Functionalization of aliphatic tertiary amines mediated by hexachloroethane/cat. copper: synthesis of propargylic amines and methylene-bridged *bis*-1,3-dicarbonyl derivatives

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Abstract
Copper-catalyzed functionalization of aliphatic tertiary amines with the assistance of C_2Cl_6 is described. This method details the alkynylation of aliphatic tertiary amines and the synthesis of methylene-bridged *bis*-1,3-dicarbonyl derivatives. The mechanism of the selective oxidation of aliphatic tertiary amines was also discussed. A broad spectrum of aliphatic tertiary amines was examined in this methodology.

Keywords: Copper, aliphatic tertiary amine, hexachloroethane, C-H functionalization

Introduction

Carbon-hydrogen bond activation or oxidation has stimulated great interest in the past decades since it can conveniently enable the carbon-carbon or carbon-hetero bond formation without the pre-functionalization of substrates.[1] Considerable progress has been made recently to carry out this kind of unconventional bond formation in which, oxidative dehydrogenation and functionalization of the sp^3 CH bond adjacent to the heteroatom or functional groups have successfully been realized.[2]

Among these carbon-hydrogen oxidative dehydrogenation couplings, large efforts have been focused on the functionalizations of sp^3 C-H bond adjacent to nitrogen atom of the tertiary amines. A lot of oxidants were used in this oxidative dehydrogenation coupling system, such as O_2,[3] benzoyl peroxide,[4] tert-butyl peroxide,[5] NBS,[6] DDQ,[7] DEAD,[8] and $PhI(OAc)_2$[9]. To activate the oxidative dehydrogenation coupling more efficiently, the assistance of transition metal such as rhodium,[10] ruthenium,[11] copper,[2] or iron,[12] was frequently necessary. Mediated by a catalytic amount of transition metal and a suitable oxidant, several kinds of functionalizations with

aromatic tertiary amines as the substrates were reported. However, research of aliphatic tertiary amines was relatively rare[13] owing probably to the relatively reduced stability of the reaction intermediates formed, and at the same time, the regioselectivity of oxidative dehydrogenation of aliphatic tertiary amines is hard to control.

Results and Discussion

Polyhalohydrocarbons were rarely used as the reactants since most of them are frequently very stable.[14] Rare typical example is the Appel reaction, where the combination of PPh_3 and CCl_4 enabled the transformation of an alcohol into an alkyl chloride.[15] Because of the similarity of tertiary phosphine and tertiary amine, the system of tertiary amine and polyhalohydrocarbon in organic synthesis should be worth investigating. Literature screening revealed that the reaction mechanism of aliphatic amines and polyhalohydrocarbons was studied intensively around 1960s.[16] Malik and Vofsi[17] described the mechanism as an initial free-radical chain process followed by a number of ionic steps.

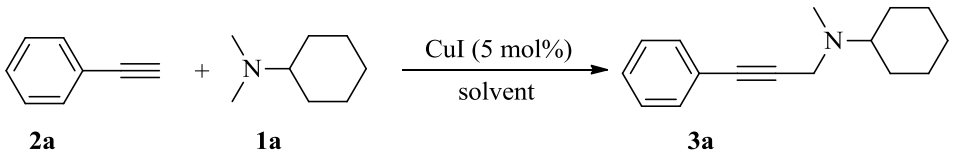
Despite the extensive investigation on the mechanism for this system, the application of polyhalohydrocarbon in organic synthesis has not been fully explored. Recently we reported that the combination of cat. CuCl and CCl_4 mediated the synthesis of sulfonyl amidines from tertiary amines and sulfonyl azides.[18] Herein we wish to report on the functionalizations of aliphatic tertiary amines mediated by hexachloroethane/catalytic copper salts.

