 Hz, 1H), 7.68-7.70 (m, 2H), 7.73 (t, $J$ = 8.0 Hz, 1H), 7.90 (d, $J$ = 15.5 Hz, 1H), 8.35-8.37 (m, 1H), 8.44-8.46 (m, 1H), 8.84 (t, $J$ = 1.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 120.7, 123.3, 127.1, 128.8, 129.1, 129.9, 131.2, 134.1, 134.3, 139.5, 146.8, 148.4, 188.0. GC-MS: calcd for C$_{15}$H$_{11}$NO$_3$ (M$^+$): m/z = 253, found: 253; Melting Point: 124-126 °C.

(E)-1-(naphthalen-2-yl)-3-phenylprop-2-en-1-one (CAS Registry Number 4782-69-8)

This product (3ka) was synthesized from the reaction of 2-naphthaldehyde (1k) and phenylacetylene (2a) following the general procedure. Purification via silica gel column
chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (71 mg, 55% yield, E/Z = 8 : 1). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.43-7.46 (m, 3H), 7.54-7.61 (m, 3H), 7.68-7.72 (m, 3H), 7.88 (d, $J$ = 15.5 Hz, 1H), 7.94-8.01 (m, 2H), 8.09-8.12 (m, 1H), 8.55 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 122.1, 124.5, 126.8, 127.9, 128.4, 128.5, 128.6, 128.6, 129.6, 130.0, 130.6, 132.6, 135.0, 135.5, 135.6, 144.8, 190.4. GC-MS: calcd for C$_{19}$H$_{14}$O (M$^+$): m/z = 258, found: 258; Melting Point: 90-94 °C.

(E)-3-phenyl-1-(pyridin-3-yl)prop-2-en-1-one (CAS Registry Number 6314-59-6)

This product (3la) was synthesized from the reaction of nicotinaldehyde (1l) and phenylacetylene (2a) Purification via silica gel column chromatography (petroleum ether/EtOAc = 10/1 v/v) afforded the desired product as a white solid (71 mg, 68% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.44-7.45 (m, 5H), 7.65-7.67 (m, 5H), 7.85 (d, $J$ = 15.5 Hz, 1H), 8.29-8.31 (m, 1H), 8.82 (s, 1H), 9.25 (s, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 121.4, 128.6, 129.1, 131.0, 134.4, 135.9, 146.1, 149.8, 153.2, 189.2. GC-MS: calcd for C$_{14}$H$_{11}$NO (M$^+$): m/z = 209, found: 209; Melting Point: 86-92 °C.

(E)-1-phenyl-3-(m-tolyl)prop-2-en-1-one (CAS Registry Number 16619-29-7)

This product (3ab) was synthesized from the reaction of benzaldehyde (1a) and phenylacetylene (2b) Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (72mg, 65% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 2.40 (s, 3H), 7.22-7.25 (m, 1H), 7.32 (t, $J$ = 7.0 Hz, 1H), 7.41-7.46 (m, 3H), 7.49-7.54 (m, 3H), 7.57-7.60 (m, 1H), 7.78 (d, $J$ = 16.0 Hz, 1H), 8.01-8.03 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 21.4, 121.9, 125.3, 128.5, 128.6, 128.9, 129.1, 131.4, 132.7, 134.9, 138.3, 138.6, 145.1, 190.6. GC-MS: calcd for C$_{16}$H$_{14}$O (M$^+$): m/z = 222, found: 222; Melting Point: 60-63 °C.

(E)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (CAS Registry Number 956-04-7)
This product (3ac) was synthesized from the reaction of benzaldehyde (1a) and 1-chloro-4-ethynylbenzene (2c) Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (86 mg, 71%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.39\) (d, \(J = 8.5\) Hz, 2H), 7.49-7.53 (m, 3H), 7.57-7.61 (m, 3H), 7.76 (d, \(J = 15.5\) Hz, 1H), 8.01-8.02 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta = 122.5, 128.5, 128.7, 129.3, 129.6, 132.9, 133.4, 136.4, 138.0, 143.3, 190.2\). GC-MS: \(\text{calcd}\) for C\(_{15}\)H\(_{11}\)OC\(_1\): \(m/z = 242\), found: 242; Melting Point: 105-107 °C.

