Reusable polymer-anchored amino acid copper complex for the synthesis of propargylamines

Liang Wang and Chun Cai*

Chemical Engineering College, Nanjing University of Science & Technology, Nanjing 210094, P.R. China

An amino acid was anchored to chloroacetylated polystyrene beads and the polymeric ligand containing N, O donor sites was treated with a solution of CuI to form the supported copper complex. The one-pot synthesis of propargylamines was then achieved efficiently via a three-component coupling of aldehydes, alkynes and amines using the supported copper catalyst under mild conditions. The catalyst could be recovered by simple filtration and reused several times without significant loss of activity.

Keywords: polymer-supported copper catalyst, propargylamines, amino acid, chloroacetylated polystyrene

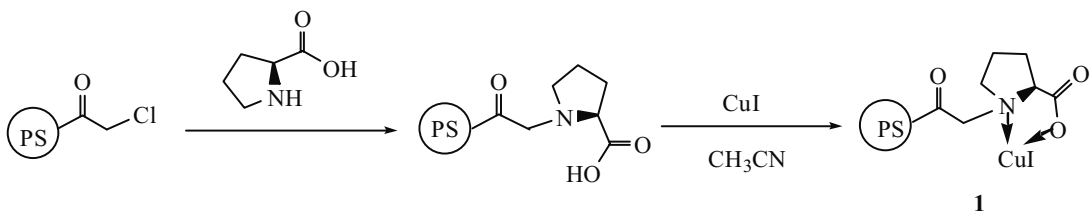
Propargylamines are important synthetic intermediates for potential therapeutic agents and polyfunctional amino derivatives.[1,2] Traditionally, propargylamines are synthesised by the nucleophilic attack of lithium acetylides or Grignard reagents on imines or their derivatives.[3-5] Unfortunately, these reagents are required in stoichiometric quantities, are highly moisture sensitive and require strictly controlled reaction conditions. Progress has been made in expanding the scope of the direct addition of alkynes to carbon–nitrogen double bonds by employing various transition metal catalysts such as copper,[6,7] silver,[8,9] gold,[10] iridium,[11] zinc,[12-14] zirconium[15] and rhenium.[16] Among the emerging methods, copper-catalysed reactions have received increasing attention. Despite the advantages of homogeneous metal catalysts, difficulties in recovering the catalysts from the reaction mixture severely restrict their wide use in industry. Research has been directed at the introduction and application of effective and eco-friendly heterogeneous catalysts.[17] Immobilisation of catalysts on polymer supports often offers advantages for carrying out organic transformations.[18] Ease of work-up, higher yields, product selectivity and reusability of the catalysts make them more attractive than their homogeneous counterparts.

Recently, advances have been made in the modification of copper-catalysed reactions. By using some special ligands such as *N,N*- and *N,O*-bidentate compounds, many CuI-catalysed C–N,[19] C–O,[20] C-S,[21] C–C[22] bond formation reactions can be carried out under relatively mild conditions. Although the detailed function for these ligands awaits further exploration,[23] new transformations using them are being discovered.[24] We considered that anchoring a *N,O*-bidentate ligand such as an amino acid onto a polymer matrix could be useful in polymer-supported copper-catalysed reactions.

We report preparation of a new amino acid functionalised resin and its use as a ligand for the copper-catalysed one-pot synthesis of propargylamines.

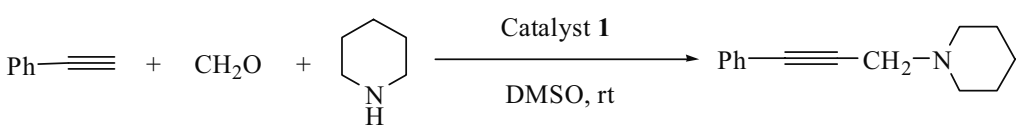
Catalyst **1** was readily accessible in two steps from chloroacetylated polystyrene. Treatment of the polymer with L-proline provided the corresponding amino acid functionalised polystyrene, which was then treated with copper iodide in acetonitrile to yield the catalyst as dark green beads (Scheme 1). Characterisation of the catalyst was performed by IR, elemental analysis, TGA and ICP analysis. The representative IR peaks at 3440, 1668, 1647, 1450 and 1082 cm^{-1} indicated the successful attachment of L-proline on to the resin. The thermal studies (TGA) showed that the support was stable up to 130 °C, whilst the catalyst was even more stable, with a decomposition temperature being higher than 150 °C. The copper content of the catalyst was 1.26 mmol/g as determined by ICP analysis.