Alkynylation of aliphatic tertiary methylamine with a terminal alkyne

Propargylic amine derivatives have drawn much attention and their synthesis is of high interest because of their important utility as synthons for drug synthesis,[19] and for their interesting bioactivity.[20] The nucleophilic alkynylation of functionalized amines and transition metal-catalyzed Mannich type reaction of terminal alkynes to imines were the typical ways to synthesize these compounds.[21] However in these effective traditional methods, the presence of a leaving group or the use of imines prepared from the prefunctionalized aldehydes and amines is necessary. Recently, the direct alkynylation to sp^3 C-H bond adjacent to nitrogen of a tertiary amine has emerged as an interesting method. Mild and efficient catalytic systems applied to dehydrogenation of tertiary amines were developed by several groups.[18,2]

In order to optimize the reaction conditions, several polyhalohydrocarbons, solvents and copper catalysts were screened (Table 1). We first chose CCl_4 as a promoter. CuI proved to be the best catalyst over CuBr and CuCl (entries 1-3). CH_3CN was the best solvent in contrast to other solvents such as ethyl acetate, hexane, 1,4-dioxane, DMSO, DMF, $ClCH_2CH_2Cl$ (entries 4-9). Even with the use of CuI, the yield was still rather low until we found that C_2Cl_6 could be an alternative to CCl_4 (entry 11). In this specific case, 3 equiv of *N*,*N*-dimethylcyclohexylamine was added, and the desired product was isolated in satisfactory yield (entry 12).

Table 1. Reaction of phenylacetylene with *N*,*N*-dimethylcyclohexylamine: optimization of conditions[a]



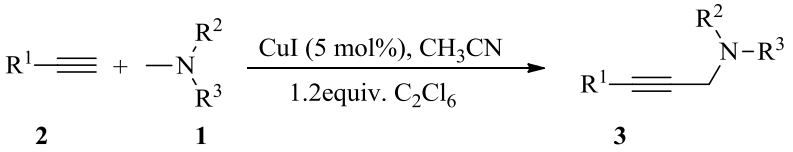
2a **1a** **3a**

Entry	Polyhalohydrocarbon	Catalyst	Solvent	Yield (%)[b]
1	CCl_4	CuBr	CH_3CN	23
2	CCl_4	CuCl	CH_3CN	36
3	CCl_4	CuI	CH_3CN	41
4	CCl_4	CuI	EtOAc	30
5	CCl_4	CuI	hexane	21
6	CCl_4	CuI	1,4-dioxane	19
7	CCl_4	CuI	DMSO	32
8	CCl_4	CuI	DMF	15
9	CCl_4	CuI	$ClCH_2CH_2Cl$	21
10	CBr_4	CuI	CH_3CN	3
11	C_2Cl_6	CuI	CH_3CN	53
6c	C_2Cl_6	CuI	CH_3CN	72

[a]Phenylacetylene (1 mmol), *N*,*N*-dimethylcyclohexylamine (2 mmol), polyhalohydrocarbon (1.1 mmol), solvent (4 mL), 24hrs, rt. [b]Isolated yields based on phenylacetylene. [c]*N*,*N*-dimethylcyclohexylamine (3mmol).

Under the optimized conditions, a variety of terminal alkynes and aliphatic tertiary methylamines were investigated, and the corresponding alkynylation products were obtained in good to excellent yields (Table 2). There is no remarkable electronic and position effect of the substituents on the aryl ring of the terminal alkynes on this reaction (entries 2-6). Benzyl acetylene also served as a good candidate (entry 8). Especially, it should be noted that the 3-ethynylthiophene as the starting material successfully afforded the corresponding propargylic amine (entry 9). The aliphatic alkyne 1-hexyne afforded the desired product in good yield as well (entry 10). Trimethylsilyl could be tolerated under the conditions (entry 11). A distinguishing feature was that several types of aliphatic tertiary methylamines can be used in this study, which was in sharp contrast with the previous results (entries 12-14). *N*-methyldicyclohexylamine also gave a better result (entry 15). Some aliphatic tertiary methylamines bearing cycloalkanes gave also better yields (entries 16-17).

Table 2. Synthesis of **3** promoted by CuI/C_2Cl_6[a]