(E)-3-(4-bromophenyl)-1-phenylprop-2-en-1-one (CAS Registry Number 1774-66-9)

This product (3ad) was synthesized from the reaction of benzaldehyde (1a) and 1-chloro-4-ethynylbenzene (2d) Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (64 mg, 45%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.50-7.57\) (m, 7H), 7.58-7.62 (m, 1H), 7.74 (d, \(J = 16.0\) Hz, 1H), 8.00-8.03 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta = 122.6, 124.8, 128.5, 128.7, 129.8, 132.2, 133.0, 133.8, 138.0, 143.4, 190.3\). GC-MS: \(\text{calcd}\) for C\(_{15}\)H\(_{11}\)OBr (M\(^+\)): \(m/z = 286; 288\), found: 286; 288; Melting Point: 120-122 °C.

(E)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (CAS Registry Number 1608-51-1)

This product (3ae) was synthesized from the reaction of benzaldehyde (1a) and 1-ethynyl-4-fluorobenzene (2e) Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (80 mg, 71%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.11\) (t, \(J = 8.5\) Hz, 2H), 7.45-7.51 (m, 3H), 7.58-7.59 (m, 1H), 7.61-7.64 (m, 2H), 7.78 (d, \(J = 15.5\) Hz, 1H), 8.01-8.02 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta = 116.1\) (\(J_{\text{CF}} = 21.9\) Hz), 121.8, 128.5 (d, \(J_{\text{CF}} = 21.9\) Hz), 130.3, 130.3, 131.2, 132.8, 138.1, 143.5, 164.1 (d, \(J_{\text{CF}} = 250.4\) Hz),
GC-MS: calcd for C_{15}H_{11}OF (M⁺): m/z = 226, found: 226; Melting Point: 78-82 °C.

\((E)-3-(3\text{-fluorophenyl})-1\text{-phenylprop-2-en-1-one}\) (CAS Registry Number 1608-52-2)

![Chemical structure of (E)-3-(3-fluorophenyl)-1-phenylprop-2-en-1-one](image)

This product \((3af)\) was synthesized from the reaction of benzaldehyde \((1a)\) and 1-ethynyl-3-fluorobenzene \((2f)\). Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (73 mg, 69%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.10-7.13\) (m, 1H), 7.34-7.42 (m, 3H), 7.59-7.62 (m, 1H), 7.76 (d, \(J = 15.5\) Hz, 1H), 8.01-8.03 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta = 114.4\) (d, \(J_{CF} = 21.8\) Hz), 117.3 (d, \(J_{CF} = 21.2\) Hz), 123.2, 124.5, 128.6 (d, \(J_{CF} = 21.4\) Hz), 130.5, 130.5, 133.0, 131.2 (d, \(J_{CF} = 6.4\) Hz), 137.9, 143.3, 163.1 (d, \(J_{CF} = 245.5\) Hz), 190.2. GC-MS: calcd for C_{15}H_{11}OF (M⁺): m/z = 226, found: 226; Melting Point: 87-92 °C.

\((E)-1\text{-phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one}\) (CAS Registry Number 61637-11-4)

![Chemical structure of (E)-1-phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one](image)

This product \((3ag)\) was synthesized from the reaction of benzaldehyde \((1a)\) and 1-ethynyl-3-fluorobenzene \((2g)\). Purification via silica gel column chromatography (petroleum ether/EtOAc = 50/1 v/v) afforded the desired product as a white solid (93 mg, 68%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.51-7.55\) (m, 2H), 7.58-7.63 (m, 2H), 7.67-7.76 (m, 4H), 7.81 (d, \(J = 16.0\) Hz), 8.02-8.05 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta = 123.6, 123.8 (q, J_{CF} = 259.6\) Hz), 125.9, 128.5, 128.6, 128.8, 125.9 (m), 131.8, 132.0, 133.1, 137.8, 138.3, 142.7, 190.6. GC-MS: calcd for C_{16}H_{11}F_{3}O (M⁺): m/z = 276, found: 276; Melting Point: 122-123 °C.

3. Control Experiments

3.1 Use of morpholine and pyrrolidine instead of piperidine
To a 25 mL schlenk tube was added anhydrous CuSO₄ (16.0 mg, 0.1 mmol). Then, benzaldehyde 1a (52 μL, 0.5 mmol), phenylacetylene 2a (75 μL, 0.75 mmol), morpholine (65 μL, 0.75 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phases were combined, dried by anhydrous NaSO₄ and concentrated under vacuum. Two products 3aa and 4aa' were detected by GC-MS and separated by chromatography on silica gel with ethyl acetate/petroleum ether (1/50 v/v) to afford yellow oils (27 mg and 81 mg, respectively).