Initially, in an effort to develop an optimal catalytic system, various reaction parameters were studied via a three-component coupling of phenylacetylene, formaldehyde and piperidine in a solvent at room temperature (Scheme 2). The results are summarised in Table 1. The solvent had a pronounced effect on the reactions (Table 1, entries 1–6). As seen from Table 1, acetonitrile was less efficient than DMSO, whilst methanol, THF and toluene afforded low yields and water did not afford any product at all. The effect of catalyst loading on the reaction was evaluated next. In the absence of catalyst, there was no reaction at all. When 2 mol% of catalyst was added, the reaction was obviously accelerated, but the yield was unsatisfactory. As the catalyst was increased to 5 mol%, it gave a nearly quantitative yield. Hence, 5 mol% of catalyst was sufficient for the reaction system. Various



1

Scheme 1



Scheme 2

* Correspondent. E-mail: c.cai@mail.njust.edu.cn.

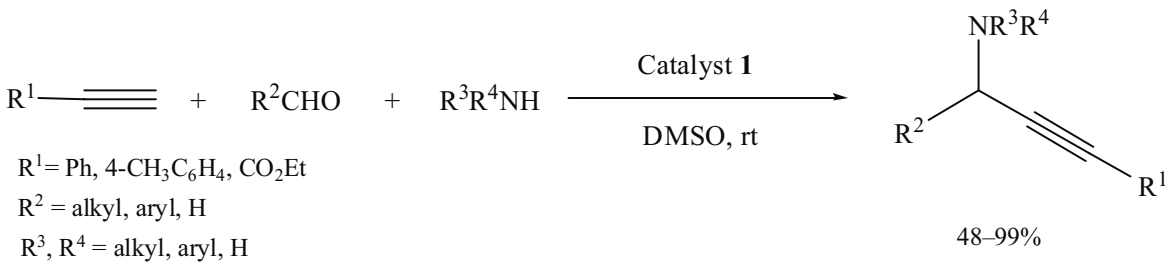
Table 1 Screening of reaction parameters for the one-pot synthesis of propargylamine[a]

Entry	Catalyst/mol%	Solvent	Yield/%[b]
1	**1**(5)	MeOH	25
2	**1**(5)	Toluene	30
3	**1**(5)	THF	42
4	**1**(5)	CH_3CN	87
5	**1**(5)	H_2O	–
6	**1**(5)	DMSO	99
7	**1**(5)	DMSO	99, 99, 98, 95, 90,90
8	**1**(0)	DMSO	–
9	**1**(2)	DMSO	87
10	**1**(10)	DMSO	99
11[c]	**1**(5)	DMSO	–
12	CuI(5)	DMSO	97
13	CuBr(5)	DMSO	65
14	CuCl(5)	DMSO	23
15	$CuSO_4$(5)	DMSO	–
16	Cu(5)	DMSO	–

[a]All reactions were carried out at room temperature for 2 h (see experimental section).
[b]Isolated yields.
[c]The catalyst was filtered after 10 minutes.

copper catalysts such as CuI, CuBr, CuCl, $CuSO_4$ and Cu were also investigated for the reaction, however, only the supported catalyst as well as CuI was found to be effective (Table 1, entries 6, 12–16). Meanwhile, in order to find out whether the reaction took place in the solid matrix or whether CuI released into the reaction system was responsible for the reaction, the catalyst was filtered after 10 minutes and the filtrate kept stirring for 2 h. However, no reaction was observed (Table 1, entry 11). Furthermore, the recyclability of the supported catalyst was investigated. It is worth noting that the catalyst was recovered quantitatively and reused for at least six cycles with a slight decrease in activity (Table 1, entry 7).