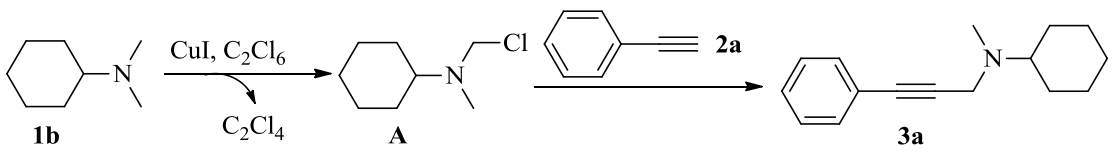


2 **1** **3**

Entry	R^1	R^2; R^3	Yield (%)[b]
1	Ph (**2a**)	Me; c-hexyl (**1a**)	71 (**3a**)
2	4-$MeOC_6H_4$ (**2b**)	**1a**	66 (**3b**)
3	4-ClC_6H_4 (**2c**)	**1a**	87 (**3c**)
4	4-MeC_6H_4 (**2d**)	**1a**	87 (**3d**)
5	3-FC_6H_4 (**2e**)	**1a**	70 (**3e**)
6	4-$CH_3(CH_2)_2C_6H_4$ (**2f**)	**1a**	68 (**3f**)
7	3-MeC_6H_4 (**2g**)	**1a**	93 (**3g**)
8	$PhCH_2$ (**2h**)	**1a**	61 (**3h**)
9	3-thienyl (**2i**)	**1a**	90(**3i**)
10	n-butyl (**2j**)	**1a**	51 (**3j**)
11	Me_3Si (**2k**)	**1a**	55 (**3k**)
12	**2a**	Me; Et (**1b**)	17 (**3l**)
13	**2a**	Me; n-butyl (**1c**)	35 (**3m**)
14	**2a**	Me; Pr^i (**1d**)	54 (**3n**)
15	**2a**	c-hexyl; c-hexyl (**1e**)	50 (**3o**)
16	**2a**	Me; c-heptyl (**1f**)	61 (**3p**)
17	**2a**	Me; c-pentyl (**1g**)	65 (**3q**)

[a]C_2Cl_6 (1.1 mmol), aliphatic tertiary methylamine (3 mmol), alkyne (1.0 mmol), CuI (0.05 mmol), CH_3CN (4 mL), 12-24h. [b]Isolated yields.

A possible mechanism is postulated in Scheme 1. By the action of CuI and *N*,*N*-dimethylcyclohexylamine, hexachloroethane underwent the homolysis cleavage of one C-Cl to produce $\cdot C_2Cl_5$, which abstracted one hydrogen atom from methyl of *N*,*N*-dimethylcyclohexylamine to form one molecule of HCl. The reaction intermediate **A** reacted with copper alkynylide to give the product **3a**.



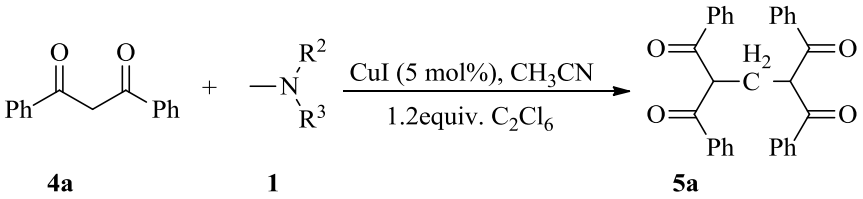
1b **A** **3a**

Scheme 1. Plausible mechanism for the formation of **3**.

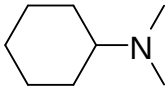
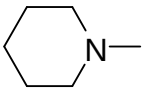
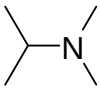
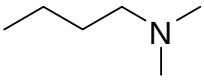
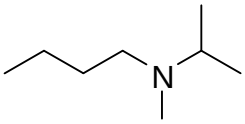
Selective oxidation of aliphatic tertiary methylamines: synthesis of methylene-bridged bis-1,3-dicarbonyl derivatives

Recently, Li developed a new method of synthesizing methylene-bridged bis-1,3-dicarbonyl derivatives[22] by iron-catalyzed oxidative reactions of 1,3-dicarbonyl compounds and *N*,*N*-dimethylaniline derivatives. Herein, we further extended the tertiary amines methodology to aliphatic tertiary methylamines using our recently developed approach. Similar to the optimization conditions described above for the alkynylation, it was found the best result could be obtained by using 3.0 equiv of *N*,*N*-dimethylcyclohexylamine and 1.0 equiv of 1,3-dibenzoylmethane. As shown in Table 3, a series of aliphatic tertiary methylamines were screened. The chained aliphatic tertiary methylamines gave the desired product in shorter time (entries 3-4), and slightly heating to 50 °C (entry 1) could accelerate the reaction remarkably. Cyclic amines showed lower activity than that of the acyclic amines (entry 2), which may indicate the difference in the stability of the corresponding iminium species.

