DOI: 10.1002/cjoc.201300047

Rare-Earth Metal Chlorides Catalyzed One-pot Syntheses of Quinolines under Solvent-free Microwave Irradiation Conditions

Lijun Zhang,*,[a] Bing Wu,[a] Yongqing Zhou,[a] Jing Xia,[a] Shuangliu Zhou,[a] and Shaowu Wang*,[a,b]

[a] *Laboratory of Functionalized Molecular Solids, Ministry of Education, Anhui Laboratory of Molecule-Based Materials, Institute of Organic Chemistry, College of Chemistry and Materials Science, Anhui Normal University, Wuhu, Anhui 241000, China*

[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Shanghai 200032, China*

Under microwave irradiation and solvent-free conditions, rare-earth metal chlorides ($RECl_3$) have been efficient catalysts for one-pot synthesis of quinoline derivatives to give products in good to excellent yields through the multi-component reactions of aldehydes, amines, and alkynes. The rare-earth metal chlorides can be recycled for six times without notable loss of catalytic activities. This new synthetic approach has prominent features of a short reaction time, high yields of products, operational simplicity, broad substrate scopes, environmentally friendly property and commercially available catalysts. It extends the applications of rare-earth metal compounds as catalysts in organic synthesis.

Keywords rare earth, quinoline, multi-component reaction, microwave irradiation, recyclable

Introduction

Quinoline derivatives are ubiquitous structural motifs in many natural products and biologically active pharmaceuticals such as anti-ulcerative, anticancer and antihistaminic.[1] Additionally, substituted quinoline derivatives have also been employed as ligands for the preparation of OLED phosphorescent complexes[2] and fluorescent probes in bioimaging studies.[3] Owing to various applications of quinoline derivatives, their syntheses had been extensively studied. The syntheses of this type of compounds can be achieved from the classic Skraup reaction,[4] Skraup-Doebner-Von Miller reaction[5] Friedländer reaction,[6] Povarov reaction,[7] Morita-Baylis-Hillman reaction,[8] and the dimerization reaction.[9] However, most of these synthetic methods required use of complicated or unstable starting materials such as 2-aminobenzaldehyde, and provided low yields of products due to low reaction efficiency. Thus, development of a new synthetic strategy for the efficient construction of quinolines and some related heterocycles is still attractive. This leads to the recent development of cascade (domino) reactions[10] for the generation of quinolines, including $Rh(cod)^{2+}BF_4/2\ PPh_3$[11] and solid acid[12] catalyzed domino reactions. Meanwhile, the usage of simple substrates as starting materials has also been reported.[13] For example, the $AuCl_3/CuBr$[14] and $FeCl_3$[15] catalyzed three-component reaction of aldehydes, alkynes, and amines have been reported recently. However, most of these improved synthetic methods used expensive catalysts or a long reaction time and provided relatively low yields of products. To increase the compatibility with the environment, studies on the recyclable catalysts in the syntheses of quinolines have attracted growing research interests. However, only few reports have been reported and generally required PEG or ionic liquids as the media.[16]

Rare-earth metal chlorides (RE＝Y, Ln), as simple Lewis acid catalysts,[17] have shown high catalytic activities in many organic reactions such as the Biginelli-type reaction for the synthesis of 1,5-benzodiazepine derivatives,[18] the condensation reaction for the synthesis of α-amino phosphonate,[19] the C-acylation of 1,3-dicarbonyl compounds,[20] the reductive dehalogenation of halogen-containing hydrocarbons with diisobutylaluminum hydride.[21] Our previous studies have shown that rare-earth metal chlorides displayed high catalytic activities on the Cannizzaro-reaction of aldehydes and lithium amide giving amides and alcohols,[22] and the introduction of microwave irradiation can improve the performance of these catalysts.[23] Herein, we report a $RECl_3$-catalyzed one-pot syntheses of quinoline

---

* E-mail: zljun@mail.ahnu.edu.cn; swwang@mail.ahnu.edu.cn; Tel.: (86)553-3869310; Fax: (86)553-3883517
Received January 17, 2013; accepted March 4, 2013; published online April 3, 2013.
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cjoc.201300047 or from the author.

derivatives under microwave irradiation and solvent-free conditions.

Experimental

General experimental procedures

The reagents were purchased and used without further purification unless otherwise stated. All of the microwave-assisted reactions were performed in a CEM Discover monomode apparatus at the indicated maximum temperature and power setting. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-300 MHz spectrometer in $CDCl_3$. Mass spectra were performed on a Micromass GCT-MS.

General procedure for the $RECl_3$-catalyzed syntheses of quinoline derivatives

To a 10 mL flask were charged with $RECl_3$ (0.15 mmol), aldehyde (1.0 mmol), amine (1.0 mmol) and alkyne (1.50 mmol) under atmosphere. The mixture was stirred at room temperature for a few minutes then it was exposed to the MW (700 W) irradiation condition in Al_2O_3 bath at 180 ℃ for 8 min. The mixture was cooled to room temperature and extracted with Et_2O. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate＝100/1, *V*/*V*) to afford compounds **4a**—**4q**.