Under the optimised reaction conditions, we carried out the coupling reactions of a variety of aldehydes, amines and alkynes to examine the scope and generality of the catalyst reactions (Scheme 3), and the results were shown in Table 2. As can be seen from Table 2, when the formaldehyde was chosen as the substrate, all of the secondary amines gave excellent yields with phenylacetylene within 2 h (Table 2, entries 1–4). An excellent yield was also obtained when the

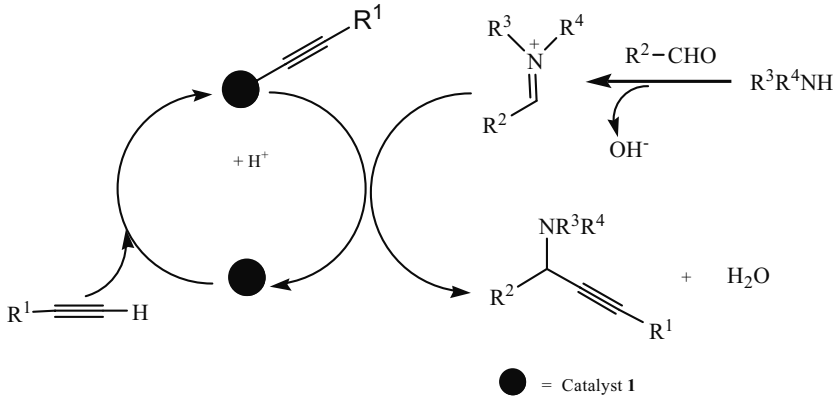


Scheme 3

Table 2 Synthesis of propargylamines[a]

Entry	R^1	R^2	R^3, R^4	Time/h	Yield/%[b]
1	Ph	H	$(CH_2)_5$	2	99
2	Ph	H	$(CH_2)_2O(CH_2)_2$	2	99
3	Ph	H	Et, Et	2	92
4	Ph	H	i-Pr, i-Pr	2	94
5	Ph	H	n-Bu, H	12	78
6	Ph	H	$PhCH_2$, H	12	81
7	4-$CH_3C_6H_4$	H	$(CH_2)_5$	2	94
8	4-$CH_3C_6H_4$	H	i-Pr, i-Pr	2	91
9	CO_2Et	H	$(CH_2)_5$	2	92
10	CO_2Et	H	Et, Et	2	89
11	Ph	Ph	$(CH_2)_5$	12	Trace
12[c]	Ph	Ph	$(CH_2)_5$	12	Trace
13[d]	Ph	Ph	$(CH_2)_5$	12	72
14[d]	Ph	4-ClC_6H_4	$(CH_2)_5$	12	63
15[d]	Ph	4-MeC_6H_4	$(CH_2)_5$	12	57
16[d]	Ph	4-$MeOC_6H_4$	$(CH_2)_5$	12	48
17[d]	Ph	2-Furfuryl	$(CH_2)_5$	12	75
18	Ph	n-C_3H_7	$(CH_2)_5$	12	82
19	Ph	Cyclohexyl	$(CH_2)_5$	12	79
20	Ph	paraformaldehyde	$(CH_2)_5$	12	96

[a]Reaction conditions as exemplified in the experimental procedure.
[b]Isolated yields.
[c]1.2 equiv Na_2CO_3 or NEt_3 was used.
[d]Reactions were carried out at 60 °C and 10 mol% of catalyst was used.



Scheme 4

substrate was changed to paraformaldehyde by prolonging the time to 12 h due to its slow depolymerisation (Table 2, entry 20). Less basic amines, and even primary amines, gave good yields after 12 h (Table 2, entries 5 and 6). Further, we examined the effect of a variety of terminal alkynes in the reaction. It was noteworthy that there were no obvious difference between the alkynes and all of the reactions proceeded smoothly to give excellent yields (Table 2, entries 1, 7–10). Then the reaction was extended to different aldehydes. However, no reaction was observed with aromatic and heteroaromatic aldehydes at room temperature. Even an additive such as Na_2CO_3, NEt_3 did not have any effect (Table 2, entries 11 and 12). Moderate yields were obtained when increasing the catalyst to 10 mol% and carrying out the reaction at 60 °C for 12 h. Meanwhile, aldehydes bearing electron donating groups gave relatively lower yields (Table 2, entries 15 and 16). Aliphatic aldehydes (Table 2, entries 18 and 19), on the other hand, displayed higher reactivity and gave higher yields.