Table 3. Reactions of **4a** with aliphatic tertiary methylamines[a]



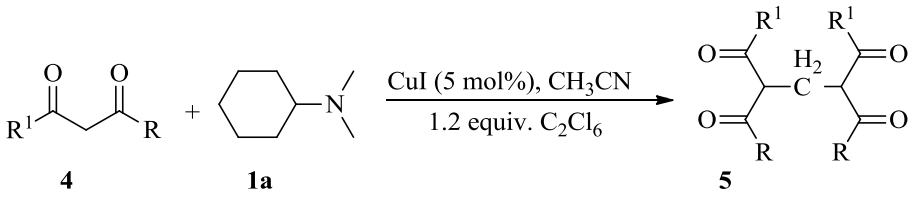
4a **1** **5a**

Entry	**1**	Time (h)	Yield (%)[b]
1	 **1a**	8; 4[c]	95; 95
2	 **1h**	12	49
3	 **1d**	3	86
4	 **1c**	5	81
5	 **1i**	5	90

[a]1,3-Diphenylpropane-1,3-dione (1 mmol), CuI (0.05 mmol), CH_3CN (4 mL), rt. [b]Isolated yields. [c]4h at 50 °C.

As shown in Table 4, several aromatic 1,3-diketones gave the corresponding methylene-bridged bis-1,3-dicarbonyl products in good to excellent yields. The electronic effect of the substituents on the benzene ring has a great influence on the yields of the products. The substrates with electron-withdrawing group gave moderate yields, whereas those with electron-donating groups gave excellent yields. Also satisfactory yields were obtained when a thienyl substituted substrate was used.

Table 4. Synthesis of methylene-bridged bis-1,3-dicarbonyl derivatives[a]

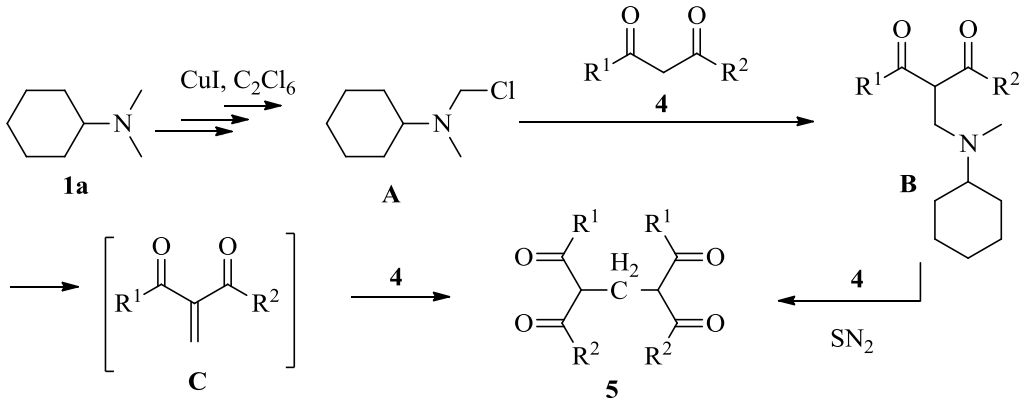


4 **1a** **5**

Entry	R	R^1	Yield (%)[b]
1	Ph	Ph	95 (**5a**)
2	Ph	CH_3	58 (**5b**)
3	Ph	4-$CH_3OC_6H_4$	98 (**5c**)
4	Ph	2-thienyl	75 (**5d**)

[a]**4** (1 mmol), **1** (3 mmol), CuI (5% mmol), C_2Cl_6 (1.2 mmol), CH_3CN (4 mL), rt, 4h.
[b]Isolated yield.

The mechanism of this reaction was depicted in Scheme 2: first, *N*,*N*-dimethylcyclohexylamine reacted with C_2Cl_6 in the presence of CuI to give **A**, on which **4** performed a nucleophilic attack to give **B**. Product **5** was formed by either nucleophilic substitution reaction or a tandem Cope elimination and Michael addition *via* intermediate **C**.



