Zn(OTf)$_2$ mediated expeditious and solvent-free synthesis of propargylamines via C-H activation of phenylacetylene

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**General Information:**

All solvents and chemicals were obtained commercially and were used as received. All reactions were monitored by thin-layer chromatography (TLC). The silica gel used for purification purposed (100–200 mesh size) for column chromatography. NMR spectra were taken with a Bruker Avance II at 400 MHz/ Bruker DMX spectrometer at 500 MHz using CDCl₃ as the solvent. All chemical shifts are reported in ppm are referenced to tetramethylsilane using residual ¹H signals of the deuterated solvents as internal standards.

**Preparation of Zn(OTf)₂**

Triflic acid (0.056mol) was added drop wise to a suspension of zinc carbonate (0.02 mol) in dry methanol (20 ml) at room temperature. During the addition, CO₂ was evolved. The reaction mixture was stirred at 25°C for 20 min. and then refluxed for 2 h. The clear solution was cooled to 25°C and concentrated under reduced pressure. The resulting white powder was dried at 125°C for 2 h to afford Zn(OTf)₂ (98% yield).

**General procedure for the preparation of propargylamines 4a-t:**

To a 25 mL flask, sequentially added aldehydes 1a-k (1.0 mmol), amine 2a-c (1.2 mmol), alkyne 3a-b (1.5 mmol) and Zn(OTf)₂ (0.05 mmol) under an air atmosphere. The reaction mixture was stirred at 100°C till the complete consumption of starting aldehydes (TLC monitoring). The reaction mixture was cooled to room temperature and diluted with ethyl acetate, and then washed with cold water (2 X 5 mL). The organic phase was separated, and the aqueous layer was washed with ethyl acetate (2 X 5 mL). Concentration of the combined organic layer afforded the crude product, which was further purified by by column chromatography on 100-200 silica gel (hexane/ethyl acetate, 20:1) to afford propargylamines 4a-t. The catalyst was
recovered from the aqueous layer via evaporation under reduced pressure and dried at 120°C for 2 h to get pure Zn(OTf)2. The recovered catalyst was reused for the next run in the same way.

Spectral Data of Compounds

1. 1-(1,3-diphenylprop-2-yn-1-yl)piperidine 4a

   Pale yellow oil; yield 0.284g, 96%; Rf 0.8 (5% EtOAc:hexane); 1H NMR (500 MHz, Chloroform-d) δ 7.65-7.63 (m, 2H), 7.55-7.51 (m, 2H), 7.38 – 7.29 (m, 6H), 4.81 (s, 1H), 2.62-2.55 (m, 4H), 1.63-1.57 (m, 4H), 1.47-1.45 (m, 2H).

2. 1-(1-(2-chlorophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4b

   Pale yellow oil; yield 0.316g, 95%; Rf 0.7 (5% EtOAc:hexane); 1H NMR (500 MHz, Chloroform-d): δ 7.75 (dd, J = 7.5, 2.0 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.40-7.38 (m, 1H), 7.34 – 7.31 (m, 3H), 7.29 – 7.22 (m, 2H), 5.10 (s, 1H), 2.62-2.60 (m, 4H), 1.60-1.54 (m, 4H), 1.44 – 1.41 (m, 2H).

3. 1-(1-(4-chlorophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4c
Pale yellow oil; yield 0.296g, 89%; Rf 0.7 (5% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$): $\delta$ 7.59 – 7.52 (m, 2H), 7.51 – 7.50 (m, 2H), 7.35 – 7.31 (m, 5H), 4.76 (s, 1H), 2.55-2.52 (m, 4H), 1.60 – 1.54 (m, 4H), 1.46 – 1.44 (m, 2H).

4. 1-(1-(2-bromophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4d

Pale yellow oil; yield 0.349g, 92%; Rf 0.8(5% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.72-7.70 (m, 1H), 7.54-7.52 (m, 1H), 7.47 – 7.44 (m, 2H), 7.29 – 7.24 (m, 4H), 7.11-7.08 (m, 1H), 4.99 (s, 1H), 2.57-2.55 (m, 4H), 1.57-1.50 (m, 4H), 1.48-1.36 (m, 2H).