A tentative mechanism may be proposed involving the activation of the C–H bond of alkyne by the supported copper catalyst.[10] The copper acetylide intermediate thus generated reacted with the immonium ion generated in situ from aldehyde and amine to give the corresponding propargylamine and regenerate the supported copper catalyst for further reactions (Scheme 4).

In conclusion, a mild and efficient polymer-supported copper-catalysed three-component coupling of aldehyde, alkyne and amine via C–H activation has been achieved. This protocol is an environmentally friendly process and can be used to generate a diverse range of propargylamines in moderate to excellent yields. The simple procedure for catalyst preparation, easy recovery and reusability of the catalyst is expected to contribute to its utilisation for the development of benign chemical process and products.

Experimental

Reagents were obtained from commercial sources. IR spectra were recorded with a Bomem Michelson model 102 FTIR. Elemental analysis were performed on a Yanagimoto MT3CHN recorder. Metal content was measured by ICP on a Varian AA240 analyser. Thermogravimetric analysis were carried out on a Shimadzu DT-30 instrument at a heating rate of 20 °C. min^{-1} under an atmosphere of nitrogen. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker Advance RX300 analyser in $CDCl_3$ with TMS as internal standard.

Preparation of L*-proline grafted polystyrenes:* Pre-washed chloroacetylated polystyrene beads (4.1 mmol Cl) 1.0 g were swollen in 1,2-dichloroethane 30 ml for 12 h, then L-proline10 mmol, TEBA 0.2 g, 25% sodium hydroxide solution 10 ml were added subsequently, and the mixture was stirred for 8 h at 90 °C. After cooling to room temperature, the pH was adjusted to 5.0 and the colour of the beads changed to yellow. The beads were filtered and washed thoroughly with water, 5% HCl solution and methanol, dried at 80 °C under vacuum overnight. Elemental analysis for nitrogen after ligand attachment gave values of 3.5%, which corresponds to 2.5 mmol of L-proline anchored per gram of resin.

Preparation of polymer-supported copper catalyst: The functionalised beads (1.0 g) were kept in contact with acetonitrile (10 ml) for 1 h. To this was added an acetonitrile solution (10 ml) of copper (I) iodide (0.475 g, 2.5 mmol) and the mixture was stirred for 24 h at room temperature under nitrogen. Then the dark green beads were filtered, washed thoroughly with water, acetone and methanol, dried at 60 °C under vacuum overnight.

Typical procedure for the synthesis of propargylamines: A mixture of aldehyde (1 mmol), terminal alkyne (0.5 mmol), amine (0.6 mmol), DMSO (1 ml) and catalyst (20 mg, 5 mol%) was placed in a round-bottomed flask and stirred at room temperature. After completion of the reaction (monitored by TLC), the catalyst was removed by filtration. After extraction with ether and basic aqueous workup, the solvent was removed to afford the crude product which was further purified by column chromatography on silica gel (hexane/ethyl acetate = 9:1) to afford the pure product. Previously reported materials were identified by comparing of their physical, ^{1}H NMR, ^{13}C NMR and element analysis with those reported in the literature.

1-(3-phenyl-2-propynyl)piperidine (Table 2, entry 1): Oil;[25] IR (film): 2933, 2278, 2749, 1598, 1456, 1321, 1154, 750 cm^{-1}; ^{1}H NMR (300 MHz, CDCl3) δ: 7.45–7.41 (m, 2H), 7.27–7.25 (m, 3H), 3.46 (s, 2H), 2.55 (s, 4H), 1.67–1.59 (m, 4H), 1.45 (t, J = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 131.4, 127.9, 127.7, 123.1, 84.8, 82.7, 53.2, 48.2, 25.7, 23.7; Anal. Calcd for $C_{14}H_{17}N$: C, 84.42; H, 8.54; N, 7.04; Found: C, 84.40; H, 8.52; N, 7.01%.