2,4-Diphenylquinoline (4a)[24] Yield 92%; yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.28—8.19 (m, 3H), 7.93—7.72 (m, 4H), 7.56—7.50 (m, 8H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 156.9, 153.5, 149.3, 148.8, 139.6, 138.4, 130.1, 129.6, 129.4, 128.9, 128.6, 128.4, 127.6, 126.4, 125.7, 119.4, 115.1; HRMS (EI) calcd for $C_{21}H_{15}N$ (M^+) 281.1204, found 281.1196.

2-(4-Methoxyphenyl)-4-phenylquinoline (4b)[25] Yield 91%; yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.24—8.17 (m, 3H), 7.88 (d, *J*＝8.25 Hz, 1H), 7.78—7.69 (m, 2H), 7.56—7.39 (m, 5H), 7.20 (d, *J*＝7.92 Hz, 1H), 7.06 (d, *J*＝8.37 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 160.7, 156.5, 149.1, 148.8, 138.5, 132.2, 129.9, 129.6, 129.5, 128.9, 128.6, 128.4, 126.0, 125.6, 125.5, 118.9, 114.2, 55.4; MS (EI) calcd for $C_{22}H_{17}NO$ (M^+) 311.1, found 312.2.

4-Phenyl-2-(*p*-tolyl)quinoline (4c)[26] Yield 89%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.25 (d, *J*＝7.65 Hz, 2H), 8.11 (d, *J*＝6.69 Hz, 2H), 7.90 (d, *J*＝7.74 Hz, 2H), 7.81 (s, 1H), 7.73 (s, 1H), 7.56—7.47 (m, 5H), 7.34 (d, *J*＝6.57 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 156.9, 149.1, 148.8, 139.5, 138.5, 136.9, 130.1, 129.6, 129.5, 128.6, 128.4, 127.5, 126.2, 125.7, 125.6, 119.2, 21.4; MS (EI) calcd for $C_{21}H_{17}N$ (M^+) 295.1, found 296.2.

2-(4-Chlorophenyl)-4-phenylquinoline (4d)[24] Yield 82%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.24—8.15 (m, 3H), 7.89 (s, 2H), 7.79—7.75 (m, 3H), 7.56—7.49 (m, 6H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 155.6, 149.5, 148.8, 138.3, 138.0, 135.6, 130.1, 129.7, 129.6, 129.0, 128.9, 128.7, 128.5, 126.6, 125.8, 125.7, 118.9; MS (EI) calcd for $C_{21}H_{14}NCl$ (M^+) 315.6, found 316.1.

2-(4-Nitrophenyl)-4-phenylquinoline (4e)[25] Yield 61%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.40 (s, 3H), 8.27 (d, *J*＝7.8 Hz, 2H), 7.95 (d, *J*＝7.74 Hz, 1H), 7.87 (s, 1H), 7.80 (s, 2H), 7.57 (s, 5H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 154.1, 149.9, 148.8, 148.4, 145.5, 137.9, 130.3, 130.1, 129.5, 128.7, 128.4, 127.3, 126.2, 125.8, 124.0, 119.1; MS (EI) calcd for $C_{21}H_{14}N_2O_2$ (M^+) 326.1, found 327.2.

2-(2-Methoxyphenyl)-4-phenylquinoline (4f) Yield 79%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.87 (s, 1H), 7.94—7.84 (m, 3H), 7.74—7.72 (m, 1H), 7.57—7.41 (m, 7H), 7.17—7.14 (m, 1H), 7.04 (d, *J*＝7.89 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 157.2, 156.7, 148.8, 147.4, 138.6, 131.5, 130.4, 130.0, 129.7, 129.1, 128.5, 128.2, 126.3, 125.6, 123.7, 121.3, 111.4, 55.7; HRMS (EI) calcd for $C_{22}H_{17}NO$ (M^+) 311.1310, found 311.1304.

2-(2,4-Dichlorophenyl)-4-phenylquinoline (4g) Yield 74%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.24 (d, *J*＝7.71 Hz, 1H), 7.99 (d, *J*＝8.37 Hz, 1H), 7.77—7.69 (m, 3H), 7.55—7.40 (m, 6H), 7.26—7.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 156.8, 148.6, 148.3, 138.1, 137.9, 135.2, 133.2, 132.7, 130.8, 130.0, 129.9, 129.7, 129.6, 128.7, 128.6, 127.6, 127.0, 125.8, 122.8; HRMS (EI) calcd for $C_{21}H_{13}Cl_2N$ (M^+) 349.0425, found 349.0419.

2-Mesityl-4-phenylquinoline (4h) Yield 78%; yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.25 (d, *J*＝6.72 Hz, 1H), 8.01 (d, *J*＝8.16 Hz, 1H), 7.75—7.73 (m, 1H), 7.54 (dd, *J*＝6.09, 6.09 Hz, 5H), 7.33 (s, 2H), 6.97 (s, 2H), 2.34 (s, 3H), 2.12 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 160.2, 148.7, 148.6, 138.1, 137.8, 137.7, 135.7, 130.0, 129.7, 129.4, 128.6, 128.5, 128.4, 126.4, 125.7, 125.2, 123.1, 21.1, 20.3; HRMS (EI) calcd for $C_{24}H_{21}N$ (M^+) 323.1674, found 323.1670.