Scheme 2. Plausible mechanism for the formation of **5.**

Conclusions

In summary, functionalizations of aliphatic tertiary amines mediated by a catalytic amount of copper salt and hexachloroethane are established. The transformations including the alkynylation of aliphatic tertiary methylamines with terminal alkynes and the synthesis of methylene-bridged bis-1,3-dicarbonyl derivatives by selective oxidation of aliphatic tertiary methylamines were realized. The reactions described here are mild, general and efficient.

Experimental Section

General. Column chromatography was carried out on silica gel (200-300 mesh). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX-500 MHz instrument and the chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. The coupling constants, *J*, are reported in Hertz (Hz). Low-resolution MS was obtained using ESI ionization. HRMS was obtained using ESI ionization. GC-MS spectra were performed on an Agilent GC-6890, MS-5973 instrument. GC-HRMS spectra were performed on a Waters GCT Premier, HRMS-PerkinElmer Elan DRC-e instrument. All reagents were weighed and handled in air at room temperature and all reactions were performed without exclusion of air or moisture. Unless otherwise noted, all tertiary amines and alkynes were purchased from Sigma-Aldrich Company and used without further purification. 1,3-Dicarbonyl compounds were synthesized according to the literatures.[23]

General procedure for propargylic amines (3a-3q)

CuI (0.05 mmol), C_2Cl_6 (1.2 mmol) were put into a 10 mL two-necked flask. CH_3CN (4 mL), tertiary methylamine (3.0 mmol) were added successively by micro-syringe. The reaction mixture was stirred at room temperature for 1 h and then alkyne (1 mmol) was added. The resulting mixture was stirred for 24 hours at room temperature. When the reaction was completed, ethyl acetate (20 mL) and water (30 mL) were then added to the reaction mixture. The organic layer was extracted with ethyl acetate (3×20 mL). The combined organic phase was washed with brine and dried over sodium sulfate. The solvent was evaporated and purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3:1 - 8:1) as eluent to give the product.

***N*-Methyl-*N*-(3-phenylprop-2-ynyl)cyclohexanamine (3a).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43-7.41 (m, 2H), 7.29-7.27 (m, 3H), 3.62 (s, 2H), 2.44-2.42 (m, 3H), 1.97-1.94 (m, 2H), 1.80-1.77 (m, 2H), 1.63-1.59 (m, 1H), 1.29-1.11 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 131.6, 128.1, 127.7, 123.4, 85.6, 84.7, 61.0, 43.6, 38.4, 29.8, 26.0, 25.4.

***N*-(3-(4-Methoxyphenyl)prop-2-ynyl)-*N*-methylcyclohexanamine (3b).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.34 (m, 2H), 6.82-6.79 (m, 2H), 3.76 (s, 3H), 3.60 (s, 2H),

2.43-2.40 (m, 4H), 1.96-1.93 (m, 2H), 1.80-1.77 (m, 2H), 1.62-1.59 (m, 1H), 1.28-1.14 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 132.8, 115.4, 113.6, 84.4, 83.9, 60.8, 55.0, 43.5, 38.3, 29.6, 26.0, 25.4.

***N*-(3-(4-Chlorophenyl)prop-2-ynyl)-*N*-methylcyclohexanamine (3c).** Light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.33 (d, *J* 8.5 Hz, 2H), 7.26-7.24 (d, *J* 8.5 Hz, 2H), 3.60 (s, 2H), 2.40 (s, 4H), 1.95-1.93 (m, 2H), 1.80-1.77 (m, 2H), 1.63-1.59 (m, 1H), 1.28-1.13 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 133.6, 132.7, 128.3, 121.7, 86.7, 83.5, 60.9, 43.5, 38.3, 29.6, 25.9, 25.3; MS (ESI): 262.1 $[M+H]^+$; HRMS (ESI) calcd for $C_{16}H_{20}ClN$ ($[M+H]^+$): 262.1363, found 262.1356; Anal. calcd for $C_{16}H_{20}ClN$: C 73.41, H 7.70, N 5.35, found C 73.59, H 7.67, N 5.42.

***N*-Methyl-*N*-(3-p-tolylprop-2-ynyl)cyclohexanamine (3d).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.30 (d, *J* 8.0 Hz, 2H), 7.08-7.06 (d, *J* 8.0 Hz, 2H), 3.60 (s, 2H), 2.43-2.41 (m, 4H), 2.31 (s, 3H), 1.96-1.94 (m, 2H), 1.80-1.76 (m, 2H), 1.62-1.59 (m, 1H), 1.28-1.11 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.6, 131.4, 128.8, 120.3, 84.7, 60.8, 43.5, 38.3, 29.6, 26.0, 25.4, 21.2.