1-(3-phenyl-2-propynyl)morpholine (Table 2, entry 2): Oil;[26] IR (film): 3057, 2958, 2362, 1599, 1489, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.30–7.50 (m, 5H), 3.78 (t, J = 5.4 Hz, 4H), 3.46 (s, 2H), 2.65 (t, J = 5.4 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 132.0, 127.9, 123.1, 85.5, 83.2, 66.7, 52.3, 47.9; Anal. Calcd for $C_{13}H_{15}NO$: C, 77.61; H, 7.46; N, 6.97; O, 7.96; Found: C, 77.65; H, 7.43; N, 6.92; O, 7.90%.

N,N-Diethyl-(3-phenyl-2-propynyl)amine (Table 2, entry 3): Oil;[27] IR (film): 2970, 2230, 1599, 1489, 1443, 1200, 1092, 1069 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42–7.39 (m, 2H), 7.28–7.26 (m, 3H), 3.63 (s, 2H), 2.61 (q, J = 5.4 Hz, 4H), 1.10 (t, J = 5.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 131.6, 128.1, 127.6, 123.2, 84.9, 84.3, 47.3, 41.5, 12.8; Anal. Calcd for $C_{13}H_{17}N$: C, 83.42; H, 9.09; N, 7.49; Found: C, 83.38; H, 9.03; N, 7.45%.

N,N-Diisopropyl-(3-phenyl-2-propynyl)amine (Table 2, entry 4): Oil;[27] IR (film): 2966, 2192, 1598, 1488, 1380, 1203, 1176, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.41–7.38 (m, 2H), 7.28–7.26 (m, 3H), 3.65 (s, 2H), 3.26 (sept, J = 5.0 Hz, 2H), 1.15 (d, J = 5.0 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 131.2, 128.0, 127.6, 123.2, 88.9, 83.4, 48.3, 34.5, 20.8; Anal. Calcd for $C_{15}H_{21}N$: C, 83.72; H, 9.77; N, 6.51; Found: C, 83.80; H, 9.75; N, 6.47%.

N-Butyl-(3-phenyl-propynyl)amine (Table 2, entry 5): Oil;[28] IR (film): 3100, 2957, 2235, 1598, 1384, 1156, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.46–7.41 (m, 2H), 7.36–7.26 (m, 3H), 3.58 (s, 2H), 2.62 (m, 2H), 2.10 (s, 1H), 1.41–1.33 (m, 4H), 0.96 (t, J = 5.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 131.6, 128.1, 127.6, 123.2, 86.8, 84.3, 47.3, 36.6, 33.5, 20.5, 13.7; Anal. Calcd for $C_{13}H_{17}N$: C, 83.42; H, 9.09; N, 7.49; Found: C, 83.37; H, 9.07; N, 7.51%.

N-Benzyl-(3-phenyl-2-propynyl)amine (Table 2, entry 6): Oil;[29] IR (film): 3076, 2956, 2218, 1488, 1210, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.48–7.44 (m, 2H), 7.38–7.23 (m, 8H), 3.62 (s, 2H), 3.49 (s, 2H), 2.10 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 138.3, 131.6, 129.1,

128.1, 127.9, 127.1, 123.2, 85.6, 84.3, 60.1, 45.6; Anal. Calcd for $C_{16}H_{15}N$: C, 86.88; H, 6.79; N, 6.33; Found: C, 86.77; H, 6.73; N, 6.35%.

1-[3-(p-tolyl)-2-propynyl]piperidine (Table 2, entry 7): Oil;[30] IR (film): 3010, 2938, 2258, 1592, 1458, 1154, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.34–7.30 (d, 2H), 7.11–7.07 (d, 2H), 3.46 (s, 2H), 2.50–2.61 (t, 4H), 2.32 (s, 3H), 1.59–1.70 (t, 4H), 1.36–1.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 137.7, 131.5, 128.8, 120.2, 85.0, 53.4, 48.4, 25.9, 23.7, 21.3; Anal. Calcd for $C_{15}H_{19}N$: C, 84.51; H, 8.92; N, 6.57; Found: C, 84.54; H, 8.90; N, 6.50%.