2-Cyclopentyl-4-phenylquinoline (4i) Yield 50%; yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.13 (d, *J*＝8.31 Hz, 1H), 7.83 (d, *J*＝8.28 Hz, 1H), 7.71 (dd, *J*＝7.50, 7.50 Hz, 1H), 7.54—7.43 (m, 5H), 7.30—7.29 (m, 2H), 3.48—3.41 (m, 1H), 2.25—2.23 (m, 4H), 1.93—1.79 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 165.8, 148.5, 148.2, 138.5, 129.6, 129.3, 129.2, 128.5, 128.3, 125.7, 125.6, 125.5, 120.2, 48.9, 33.7, 26.1; HRMS (EI) calcd for $C_{21}H_{19}N$ (M^+) 273.1517, found 273.1509.

6-Methyl-2,4-diphenylquinoline (4j)[27] Yield 93%; yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.17 (dd, *J*＝7.64, 7.64 Hz, 3H), 7.78 (s, 1H), 7.65 (s, 1H), 7.56—7.46 (m, 9H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 156.0, 148.5, 147.4, 139.8, 138.7, 136.3, 131.8, 129.8, 129.6, 129.2, 128.8, 128.6, 128.3, 127.5, 125.7, 124.4, 119.5, 21.8; MS (EI) calcd for $C_{22}H_{17}N$ (M^+) 295.1, found 296.2.

6-Methoxy-2,4-diphenylquinoline (4k)[24] Yield 91%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.16 (d, *J*＝7.8 Hz, 3H), 7.78 (s, 2H), 7.58—7.39 (m, 8H), 7.20 (s, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.0 MHz)

δ: 157.8, 154.7, 147.8, 144.9, 139.8, 138.8, 131.6, 129.4, 129.0, 128.8, 128.7, 128.4, 127.3, 126.7, 121.9, 119.7, 103.7, 55.5; MS (EI) calcd for $C_{22}H_{17}N$ (M^+) 311.1, found 312.2.

6-Bromo-2,4-diphenylquinoline (4l)[28] Yield 82%; white solid. m.p. 157—159 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.19 (d, J=7.11 Hz, 2H), 8.12 (d, J=8.88 Hz, 1H), 8.04 (s, 1H), 7.84—7.79 (m, 2H), 7.56—7.51 (m, 8H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 157.2, 148.4, 147.4, 139.2, 137.7, 133.0, 131.8, 129.7, 129.5, 128.9, 128.8, 128.7, 127.8, 127.6, 127.0, 120.5, 120.1; MS (EI) calcd for $C_{21}H_{14}NBr$ (M^+) 359.0, found 360.1.

8-Methyl-2,4-diphenylquinoline (4m)[29] Yield 73%; yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.30 (d, J=7.05 Hz, 2H), 7.85 (s, 1H), 7.74 (d, J=8.22 Hz, 1H), 7.61—7.47 (m, 9H), 7.37 (dd, J=7.56, 7.56 Hz, 1H), 2.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 155.0, 149.3, 147.7, 139.8, 139.0, 138.0, 132.6, 129.6, 129.3, 128.8, 128.5, 128.3, 127.5, 126.0, 125.7, 123.6, 118.7, 18.4; MS (EI) calcd for $C_{22}H_{17}N$ (M^+) 295.1, found 296.2.

6-Nitro-2,4-diphenylquinoline (4n)[24] Yield 63%; Yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.87 (s, 1H), 8.51 (d, J=7.71 Hz, 1H), 8.36—8.26 (m, 4H), 7.99 (s, 1H), 7.61 (s, 7H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 160.1, 151.3, 149.1, 145.4, 138.5, 136.9, 131.8, 130.5, 129.5, 129.3, 129.2, 129.1, 127.9, 124.8, 123.1, 122.9, 120.7; MS (EI) calcd for $C_{22}H_{17}NO$ (M^+) 326.1, found 327.2.

7-Nitro-2,4-diphenylquinoline (4o) Yield 69%; brown solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.47 (d, J=8.16 Hz, 1H), 8.23 (d, J=6.42 Hz, 2H), 7.95 (s, 1H), 7.88 (d, J=7.14 Hz, 1H), 7.79 (dd, J=7.50, 7.80 Hz, 1H), 7.56—7.43 (m, 8H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 158.0, 149.5, 148.4, 147.1, 138.8, 138.2, 135.1, 130.2, 129.0, 128.9, 128.7, 127.8, 127.7, 127.4, 123.5, 117.8, 103.2; HRMS (EI) calcd for $C_{21}H_{14}N_2O_2$ (M^+) 326.1055, found 326.1050.