***N*-(3-(3-Fluorophenyl)prop-2-ynyl)-*N*-methylcyclohexanamine (3e).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.18 (m, 2H), 7.13-7.10 (m, 1H), 7.00-6.96 (m, 1H), 3.62 (s, 2H), 2.44-2.40 (m, 4H), 1.96-1.93 (m, 2H), 1.81-1.78 (m, 2H), 1.64-1.60 (m, 1H), 1.29-1.11 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2, 161.2, 129.6, 127.4, 125.2, 118.3, 115.0, 86.8, 83.5, 61.0, 43.5, 38.4, 29.7, 26.0, 25.4.

***N*-Methyl-*N*-(3-(4-propylphenyl)prop-2-ynyl)cyclohexanamine (3f).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.33 (d, *J* 8.0 Hz, 2H), 7.10-7.08 (d, *J* 8.5 Hz, 2H), 3.62 (s, 2H), 2.57-2.54 (t, *J* 7.75 Hz, 2H), 2.44-2.41 (m, 4H), 1.97-1.95 (m, 2H), 1.80-1.77 (m, 2H), 1.63-1.59 (q, *J* 7.25 Hz, 3H), 1.28-1.14 (m, 5H), 0.93-0.90 (t, *J* 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.5, 131.4, 128.2, 120.6, 84.8, 60.9, 43.6, 38.4, 37.8, 29.7, 26.0, 25.4, 24.2, 13.6; MS (ESI): 270.2 $[M+H]^+$; HRMS (ESI) calcd for $C_{19}H_{27}N$ ($[M+H]^+$): 270.2222, found 270.2222; Anal. calcd for $C_{19}H_{27}N$: C 84.70, H 10.10, N 5.20, found C 84.53, H 10.21, N 5.37.

***N*-Methyl-*N*-(3-m-tolylprop-2-ynyl)cyclohexanamine (3g).** Light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.22 (m, 2H), 7.17-7.14 (t, *J* 7.5 Hz, 1H), 7.08-7.06 (m, 1H), 3.61 (s, 2H), 2.43-2.40 (m, 4H), 2.30 (s, 3H), 1.96-1.94 (m, 2H), 1.80-1.77 (m, 2H), 1.63-1.59 (m, 1H), 1.31-1.11 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.6, 132.1, 128.6, 127.9, 123.1, 85.0, 84.8, 60.8, 43.5, 38.4, 29.7, 26.0, 25.4, 21.0; MS (ESI): 242.2 $[M+H]^+$; HRMS (ESI) calcd for $C_{17}H_{23}N$ ($[M+H]^+$): 242.1909, found 242.1912; Anal. calcd for $C_{17}H_{23}N$: C 84.59, H 9.60, N 5.80, found C 84.57, H 9.52, N 5.99.

***N*-Methyl-*N*-(4-phenylbut-2-ynyl)cyclohexanamine (3h).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.36 (m, 2H), 7.34-7.31 (m, 2H), 7.25-7.24 (m, 1H), 3.65 (s, 2H), 3.48-3.47 (m, 2H), 2.45-2.40 (m, 4H), 1.96-1.94 (m, 2H), 1.82-1.78 (m, 2H), 1.65-1.62 (m, 1H), 1.31-1.12 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.0, 128.2, 127.7, 126.3, 82.0, 78.0, 60.6, 43.2, 38.3, 29.6, 25.9, 25.4, 25.0.

***N*-Methyl-*N*-(3-(thiophen-3-yl)prop-2-ynyl)cyclohexanamine (3i).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.37 (m, 1H), 7.22-7.20 (m, 1H), 7.08-7.07 (m, 1H), 3.60 (s, 2H), 2.40 (s, 4H), 1.95-1.93 (m, 2H), 1.80-1.76 (m, 2H), 1.62-1.59 (m, 1H), 1.28-1.10 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 129.8, 127.9, 124.8, 122.2, 85.1, 79.6, 60.8, 43.5, 38.3, 29.6, 25.9, 25.3.