5. 1-(1-(3-bromophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4e

Pale yellow oil; yield 0.323g, 85%; Rf 0.7(5% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$): $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.80 (s, 1H), 7.60-7.57 (m, 1H), 7.54 – 7.51 (m, 2H), 7.43-7.41 (m, 1H), 7.35 – 7.32 (m, 3H), 7.24-7.21 (m, 1H), 4.76 (s, 1H), 2.55-2.53 (m, 4H), 1.64-1.56 (m, 4H), 1.46 – 1.43 (m, 2H).
6. **1-(1-(4-bromophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4f**

![Chemical Structure](image)

Pale yellow oil; yield 0.311g, 82%; Rf 0.7(5% EtOAc:hexane); \(^1\)H NMR (500 MHz, Chloroform-\(d\)): \(\delta\) 7.54 – 7.50 (m, 4H), 7.49-7.46 (m, 2H), 7.35 – 7.32 (m, 3H), 4.75 (s, 1H), 2.55-2.53 (m, 4H), 1.65-1.54 (m, 4H), 1.47 – 1.42 (m, 2H).

7. **1-(3-phenyl-1-(p-tolyl)prop-2-yn-1-yl)piperidine 4g**

![Chemical Structure](image)

Pale yellow oil; yield 0.233g, 75%; Rf 0.8(5% EtOAc:hexane); \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta\) 7.53-7.49 (m, 4H), 7.33-7.27 (m, 3H), 7.17-7.15 (m, 2H), 4.75 (s, 1H), 2.56-2.44 (m, 4H), 2.35 (s, 3H), 1.64-1.53 (m, 4H), 1.46-1.42 (m, 2H).

8. **4-(1,3-diphenylprop-2-yn-1-yl)morpholine 4h**

![Chemical Structure](image)

Pale yellow oil; yield 0.262g, 88%; Rf 0.7(10% EtOAc:hexane); \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta\) 8.08-7.63 (m, 2H), 7.53 – 7.50 (m, 2H), 7.39 – 7.30 (m, 6H), 4.79 (s, 1H), 3.77-3.70(m, 4H), 2.65 – 2.64 (m, 4H).

9. **4-(1-(2-chlorophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4i**

![Chemical Structure](image)
S6

Pale yellow oil; yield 0.281g, 84%; Rf 0.5(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.75–7.74 (m, 1H), 7.50–7.47 (m, 2H), 7.42–7.39 (m, 1H), 7.34–7.30 (m, 3H), 7.28–7.23 (m, 2H), 5.12 (s, 1H), 3.75–3.65 (m, 4H), 2.68–2.65 (m, 4H).

10. 4-(1-(4-chlorophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4j

Pale yellow oil; yield 0.284g, 85%; Rf 0.7(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.59–7.57 (m, 2H), 7.52–7.50 (m, 2.5 Hz, 2H), 7.36–7.33 (m, 5H), 4.76 (s, 1H), 3.76–3.68 (m, 4H), 2.63–2.60 (m, 4H).

11. 4-(1-(2-bromophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4k

Pale yellow oil; yield 0.317g, 83%; Rf 0.6 (10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.76 (dd, $J = 7.7$, 1.8 Hz, 1H), 7.60 (dd, $J = 7.9$, 1.3 Hz, 1H), 7.51–7.48 (m, 2H), 7.35–7.30 (m, 4H), 7.17 (td, $J = 7.6$, 1.7 Hz, 1H), 5.07 (s, 1H), 3.72–3.66 (m, 4H), 2.70–2.62 (m, 4H).

12. 4-(1-(3-bromophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4l

S6
Pale yellow oil; yield 0.344g, 90%; Rf 0.5(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.80 (s, 1H), 7.58 (ddd, $J = 7.7, 1.8, 0.9$ Hz, 1H), 7.54 – 7.49 (m, 2H), 7.44 (dt, $J = 8.0, 1.6$ Hz, 1H), 7.37 – 7.32 (m, 3H), 7.23 (d, $J = 7.9$ Hz, 1H), 4.77 (s, 1H), 3.79-3.69 (m, 4H), 2.64-2.61 (m, 4H).

13. 4-(1-(4-bromophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4m$^5$

Pale yellow oil; yield 0.325g, 85%; Rf 0.6(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.54 – 7.48 (m, 6H), 7.36 – 7.32 (m, 3H), 4.74 (s, 1H), 3.76-3.69 (m, 4H), 2.62-2.60 (m, 4H).

14. 4-(3-phenyl-1-(p-tolyl)prop-2-yn-1-yl)morpholine 4n$^5$
Pale yellow oil; yield 0.266g, 85%; Rf 0.5(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.52 – 7.48 (m, 4H), 7.35 – 7.31 (m, 3H), 7.18 (d, $J = 7.8$ Hz, 2H), 4.75 (s, 1H), 3.77-3.68 (m, 4H), 2.68-2.58 (m, 4H), 2.36 (s, 3H).