2,4-Diphenylbenzo[*h*]quinoline (4p)[30] Yield 90%; white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.59 (d, J=7.71 Hz, 1H), 8.42 (d, J=7.26 Hz, 2H), 7.98 (s, 1H), 7.91 (d, J=7.92 Hz, 1H), 7.83—7.72 (m, 4H), 7.58—7.49 (m, 8H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 154.9, 149.1, 146.7, 139.7, 138.9, 133.6, 132.6, 129.7, 129.3, 128.9, 128.6, 128.3, 128.2, 127.6, 127.5, 127.3, 126.9, 125.3, 123.4, 122.9, 119.5; MS (EI) calcd for $C_{25}H_{117}N$ (M^+) 331.1, found 332.2.

2-Phenyl-4-(*p*-tolyl)quinoline (4q)[31] Yield 87%; yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.28—8.20 (m, 3H), 7.95 (d, J=8.34 Hz, 1H), 7.83 (s, 1H), 7.77—7.74 (m, 1H), 7.57—7.47 (m, 6H), 7.38 (d, J=7.77 Hz, 2H), 2.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ: 156.9, 149.3, 148.9, 139.8, 138.4, 135.5, 130.2, 129.6, 129.4, 128.9, 127.7, 126.3, 125.9, 125.8, 119.4, 21.4; MS (EI) calcd for $C_{22}H_{17}N$ (M^+) 295.1, found 296.2.

Results and Discussion

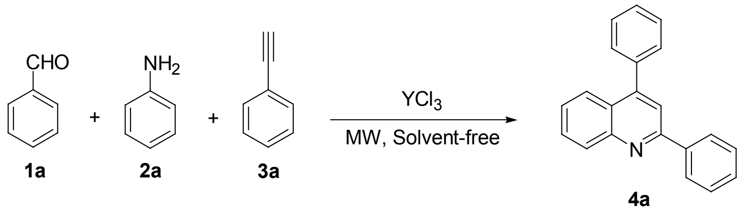
Optimization of the reaction conditions.

Initially, benzaldehyde, aniline and phenylacetylene were used as model substrates for optimization of the reaction conditions, which include the reaction temperature, microwave oven power, time of irradiation, and reactant ratios, results were summarized in Table 1. Raising the reaction temperature under conventional thermal conditions leads to an increased yield of the target product (Table 1, Entries 1—3). Microwave irradiation presents a powerful tool toward this reaction (Table 1, Entries 4—6). The microwave oven power influences the reaction efficiency of this reaction, and a 79% yield of product was achieved at 700 W (180 ℃) (Table 1, Entry 8). Increment of the microwave oven power to 800 W (180 ℃) showed no significant increasing of the yield of the product (Table 1, Entry 9). Performance of this reaction with irradiation times of 6, 8, and 10 min at 700 W (180 ℃) afforded the corresponding products with yields of 60%, 79% and 80%, respectively (Table 1, Entries 8 and 10—12). Thus the optimized microwave irradiation was set at 700 W for 8 min. Under these conditions, we then obtained that the best ratio of the substrates was 1∶1∶1.5 under solvent-free in the presence of 10 mol% YCl_3 as a catalyst (Table 1, Entry 17). Reaction of benzaldehyde, aniline and phenylacetylene catalyzed by hydrated lanthanide chloride, $YCl_3{\bullet}6H_2O$, was tested. The reaction proceeded highly efficiently (Table 1, Entry 19). So our microwave assisted reactions were performed at atmospheric condition without the usage of Schlenck technique.

Scopes of this reaction

Under the optimum reaction conditions, the scopes of YCl_3-catalyzed reaction were investigated, and the results were summarized in Table 2. Despite of the aromatic aldehydes having electron-donating or electron-withdrawing groups, the reaction proceeded smoothly generating the desired quinoline derivatives in moderate to good yields (Table 2, Entries 1—3 and 5). Reaction of the aldehydes having electron-withdrawing substituent such as 4-nitrobenzaldehyde, aniline and phenylacetylene gave a moderate yield of the product **4e** (Table 2, Entry 5). However, the high yields of products with the aldehydes having electron-rich substituents may be due to the enhancement of the coordination ability of aldehydes to the Lewis acid (YCl_3), which may assist the subsequent addition of amine group to the carbonyl group. For the sterically hindered substrates such as 2-$CH_3OC_6H_4CHO$, 2,4-$Cl_2C_6H_3CHO$ and 2,4,6-$(CH_3)_3$-C_6H_2CHO, the products **4f**—**4h** were obtained in moderate yields (Table 2, Entries 6—8). Additionally, the application of aliphatic aldehyde for this reaction also gave the desired product (Table 2, Entry 9) in a comparable result to the literature.[15]

Table 1 Screening the optimized reaction conditions for the synthesis of 2,4-diphenylquinoline under YCl_3-catalyzed condition[a]