N,N-Diisopropyl-[3-(p-tolyl)-2-propynyl]amine (Table 2, entry 8): Oil; IR (film): 2970, 2220, 1599, 1489, 1380, 1200, 1092, 760 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.35–7.30 (d, 2H), 7.10–7.03 (d, 2H), 3.46 (s, 2H), 2.95 (m, 2H), 2.35 (s, 3H), 1.10 (d, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 137.4, 132.0, 128.8, 123.2, 86.8, 81.4, 46.1, 35.7, 21.4, 20.8; Anal. Calcd for $C_{16}H_{23}N$: C, 83.84; H, 10.05; N, 6.11; Found: C, 83.77; H, 10.07; N, 6.08%.

Ethyl 4-piperidin-2-butynoate (Table 2, entry 9): Oil; IR (film): 2968, 2210, 1732, 1458, 1384, 1156, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.31 (q, J = 3.6 Hz, 2H), 3.46 (s, 2H), 2.55 (m, 4H), 1.67–1.59 (m, 4H), 1.45 (t, J = 6.5 Hz, 2H), 1.39 (t, J = 3.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 143.2, 84.8, 77.2, 58.2, 51.2, 40.6, 25.7, 23.7, 13.9; Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.69; H, 8.72; N, 7.18; Found: C, 67.60; H, 8.71; N, 7.20%.

Ethyl 4-diethylamino-2-butynoate (Table 2, entry 10): Oil; IR (film): 2965, 2228, 1730, 1450, 1380, 1060, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.30 (q, J = 3.0 Hz, 2H), 3.45 (s, 2H), 2.54 (m, 4H), 1.39 (t, J = 3.6 Hz, 3H), 1.10 (t, J = 5.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 143.6, 84.5, 78.8, 58.3, 51.6, 40.5, 12.8; Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.57; H, 9.29; N, 7.65; Found: C, 65.61; H, 9.25; N, 7.61%.

N-(1,3-Diphenyl-2-propynyl)piperidine (Table 2, entry 11): Oil;[31] IR (film): 3060, 2933, 2749, 1598, 1489, 1450, 1321, 1154, 756 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.67–7.62 (m, 2H), 7.55–7.50 (m, 2H), 7.40–7.26 (m, 6H), 4.81 (s, 1H), 2.61–2.50 (m, 4H), 1.70–1.50 (m, 4H), 1.50–1.40 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 138.9, 132.1, 128.8, 128.5, 128.3, 127.6, 123.6, 88.0, 86.4, 62.6, 59.9, 26.4, 24.6; Anal. Calcd for $C_{20}H_{21}N$: C, 87.27; H, 7.64; N, 5.09; Found: C, 87.41; H, 7.61; N, 5.03%.

N-(1-(4-Chlorophenyl)-3-phenyl-2-propynyl)piperidine (Table 2, entry 14): Oil;[31] IR (film): 3055, 2934, 2748, 1667, 1597, 1487, 1317, 1154, 1089, 756 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.65–7.61 (m, 2H), 7.59–7.54 (m, 2H), 7.40–7.34 (m, 5H), 4.80 (s, 1H), 2.62–2.54 (m, 4H), 1.71–1.54 (m, 4H), 1.54–1.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 137.6, 133.5, 132.1, 130.1, 128.6, 128.5, 123.8, 88.5, 85.6, 62.1, 61.9, 50.9, 26.5, 24.7; Anal. Calcd for $C_{20}H_{20}NCl$: C, 77.54; H, 6.46; N, 4.53; Cl, 11.47; Found: C, 77.61; H, 6.42; N, 4.49; Cl, 11.50%.

N-(1-(4-Methylphenyl)-3-phenyl-2-propynyl)piperidine (Table 2, entry 15): Oil;[31] IR (film): 2933, 2804, 2748, 2210, 1598, 1510, 1318, 1154, 1092, 756 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.61–7.56 (m, 4H), 7.42–7.34 (m, 3H), 7.23 (d, J = 6.0 Hz, 2H), 4.83 (s, 1H), 2.68–2.56 (m, 4H), 2.42 (s, 3H), 1.73–1.58 (m, 4H), 1.58–1.45 (m,2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 137.6, 135.9, 132.1, 130.1, 129.0, 128.7, 128.3, 123.7, 87.9, 86.7, 75, 62.3, 50.9, 26.5, 24.8, 21.4; Anal. Calcd for $C_{21}H_{23}N$: C, 87.20; H, 7.96; N, 4.84; Found: C, 87.30; H, 7.92; N, 4.79%.