4-(1,3-diphenylprop-2-yn-1-yl)morpholine (4aa') ¹H NMR (500 MHz, CDCl₃) δ = 2.60-2.66 (m, 4H), 3.69-3.76 (m, 4H), 4.81 (s, 1H), 7.28-7.32 (m, 6H), 7.49-7.52 (m, 2H), 7.62-7.64 (m, 2H). GC-MS: calcd for C₁₉H₁₉NO (M⁺): m/z = 277, found: 277.

The similar procedure was carried out with the use of pyrrolidine instead of piperidine. GC-MS analysis showed that no chalcone was obtained and the corresponding A¹ product 5aa' was only trace.

3.2 Reaction in the absence of piperidine

To a 25 mL schlenk tube was added anhydrous CuSO₄ (16.0 mg, 0.1 mmol). Then, benzaldehyde 1a (52 μL, 0.5 mmol), phenylacetylene 2a (75 μL, 0.75 mmol), pyridine (75 μL, 1 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at
130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phase was dried by anhydrous NaSO₄ and taken into analysis by GC-MS and no chalcone was detected.

3.2 Reaction in the absence of aldehyde

\[
\begin{align*}
\text{phenylacetylene} + \text{H}_2\text{O} + \text{CuSO}_4 (20 \text{ mol\%}) + \text{pyridine} (2 \text{ equiv}) & \rightarrow \text{acetophenone (trace)} \\
\text{DMSO} & \text{130 °C, 12 h}
\end{align*}
\]

To a 25 mL schlenk tube was added anhydrous CuSO₄ (16.0 mg, 0.1 mmol). Then phenylacetylene 2a (75 μL, 0.75 mmol), piperidine (74 μL, 0.75 mmol), pyridine (75 μL, 1 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phase was dried by anhydrous NaSO₄ and taken into analysis by GC-MS and only trace of acetophenone (<5%) was detected.

3.3 Transformation of the A³ product

3.3.1 Synthesis of 3aa’

\[
\begin{align*}
\text{benzaldehyde} + \text{phenylacetylene} + \text{piperidine} & \rightarrow \text{3aa’} \\
\text{toluene} & \text{100 °C, 12 h}
\end{align*}
\]

To a 100 mL schlenk tube was added anhydrous Cu(OAc)₂ (72.0 mg, 0.4 mmol). Then, benzaldehyde 1a (208 μL, 2 mmol), phenylacetylene 2a (300 μL, 3 mmol), piperidine (298 μL, 3 mmol), and toluene (10 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 100 °C for 12 h. After cooling to room temperature, the solvent was evaporated under vacuum. The residue was purified by chromatography on silica gel with ethyl acetate/petroleumether (1/50 v/v) to give the A³ product 3aa’ [1-(1,3-diphenylprop-2-yn-1-yl)piperidine] (CAS Registry Number 1036-21-1) as a yellow solid (400 mg, 73% yield). ¹H NMR (500 MHz, CDCl₃) δ = 1.43-4.45 (m, 2H),
1.55-1.64 (m, 4H), 2.57 (br, 4H), 4.81 (s, 1H), 7.27-7.37 (m, 6H), 7.50-7.52 (m, 2H), 7.63 (d, \( J = 7.5 \) Hz, 2H); \( ^{13} \text{C} \) NMR (125 MHz, CDCl\(_3\)) \( \delta = 24.4, 26.1, 50.7, 62.4, 86.0, 87.9, 123.3, 127.5, 128.1, 128.3, 128.6, 138.5. \)

3.3.2 Synthesis of D-3aa’

The D-labeled A\(^3\) product D-3aa’ was synthetic from the reaction of benzaldehyde-\( d \), phenylacetylene and piperidine procedure under the conditions as described in 3.3.1. 1-(1,3-diphenylprop-2-yn-1-yl-1-d)piperidine (D-3aa’) (62% yield, yellow oil, 91% D-labeled at the propargyl position) \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)) \( \delta = 1.43-4.45 \) (m, 2H), 1.55-1.64 (m, 4H), 2.57 (br, 4H), 4.81 (s, 0.09H), 7.27-7.37 (m, 6H), 7.50-7.52 (m, 2H), 7.62-7.66 (m, 2H).