Entry	Ratio[b]	Cat./%	Time	Solvent	*T*/℃	Yield[c]/%
1[d]	1∶1∶1	10	24 h	Toluene	r.t.	26
2[d]	1∶1∶1	10	24 h	Toluene	Reflux	38
3[d]	1∶1∶1	10	24h	—	130	45
4	1∶1∶1	10	10 min	—	130 (MW, 500W)	58
5	1∶1∶1	10	10 min	—	150 (MW, 500W)	65
6	1∶1∶1	10	10 min	—	180 (MW, 500W)	73
7	1∶1∶1	10	10 min	—	180 (MW, 600W)	73
8	1∶1∶1	10	10 min	—	180 (MW, 700W)	79
9	1∶1∶1	10	10 min	—	180 (MW, 800W)	80
10	1∶1∶1	10	12 min	—	180 (MW, 700W)	80
11	1∶1∶1	10	8 min	—	180 (MW, 700W)	79
12	1∶1∶1	10	6 min	—	180 (MW, 700W)	60
13	1∶1∶1	0	10 min	—	180 (MW, 500W)	trace
14	1∶1∶1	8	8 min	—	180 (MW, 700W)	72
15	1∶1∶1	15	8 min	—	180 (MW, 700W)	79
16	1∶1∶1.3	10	8 min	—	180 (MW, 700W)	84
17	1∶1∶1.5	10	8 min	—	180 (MW, 700W)	92
18	1∶1∶2.0	10	8 min	—	180 (MW, 700W)	93
19[e]	1∶1∶1.5	10	8 min	—	180 (MW, 700W)	90

[a] Reaction conditions: benzaldehyde (1.0 mmol), aniline (1.0 mmol), solvent (10 mL). [b] Mole ratio (benzaldehyde∶aniline∶phenylacetylene). [c] Isolated yield. [d] Performed under conventional thermal conditions. [e] Catalyzed by 10 mol% YCl_3•$6H_2O$.

Then, the scopes of amines were examined for this reaction (Table 2, Entries 10—16). It is found that aromatic amines containing either an electron-donating group or an electron-withdrawing group proceeded smoothly for this reaction to give the corresponding quinolines in moderate to good yields (Table 2, Entries 10—15). It is worth noticed that a bulky 1-naphthamine was also suitable for this reaction and smoothly generated the desired product **4p** in 90% yield (Table 2, Entry 16). Substituted phenylacetylene was also suitable for this transformation with isolation of the expected product **4q** in 89 % yield (Table 2, Entry 17).

In comparison with results obtained with other catalysts,[14,15] our reactions show the advantages of wide range of aromatic amines and phenylacetylenes and aromatic or aliphatic aldehydes producing the products in good to excellent yields within a short reaction time (8 min).

Effect of rare-earth metals

Results indicated that rare-earth metals have a little effect on the activity of this reaction. As shown in Table 3, most of the rare-earth metal chlorides exhibited well to high catalytic activities for this reaction. The absence of rare-earth metal chlorides led to only trace amount of the product.

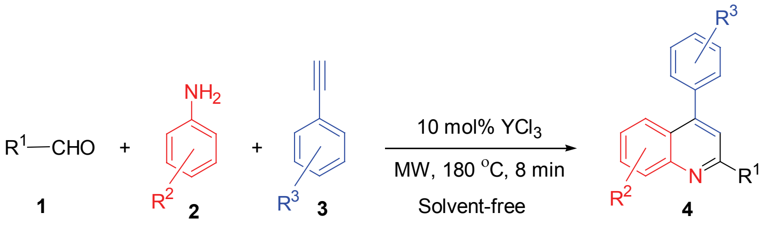
Proposed mechanism of the reaction

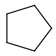
Based on these experimental results, a tentative mechanism was proposed as shown in Scheme 1. The coordination of aldehyde to $RECl_3$ with subsequent condensation with amine leads to the formation of the imine, which undergoes nucleophilic attack by phenylacetylene to give a propargylamine intermediate **A**. Intermediate **A** further undergoes intramolecular cyclization to give intermediate **B**, which undergoes isomerization and further oxidation to give the quinoline product.[16a]

Recycle of the catalyst

The facts that rare-earth metal chlorides are not very sensitive to water and air and are stable at high temperature, the recycle of catalyst was tested. Although there are many reports about the recyclization of rare-

Table 2 Synthesis of quinoline derivatives by YCl_3-catalyzed three-component reaction of aldehydes, alkynes, and amines[a]



Entry	R^1	R^2	R^3	Product	Yield[b]/%
1	C_6H_5	H	H	**4a**	92
2	$4\text{-}CH_3OC_6H_4$	H	H	**4b**	91
3	$4\text{-}CH_3C_6H_4$	H	H	**4c**	89
4	$4\text{-}ClC_6H_4$	H	H	**4d**	82
5	$4\text{-}O_2NC_6H_4$	H	H	**4e**	61
6	$2\text{-}CH_3OC_6H_4$	H	H	**4f**	79
7	$2,4\text{-}Cl_2C_6H_3$	H	H	**4g**	74
8	$2,4,6\text{-}(CH_3)_3C_6H_2$	H	H	**4h**	78
9		H	H	**4i**	50
10	C_6H_5	$4\text{-}CH_3$	H	**4j**	93
11	C_6H_5	$4\text{-}CH_3O$	H	**4k**	91
12	C_6H_5	4-Br	H	**4l**	83
13	C_6H_5	$2\text{-}CH_3$	H	**4m**	73
14	C_6H_5	$4\text{-}O_2N$	H	**4n**	63
15	C_6H_5	$3\text{-}O_2N$	H	**4o**	69
16	C_6H_5	2-Naphthyl	H	**4p**	90
17	C_6H_5	H	$4\text{-}CH_3$	**4q**	89

[a] Aldehyde (1.0 mmol); amine (1.0 mmol); alkyne (1.5 mmol), MW irradiation (700 W). [b] Isolated yield.