N-(1-(4-Methoxyphenyl)-3-phenyl-2-propynyl)piperidine (Table 2, entry 16): Oil;[31] IR (film): 2998, 2932, 2748, 1610, 1511, 1302, 1169, 1036, 756 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.61–7.54 (m, 4H), 7.38–7.32 (m, 3H), 6.96–6.91 (m, 2H), 4.78 (s, 1H), 3.82 (s, 3H), 2.65–2.52 (m, 4H), 1.70–1.53 (m, 4H), 1.53–1.41 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 159.2, 132.0, 130.9, 129.9, 128.6, 128.3, 123.6, 113.6, 87.9, 86.7, 62.1, 55.4, 50.9, 26.5, 24.8; Anal. Calcd for $C_{21}H_{23}NO$: C, 82.62; H, 7.54; N, 4.59; Found: C, 82.48; H, 7.50; N, 4.55%.

N-(1-(2-Furyl)-3-phenyl-2-propynyl)piperidine (Table 2, entry 17): Oil;[32] IR (film): 2968, 2748, 2236, 1610, 1510, 1036, 750 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.50–7.49 (m, 2H), 7.49–7.48 (m, 1H), 7.43–7.32 (m, 3H), 6.51–6.50 (m, 1H), 6.36–6.35 (m, 1H), 4.87 (s, 1H), 2.64–2.51 (m, 4H), 1.70–1.55 (m, 4H), 1.50–1.40 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 150.7, 142.8, 131.8, 128.4, 128.3, 122.5, 110.1, 109.7, 87.0, 82.8, 66.9, 56.1, 49.6, 26.4, 24.8; Anal. Calcd for $C_{18}H_{19}NO$: C, 81.51; H, 7.17; N, 5.28; Found: C, 81.48; H, 7.19; N, 5.31%.

N-(1-Propyl-3-phenyl-2-propynyl)piperidine (Table 2, entry 18): Oil;[33] IR (film): 3010, 2932, 2180, 1615, 1500, 1380, 1165, 1035, 750 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.39–7.36 (m, 2H), 7.25–7.23 (m, 3H), 3.45 (t, J = 7.2 Hz, 1H), 2.55–2.44 (m, 4H), 1.68–1.40 (m, 10H), 0.97 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 131.6, 128.1, 127.7, 123.4, 87.9, 85.5, 58.2, 35.5, 26.2, 24.4, 20.2, 13.9; Anal. Calcd for $C_{17}H_{23}N$: C, 84.65; H, 9.54; N, 5.81; Found: C, 84.58; H, 9.48; N, 5.79%.

N-(1-Cyclohexyl-3-phenyl-2-propynyl)piperidine (Table 2, entry 18): Oil;[32] IR (film): 2998, 2748, 2235, 1610, 1530, 1378, 1160, 1036, 745 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ: 7.45–7.44 (m, 2H), 7.29–7.28 (m, 3H), 3.13 (d, J = 9.6 Hz, 1H), 2.60–2.58 (m, 2H), 2.40–2.37 (m, 2H), 2.10–2.02 (m, 1H), 1.77–1.51 (m, 4H), 1.32–0.96 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ: 131.6, 128.1, 127.7, 123.3, 87.2, 86.5, 63.8, 49.8, 38.9, 30.0, 26.6, 26.1, 25.9; Anal. Calcd for $C_{20}H_{27}N$: C, 85.41; H, 9.61; N, 4.98; Found: C, 85.32; H, 9.53; N, 4.90%.