15. 4-(1-(2-ethoxyphenyl)-3-phenylprop-2-yn-1-yl)morpholine 4o

![Structure Image]

Light yellow oil; yield 0.283g, 82%; Rf 0.4(10% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.63 (dd, $J = 7.6$, 1.8 Hz, 1H), 7.48 – 7.46 (m, 2H), 7.31 – 7.26 (m, 4H), 7.25 – 6.68 (m, 2H), 5.22 (s, 1H), 4.12-4.05 (m, 2H), 3.72-3.70 (m, 4H), 2.73- 2.64 (m, 4H), 1.44 (t, $J = 7.0$ Hz, 3H).

16. 1-(3-phenylprop-2-yn-1-yl)piperidine 4p

![Structure Image]

Pale yellow oil; yield 0.197g, 92%; Rf 0.3(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.45 – 7.42 (m, 2H), 7.30- 7.27 (m, 3H), 3.48 (s, 2H), 2.57 (s, 4H), 1.65 (p, $J = 5.7$ Hz, 4H), 1.46-1.45 (m, 2H).

17. 4-(3-phenylprop-2-yn-1-yl)morpholine 4q

![Structure Image]
Pale yellow oil; yield 0.197g, 91%; Rf 0.2(10% EtOAc:hexane); $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.45 – 7.42 (m, 2H), 7.32-7.29 (m, 3H), 3.79 – 3.77 (m, 4H) , 3.51 (s, 2H), 2.66-2.64 (m, 4H).

18. 1-(1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl)pyrrolidine 4r$^{10}$

![Structure of 1-(1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl)pyrrolidine](structure.png)

Yellow oil; yield 0.266g, 85%; Rf 0.7(10% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.53 – 7.46 (m, 4H), 7.33 – 7.29 (m, 3H), 6.91 – 6.88 (m, 2H) , 4.84 (s, 1H), 3.81 (s, 3H), 2.70 – 2.66 (m, 4H), 1.83-1.79 (m, 4H).

19. 1-(1-phenylhex-1-yn-3-yl)pyrrolidine 4s$^8$

![Structure of 1-(1-phenylhex-1-yn-3-yl)pyrrolidine](structure.png)

Yellow oil; yield 0.210g, 81%; Rf 0.6(10% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.43 – 7.41 (m, 2H), 7.30 – 7.27 (m, 3H), 3.72 (t, $J = 7.5$ Hz, 1H), 2.79 – 2.70 (m, 4H), 1.82 – 1.79 (m, 4H), 1.73 – 1.70 (m, 2H), 1.63 – 1.60 (m, 1H), 1.52 – 1.48 (m, 1H), 0.97 (t, $J = 7.4$ Hz, 3H).

20. 1-(1-phenyl-3-(trimethylsilyl)prop-2-yn-1-yl)piperidine 4t$^8$
Yellow oil; yield 0.271g, 93%; Rf 0.6(10% EtOAc:hexane); $^1$H NMR (500 MHz, Chloroform-$d$)

$\delta$ 7.57 – 7.54 (m, 2H), 7.35 – 7.29 (m, 2H), 7.28 – 7.27 (m, 1H), 4.58 (s, 1H), 2.46-2.44 (m, 4H),
1.61 – 1.50 (m, 4H), 1.44-1.41 (m, 2H), 0.23 (s, 9H).
\(^1\)H of 1-(1,3-diphenylprop-2-yn-1-yl)piperidine 4a

1-(1-(2-chlorophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4b
1-(1-(4-chlorophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4c

1-(1-(2-bromophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4d
1-(1-(3-bromophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4e

1-(1-(4-bromophenyl)-3-phenylprop-2-yn-1-yl)piperidine 4f
1-(3-phenyl-1-(p-tolyl)prop-2-yn-1-yl)piperidine 4g

4-(1,3-diphenylprop-2-yn-1-yl)morpholine 4h
4-(1-(2-chlorophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4i

4-(1-(4-chlorophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4j
4-(1-(2-bromophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4k

4-(1-(3-bromophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4l
4-(1-(4-bromophenyl)-3-phenylprop-2-yn-1-yl)morpholine 4m

4-(3-phenyl-1-(p-tolyl)prop-2-yn-1-yl)morpholine 4n
4-(1-(2-ethoxyphenyl)-3-phenylprop-2-yn-1-yl)morpholine 4o

1-(3-phenylprop-2-yn-1-yl)piperidine 4p
4-(3-phenylprop-2-yn-1-yl)morpholine 4q

1-(1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl)pyrrolidine 4r
1-(1-phenylhex-1-yn-3-yl)pyrrolidine 4s

1-(1-phenyl-3-(trimethylsilyl)prop-2-yn-1-yl)piperidine 4t
References