3.3.3 Reaction of 3aa’ with water in the absence of a catalyst

To a 25 mL schlenk tube was added A\(^3\) product 3aa’ (137 mg, 0.5 mmol). Then, water (36 \( \mu \)L, 2 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phase was dried by anhydrous NaSO\(_4\) and taken into analysis by GC-MS and no chalcone was detected. The starting material remained.

3.3.4 Reaction of 3aa’ with water catalyzed by CuSO\(_4\)
To a 25 mL schlenk tube were added A product 3aa\(^{1}\) (137 mg, 0.5 mmol) and anhydrous CuSO\(_4\) (16.0 mg, 0.1 mmol). Then, water (36 μL, 2 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phase was dried by anhydrous NaSO\(_4\) and taken into quantitative analysis by GC using dodecane as the internal standard.

3.3 Isotope labeled experiments

To a 25 mL schlenk tube was added anhydrous CuSO\(_4\) (16.0 mg, 0.1 mmol). Then, benzaldehyde 1 (52 μL, 0.5 mmol), phenylacetylene 2 (75 μL, 0.75 mmol), piperidine (74 μL, 0.75 mmol), pyridine (75 μL, 1 mmol), D\(_2\)O (38 μL, 2 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate for three times. The organic phases were combined, dried by anhydrous NaSO\(_4\) and concentrated under vacuum. The residue was purified by chromatography on silica gel with ethyl acetate/petroleumether (1:50) to give corresponding product D-3aa in 66% yield. The product was then submitted to NMR analysis to identify the ratio of D-labeling on the two C=C carbons (Fig S1). It proved that partial of the hydrogen atoms on the C=C group were from water in the reaction system.
To a 25 mL schlenk tube was added anhydrous CuSO$_4$ (16.0 mg, 0.1 mmol). Then, benzaldehyde 1 (52 μL, 0.5 mmol), phenylacetylene 2 (75 μL, 0.75 mmol), piperidine (74 μL, 0.75 mmol), pyridine (75 μL, 1 mmol), H$_2$O$^{18}$ (38 μL, 2 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phases were dried by anhydrous Na$_2$SO$_4$ and submitted to GC-MS analysis to identify the origination of oxygen atom of the carbonyl carbons (Fig S2). It is shown that the O-atom of the carbonyl group was generated from water.
To a 25 mL schlenk tube were added A3 product D-3aa' (138 mg, 0.5 mmol) and anhydrous CuSO₄ (16.0 mg, 0.1 mmol). Then, water (36 μL, 2 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phase was dried by anhydrous NaSO₄ and concentrated under vacuum. The residue was purified by chromatography on silica gel with ethyl acetate/petroleumether (1:50) to give corresponding product D-3aa in 43% yield.

### Fig S2 GC-MS spectra of 3aa with H₂¹⁸O as additive

<table>
<thead>
<tr>
<th>m/z</th>
<th>Intensity</th>
<th>Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>206.95</td>
<td>814875</td>
<td>61.69</td>
</tr>
<tr>
<td>207.95</td>
<td>702585</td>
<td>53.18</td>
</tr>
<tr>
<td>209.00</td>
<td>890942</td>
<td>67.44</td>
</tr>
<tr>
<td>210.00</td>
<td>644174</td>
<td>48.76</td>
</tr>
<tr>
<td>211.00</td>
<td>96390</td>
<td>7.30</td>
</tr>
</tbody>
</table>

To a 25 mL schlenk tube were added A3 product D-3aa' (138 mg, 0.5 mmol) and anhydrous CuSO₄ (16.0 mg, 0.1 mmol). Then, water (36 μL, 2 mmol) and dimethyl sulfoxide (1.5 mL) were added in sequence by syringe with nitrogen flowing at a double-rowed pipe. The reaction tube was then sealed and the resulting mixture was stirred at 130 °C for 12 h. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic phase was dried by anhydrous NaSO₄ and concentrated under vacuum. The residue was purified by chromatography on silica gel with ethyl acetate/petroleumether (1:50) to give corresponding product D-3aa in 43% yield.
Fig S2 $^1$HNMR spectrum of D-3aa (lower field area)

4. Copies for $^1$H NMR and $^{13}$C NMR spectra
Cl

3da
3ag

[Chemical Structure Image]
3ag