Scheme 1 Proposed mechanism for the formation of quinoline derivatives

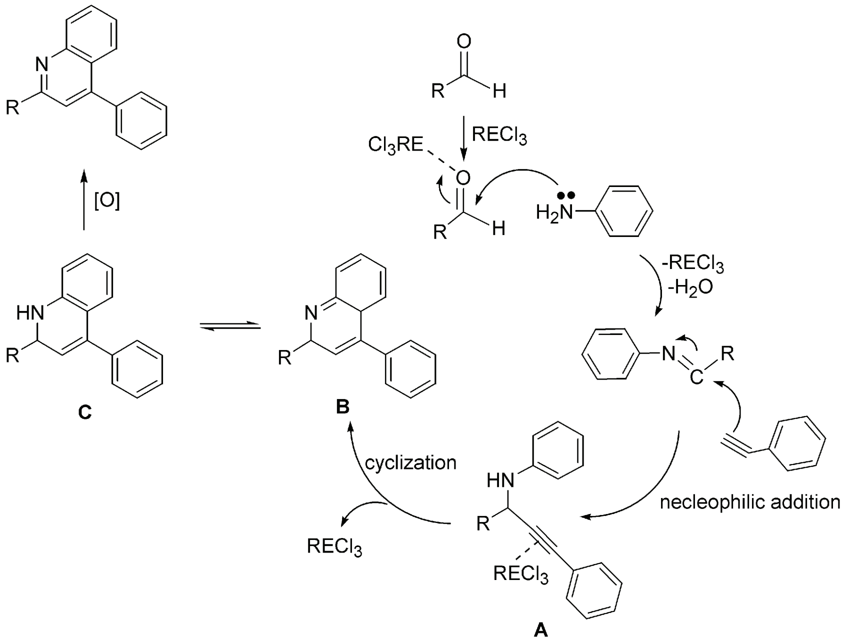


Table 3 Catalytic activities of rare earth metal chlorides[a]

RE	No	Y	La	Ce	Pr	Nd	Sm	Eu	Gd	Dy	Tm	Yb
Yield/%	trace	92	80	82	87	89	90	83	83	86	88	89

[a] Reaction of benzaldehyde (1.0 mmol), aniline (1.0 mmol) with phenylacetylene (1.5 mmol) catalyzed by 10 mol% $RECl_3$ at 180 ℃ for 8 min under MW irradiation (700 W) and solvent-free conditions.

earth triflates $RE(OTf)_3$,[32,16a] few studies have been performed on the recyclization of rare-earth metal chlorides. After the crude reaction product was extracted with diethyl ether (3×10 mL), the remaining rare-earth metal chloride was directly used as a catalyst for the reaction of benzaldehyde, aniline and phenylacetylene (1∶1∶1.5) under the above indicated conditions. As shown in Figure 1, the catalyst can be recycled for six times with only a slight decrease of the catalytical performance attributed to the slight loss of the amount of $RECl_3$ during separation of the reaction products.

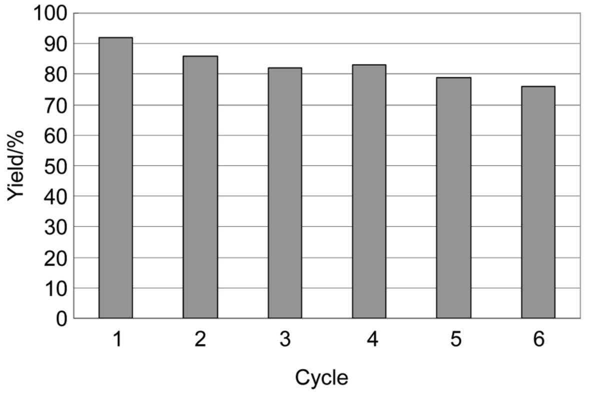


Figure 1 Results of six consecutive cycles of the catalyst.

Conclusions

In summary, we have developed a facile one-pot synthesis of the substituted quinolines from readily available simple starting materials of aldehydes, alkynes, and amines under solvent-free and microwave irradiation conditions. This reaction features a short reaction time, broad scope of substrates, solvent-free conditions, readily available and recyclable catalysts, and easy operation, which may have a potential application in the synthesis of quinoline derivatives.

Acknowledgement

The work was supported by the National Natural Science Foundation of China (21172004, 21172003 and 21072004), the National Basic Research Program of China (2012CB821604), and grants from the Ministry of Education (20103424110001).

References

[1] (a) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166; (b) Reux, B.; Nevalainen, T.; Raitio, K. H.; Koskinen, A. M. P. *Bioorg. Med. Chem.* **2009**, *17*, 4441; (c) Welsch, M. E.; Snyder, S. A.; Stockwell, B. R. *Curr. Opin. Chem. Biol.* **2010**, *14*, 347.