***N*-(Hept-2-ynyl)-*N*-methylcyclohexanamine (3j).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.37-3.36 (s, 2H), 2.37-2.33 (m, 4H), 2.21-2.18 (m, 2H), 1.92-1.89 (m, 2H), 1.79-1.75 (m, 2H), 1.63-1.59 (m, 1H), 1.50-1.40 (m, 4H), 1.27-1.10 (m, 5H), 0.93-0.90 (t, J=7.25 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 84.8, 75.7, 60.8, 43.3, 38.3, 31.0, 29.7, 26.1, 25.6, 21.9, 18.4, 13.6.

***N*-Methyl-*N*-(3-(trimethylsilyl)prop-2-ynyl)cyclohexanamine (3k).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 (s, 2H), 2.30 (s, 4H), 1.87-1.85 (m, 2H), 1.75-1.72 (m, 2H), 1.58-1.55 (m, 1H), 1.22-1.06 (m, 5H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 102.2, 89.1, 60.9, 43.8, 38.2, 29.6, 26.0, 25.4.

***N*-Ethyl-*N*-methyl-3-phenylprop-2-yn-1-amine (3l).** Light yellow oil.[24] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44-7.42 (m, 2H), 7.30-7.26 (m, 3H), 3.56 (s, 2H), 2.58-2.54 (q, *J* 7.0 Hz, 2H), 2.38 (s, 3H), 1.13-1.10 (t, *J* 7.25 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 131.7, 128.2, 128.0, 123.2, 85.2, 84.4, 49.8, 46.0, 41.5, 12.8.

***N*-Methyl-*N*-(3-phenylprop-2-ynyl)butan-1-amine (3m).** Light yellow oil.[24] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44-7.42 (m, 2H), 7.30-7.28 (m, 3H), 3.54 (s, 2H), 2.49-2.46 (m, 2H), 2.37 (s, 3H), 1.51-1.45 (m, 2H), 1.39-1.32 (m, 2H), 0.95-0.92 (t, *J* 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 131.6, 128.1, 127.8, 123.2, 85.1, 84.5, 55.7, 46.3, 41.9, 29.7, 20.5, 14.0.

***N*-isoPropyl-*N*-methyl-3-phenylprop-2-yn-1-amine (3n).** Light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44-7.42 (m, 2H), 7.29-7.27 (m, 3H), 3.58 (s, 2H), 2.90-2.85 (m, 1H), 2.39 (s, 3H), 1.11-1.10 (d, *J* 6.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 131.6, 128.1, 127.8, 123.4, 85.6, 84.7, 52.5, 43.9, 38.0, 19.5; MS (ESI): 188.1 $[M+H]^+$; HRMS (ESI) calcd for $C_{13}H_{17}N$ ($[M+H]^+$): 188.1439, found 188.1436; Anal. calcd for $C_{13}H_{17}N$: C 83.37, H 9.15, N 7.48, found C 83.42, H 9.33, N 7.37.

***N*-cycloHexyl-*N*-(3-phenylprop-2-ynyl)cyclohexanamine (3o).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.38 (m, 1H), 7.29-7.26 (m, 1H), 3.72 (s, 1H), 2.88-2.83 (m, 1H), 1.93-1.91 (m, 2H), 1.80-1.78 (m, 2H), 1.63-1.60 (m, 1H), 1.43-1.35 (m, 2H), 1.31-1.23 (m, 2H), 1.16-1.11 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 131.2, 128.0, 127.5, 88.6, 83.5, 57.4, 35.4, 30.8, 26.0, 25.9.

***N*-Methyl-*N*-(3-phenylprop-2-ynyl)cycloheptanamine (3p).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43-7.41 (m, 2H), 7.27-7.26 (m, 2H), 3.54 (s, 2H), 2.80-2.74 (m, 1H), 2.38 (s, 3H), 1.88-1.84 (m, 2H), 1.71-1.66 (m, 2H), 1.57-1.42 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 131.3, 127.9, 127.6, 123.2, 86.0, 84.1, 62.9, 43.4, 37.4, 30.0, 27.9, 25.1.