Received 11 June 2008; accepted 31 July 2008
Paper 08/5321 doi: 10.3184/030823408X349989
Published online: 8 September 2008

References

1 I. Naota, H. Takaya and S.I. Murahashi, *Chem. Rev.,* 1998, **98**, 2599.
2 G. Dyker, *Angew. Chem., Int. Ed.,* 1999, **38**, 1698.
3 C. Wei and C.-J. Li, *J. Am. Chem. Soc.,* 2002, **124**, 5638.
4 F. Tubery, D.S. Grierson and H.-P. Husson, *Tetrahedron Lett.,* 1987, **28**, 6457.
5 T. Murai, Y. Mutoh, Y. Ohta and M. Murakami, *J. Am. Chem. Soc.,* 2004, **126**, 5968.
6 C. Wei and C.-J. Li, *J. Am. Chem. Soc.,* 2002, **124**, 5638.
7 D.A. Black and B.A. Arndtsen, *Tetrahedron*, 2005, **61**, 11317.
8 W. Yan, R. Wang, Z. Xu, J. Xu, L. Lin, Z. Shen and Y. Zhou, *J. Mol. Catal. A: Chem.,* 2006, **255**, 81.
9 Z. Li, C. Wei, L. Chen, R.S. Varma and C.-J. Li, *Tetrahedron Lett.,* 2004, **45**, 2443.
10 C. Wei and C.-J. Li, *J. Am. Chem. Soc.,* 2003, **125**, 9584.
11 C. Fischer and E.M. Carreira, *Org. Lett.,* 2001, **3**, 4319.
12 D.E. Frantz, R. Fassler and E.M. Carreira, *J. Am. Chem. Soc.,* 1999, **121**, 11245.
13 L. Zani, S. Alesi, P.G. Cozzi and C. Bolm, *J. Org. Chem.,* 2006, **71**, 1558.
14 K.-Y. Lee, C.-G. Lee, J.-E. Na and J.-N. Kim, *Tetrahedron Lett.,* 2005, **46**, 69.
15 L.C. Akullian, M.L. Snapper and A.H. Hoveyda, *Angew. Chem., Int. Ed.,* 2003, **42**, 4244.
16 Y. Kuninobu, Y. Inoue and K. Takai, *Chem. Lett.,* 2006, **35**, 1376.
17 S.V. Ley, I.R. Baxendale, R.N. Bream, P.S. Jackson, A.G. Leach, D.A. Longbottom, M. Nesi, J.S. Scott, R.I. Storer and S.J. Taylor, *J. Chem. Soc. Perkin Trans.1,* 2000, **23**, 3815.
18 M.E. Wright and S.R. Pulley, *J. Org. Chem.,* 1987, **52**, 5036.
19 H. Zhang, Q. Cai and D. Ma, *J. Org. Chem.,* 2005, **70**, 5164.
20 D. Ma, Q. Cai and X. Xie, *Synlett.,* 2005, 1767.
21 W. Zhu and D. Ma, *J. Org. Chem.,* 2005, **70**, 2696.
22 D. Ma and F. Liu, *Chem. Commun.,* 2004, 1934.17 B.M. Trost and D.T. Stiles, *Org. Lett.*, 2005, **7**, 2117.
23 I.P. Beletskaya and A.V. Cheprakov, *Coord. Chem. Rev.,* 2004, **248**, 2337.
24 B.M. Trost and D.T. Stiles, *Org. Lett.*, 2005, **7**, 2117.
25 C. Mannich and F.T. Chan, *Ber.*, 1933, **66**, 418.
26 J.H. Ann, M.J. Joung and N.M. Yoon, *J. Org. Chem.,* 1999, **64**, 488.
27 H. Nakamura, T. Kamakura, M. Ishikura and J.F. Biellmann, *J. Am. Chem. Soc.,* 2004, **126**, 5958.
28 L.W. Bieber and M.F. Silva, *Tetrahedron Lett.,* 2004, **45**, 8281.
29 G. W. Kabalka, L.L Zhou, L. Wang and R.M. Pagni, *Tetrahedron*, 2006, **62**, 857.
30 El.O. Chukhadzhyan, E.O. Chukhadzhyan and A.T. Babayan, *Zh. Org. Khim.*, 1974, **10**, 46.
31 C.M. W and C.J. L, *J. Am. Chem. Soc.,* 2003, **125**, 9584.
32 E. Ramu, R. Varala, N. Sreelatha and S.R. Adapa, *Tetrahedron Lett.,* 2007, **48**, 7184.
33 B. Sreedhar, P.S. Reddy, C.S.V. Krishna and P.V. Babu, *Tetrahedron Lett.,* 2007, **48**, 7882.