[2] (a) Kim, J. I.; Shin, I.-S.; Lee, J.-K. *J. Am. Chem. Soc.* **2005**, *127*, 1614; (b) Thompson, M. E.; Ma, B.; Djurovich, P. *US 20050164031A1*, **2005**.

[3] (a) Sheng, R.; Wang, P.; Gao, Y.; Wu, Y.; Liu, W.; Ma, J.; Li, H.; Wu, S. *Org. Lett.* **2008**, *10*, 5015; (b) Jung, H. S.; Kwon, P. S.; Lee, J. W.; Kim, J. I.; Hong, C. S.; Kim, J. W.; Yan, S.; Lee, J. Y.; Lee, J. H.; Joo, T.; Kim, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 2008; (c) Laras, Y.; Hugues, V.; Chandrasekaran, Y.; Blanchard-Desce, M.; Acher, F. C.; Pietrancosta, N. *J. Org. Chem.* **2012**, *77*, 8294.

[4] (a) Manske, R. H. F.; Kulka, M. *Org. React.* **1953**, *7*, 59; (b) Ranu, B. C.; Hajra, A.; Dey, S. S.; Jana, U. *Tetrahedron* **2003**, *59*, 813.

[5] (a) Denmark, S. E.; Venkatraman, S. *J. Org. Chem.* **2006**, *71*, 1668; (b) Wu, Y.-C.; Liu, L.; Li, H.-J.; Wang, D.; Chen, Y.-J. *J. Org. Chem.* **2006**, *71*, 6592.

[6] (a) Marco-Contelles, J.; Pérez-Mayoral, E.; Samadi, A.; Carreiras, M. C.; Soriano, E. *Chem. Rev.* **2009**, *109*, 2652; (b) Dormer, P. G.; Eng, K. K.; Farr, R. N.; Humphrey, G. R.; Mc Williams, J. C.; Reider, P. J.; Sager, J. W.; Volante, R. P. *J. Org. Chem.* **2003**, *68*, 467; (c) Mc Naughton, B. R.; Miller, B. L. *Org. Lett.* **2003**, *5*, 4257; (d) Bose, D. S.; Kumar, R. K. *Tetrahedron Lett.* **2006**, *47*, 813; (e) Zolfigol, M. A.; Salehi, P.; Ghaderi, A.; Shiri, M. *Catal. Commun.* **2007**, *8*, 1214; (f) Ghorbani-Vaghei, R.; Akbari-Dadamahaleh, S. *Tetrahedron Lett.* **2009**, *50*, 1055; (g) Mierde, H. V.; Voort, P. V. D.; Verpoort, F. *Tetrahedron Lett.* **2008**, *49*, 6893; (h) Mierde, H. V.; Voort, P. V. D.; Verpoort, F. *Tetrahedron Lett.* **2009**, *50*, 201; (i) Venkatesan, H.; Hocutt, F. M.; Jones, T. K.; Rabinowitz, M. H. *J. Org. Chem.* **2010**, *75*, 3488; (j) Ryabukhin, S. V.; Naumchik, V. S.; Plaskon, A. S.; Grygorenko, O. O.; Tolmachev, A. A. *J. Org. Chem.* **2011**, *76*, 5774; (k) Rafiee, E.; Nejad, F. K.; Joshaghani, M. *Chin. Chem. Lett.* **2011**, *22*, 288.

[7] (a) Vicente-García, E.; Catti, F.; Ramön, R.; Lavilla, R. *Org. Lett.* **2010**, *12*, 860; (b) Shindoh, N.; Tokuyama, H.; Takemoto, Y.; Takasu, K. *J. Org. Chem.* **2008**, *73*, 7451; (c) Zhao, Y.-L.; Zhang, W.; Wang, S.; Liu, Q. *J. Org. Chem.* **2007**, *72*, 4985; (d) Richter, H.; Mancheno, O. G. *Org. Lett.* **2011**, *13*, 6066; (e) Gong, D.; Li, J.; Yuan, C. *Chin. J. Chem.* **2001**, *19*, 1263.

[8] (a) Han, E.-G.; Kim, H. J.; Lee, K.-J. *Tetrahedron* **2009**, *65*, 9616; (b) Lü, Y.; Lan, B.; Zhou, H.; Xu, W.; Wang, J.; Huang, Y. *Chin. J. Chem.* **2004**, *22*, 854.

[9] Sakai, N.; Annaka, K.; Konakahara, T. *J. Org. Chem.* **2006**, *71*, 3653.

[10] (a) Barluenga, J.; Rodríguez, F.; Fañanás, F. *J. Chem. Asian J.* **2009**, *4*, 1036; (b) Aitken, R. A.; Murray, L. *J. Org. Chem.* **2008**, *73*, 9781; (c) Qi, C.; Zheng, Q.; Hua, R. *Tetrahedron* **2009**, *65*, 1316; (d) Kornhaaß, C.; Li, J.; Ackermann, L. *J. Org. Chem.* **2012**, *77*, 9190; (e) Zheng, L.; Ju, J.; Bin, Y.; Hu, R. *J. Org. Chem.* **2012**, *77*, 5794.