***N*-Methyl-*N*-(3-phenylprop-2-yn-1-yl)cyclopentanamine (3q).** Light yellow oil.[8b] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45-7.43 (m, 2H), 7.31-7.26 (m, 3H), 3.62 (s, 2H), 2.83-2.76 (m, 1H),

2.42 (s, 3H), 1.94-1.88 (m, 2H), 1.73-1.68 (m, 2H), 1.63-1.56 (m, 2H), 1.46-1.40 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 131.7, 128.2, 127.9, 123.3, 85.2, 84.5, 64.8, 45.8, 41.0, 31.3, 24.1.

General procedure for the synthesis of bis-1,3-dicarbonyl compounds (5a-5d)

CuI (0.05 mmol), C_2Cl_6 (1.2 mmol), 1,3-dicarbonyl compounds **4** (1.0 mmol), were successively put into a 10 mL two-necked flask , then CH_3CN (4 mL) and *N*,*N*-dimethylcyclohexanamine (3.0 mmol) were added by micro-syringe. The resulting mixture was stirred for 4 hours at room temperature. Ethyl acetate (20 mL) and water (30 mL) were then added to the reaction mixture. The organic layer was extracted with ethyl acetate (3×20 mL). The resulting reaction mixture was evaporated and purified by flash column chromatography on silica gel with ethyl petroleum ether / ethyl acetate (10:1) as eluent to give the desired product **5**.

2,4-Dibenzoyl-1,5-diphenylpentane-1,5-dione (5a). Yellow solid, mp: 177-178 °C (lit. 179-180 °C) [25]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15-8.13 (d, *J* 7.0 Hz, 4H), 7.59-7.57 (m, 2H), 7.50-7.46 (m, 4H), 5.76-5.73 (t, *J* 7.3 Hz, 1H), 2.78-2.75 (t, *J* 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.6, 135.4, 133.9, 129.0, 128.8, 54.0, 28.9.

3,5-Dibenzoylheptane-2,6-dione (5b). Yellow solid[22]. two diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08-8.02 (m, 4H), 7.65-7.58 (m, 2H), 7.54-7.47 (m, 4H), 4.74-4.71 (t, *J* 7.0 Hz, 1H), 4.66-4.63 (t, *J* 7.0 Hz, 1H), 2.60-2.56 (m, 1H), 2.54-2.46 (m, 1H), 2.19 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.8, 203.3, 196.5, 135.8, 134.0, 129.0, 59.3, 29.3, 29.2, 27.4, 27.2.

2,4-Dibenzoyl-1,5-bis(4-methoxyphenyl)pentane-1,5-dione (5c). Yellow solid. two diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24-8.22 (m, 1H), 8.17-8.14 (m, 2H), 8.10-8.08(m, 1H), 7.59-7.55 (m, 1H), 7.51-7.44 (m, 2H), 7.01-6.96 (m, 2H), 5.72-5.69 (t, *J* 7.0 Hz, 1H), 3.88-3.86 (d, *J* 11.0 Hz, 3H), 2.78-2.75 (t, *J* 7.0 Hz,1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.7, 195.1, 164.1, 135.7, 133.7, 131.3, 128.7, 114.2, 55.5, 53.9, 29.2; MS (ESI): $[M+H]^+$, 521.2; HRMS (ESI) calcd for $C_{33}H_{28}O_6$ ($[M+H]^+$): 521.1964, found 521.1965; Anal. calcd for $C_{33}H_{28}O_6$: C 76.14, H 5.42, found C 76.35, H 5.57.

2,4-Dibenzoyl-1,5-di(thiophen-2-yl)pentane-1,5-dione (5d). Yellow solid. two diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15-8.0 (m, 3H), 7.68-7.66 (m, 1H), 7.60-7.55 (m, 1H), 7.50-7.45 (m, 2H), 7.15-7.11 (m, 1H), 5.56-5.53 (t, *J* 7.0 Hz, 1H), 2.82-2.79 (t, *J* 7.0 Hz,1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.8, 188.9, 142.8, 135.3, 133.7, 128.7, 55.1, 29.4; MS (ESI): $[M+H]^+$, 473.1; HRMS (ESI) calcd for $C_{27}H_{20}O_4S_2$ $[M+H]^+$: 473.0881, found 473.0872; Anal. calcd for $C_{27}H_{20}O_4S_2$: C 68.62, H 4.27, found C 68.75, H 4.53.

Acknowledgements

This work was supported by the grant from National Natural Science Foundation of China (No. 20872131) and Natural Science Foundation of Zhejiang Province (LY12B02017).

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