[11] Beller, M.; Thiel, O. R.; Trauthwein, H.; Hartung, C. G. *Chem. Eur. J.* **2000**, *6*, 2513.

[12] De Paolis, O.; Teixeira, L.; Török, B. *Tetrahedron Lett.* **2009**, *50*, 2939.

[13] (a) Gao, G.-L.; Niu, Y.-N.; Yan, Z.-L.; Wang, H.-L.; Wang, G.-W.; Shaukat, A.; Liang, Y.-M. *J. Org. Chem.* **2010**, *75*, 1305; (b) Zhao, J.; Peng, C.; Liu, L.; Wang, Y.; Zhu, Q. *J. Org. Chem.* **2010**, *75*, 7502; (c) Wang, Y.; Xin, X.; Liang, Y.; Lin, Y.; Zhang, R.; Dong, D. *Eur. J. Org. Chem.* **2009**, 4165; (d) Shindoh, N.; Tokuyama, H.; Takasu, K. *Tetrahedron Lett.* **2007**, *48*, 4749.

[14] Xiao, F.; Chen, Y.; Liu, Y.; Wang, J. *Tetrahedron* **2008**, *64*, 2755.

[15] Cao, K.; Zhang, F.-M.; Tu, Y.-Q.; Zhuo, X.-T.; Fan, C.-A. *Chem. Eur. J.* **2009**, *15*, 6332.

[16] (a) Kumar, A.; Rao, V. K. *Synlett* **2011**, 2157; (b) Cho, C. S.; Ren, W. X.; Yoon, N. S. *J. Mol. Catal. A*: *Chem.* **2009**, *299*, 117; (c) Cho, C. S.; Ren, W. X. *J. Organomet. Chem.* **2007**, *692*, 4182; (d) Gabriele, B.; Mancuso, R.; Lupinacci, E.; Spina, R.; Salerno, G.; Veltri, L.; Dibenedetto, A. *Tetrahedron* **2009**, *65*, 8507.

[17] (a) Gu, L.; Qin, Y.; Gao, Y.; Wang, X.; Wang, F. *Chin. J. Chem.* **2012**, *30*, 2121; (b) Cai, L.; Ji, X.; Yao, Z.; Xu, F.; Shen, Q. *Chin. J. Chem.* **2011**, *29*, 1880.

[18] (a) Zhang, H.; Zhou, Z.; Yao, Z.; Xu, F.; Shen, Q. *Tetrahedron Lett.* **2009**,

50, 1622; (b) Feng, S.-E.; Xu, F.; Shen, Q. *Chin. J. Chem.* **2008**, *26*, 1163.
[19] Xu, F.; Luo, Y.; Wu, J. *Heteroatom. Chem.* **2006**, *17*, 389.
[20] Shen, Q.; Huang, W.; Wang, J.; Zhou, X. *Org. Lett.* **2007**, *9*, 4491.
[21] Bulgakov, R. G.; Kuleshov, S. P.; Karamzina, D. S.; Dzhemilev, U. M. *Russ. J. Org. Chem.* **2006**, *42*, 1570.
[22] (a) Zhang, L.; Wang, S.; Zhou, S.; Yang, G.; Sheng, E. *J. Org. Chem.* **2006**, *71*, 3149; (b) Zhang, L.; Su, S.; Wu, H.; Wang, S. *Tetrahedron* **2009**, *65*, 10022.
[23] Zhang, L.; Wang, S.; Sheng, E.; Zhou, S. *Green Chem.* **2005**, *7*, 683.
[24] Enugala, R.; Nuvvula, S.; Kotra, V.; Varala, R.; Adapa, S. *Heterocycles* **2008**, *75*, 2523.
[25] Kobayashi, K.; Yoneda, K.; Miyamoto, K.; Morikawa, O.; Konishi, H. *Tetrahedron* **2004**, *60*, 11639.
[26] Prasad, K.; Cheng, C.-H. *J. Org. Chem.* **2006**, *71*, 7079.
[27] Song, S. J.; Cho, S. J.; Park, D. K.; Kwona, T. W.; Jenekhe, S. A. *Tetrahedron Lett.* **2003**, *44*, 255.
[28] Goswami, S.; Jana, S.; Adak, A. K. *J. Heterocycl. Chem.* **2007**, *44*, 1191.
[29] Anon, E.; Malo, M. C.; Tan, C.-Q.; Rodriguez, M. A. *Tetrahedron* **1998**, *54*, 6929.
[30] Akiyama, T.; Nakashima, S.; Yokota, K.; Fuchibe, K. *Chem. Lett.* **2004**, *33*, 922.
[31] Leardini, R.; Nanni, D.; Tundo, A.; Zanardi, G.; Ruggieri, F. *J. Org. Chem.* **1992**, *57*, 1842.
[32] (a) Barrett, A. G.; Braddock, D. C. *Chem. Commun.* **1997**, 351; (b) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W.-L. *Chem. Rev.* **2002**, *102*, 2227; (c) Wang, L.; Sui, Y.; Zhang, L. *Chin. J. Chem.* **2008**, *26*, 1105.

(Pan, B.; Fan, Y.)