Communication

One-Pot Three-Component Synthesis of 6-Bromoquinolines and 6-Iodoquinolines

Li-Qiang Wu* (武利強), Xiao Wang (王　霄),
Wei-Wei Ma (馬偉偉) and Fu-Lin Yan (閆福林)
School of Pharmacy, Xinxiang Medical University, Xinxiang, Henan 453003, P. R. China

Three-component one-pot synthesis of some novel 6-bromoquinolines **5a-5h** involving the treatment of 2-aminobenzophenone, α-methylene carbonyl compounds, and tetrabutyl-ammonium tribromide was achieved, and this reaction was extended to the preparation of 6-iodoquinolines **6a-6e** by a three-component reaction 2-aminobenzophenone, α-methylene carbonyl compounds, and benzyltrimethylammonium dichloroiodate in the presence of $ZnCl_2$.

Keywords: 6-Bromoquinolines; 6-Iodoquinolines; Friedlander reation; Tetrabutylammonium tribromide; Benzyltrimethylammonium dichloroiodate; Heterocycle; Multicomponent reaction.

INTRODUCTION

Quinoline and its derivatives are important intermediates in organic synthesis and exhibit various physiological properties and pharmacological activities, such as antiparasitic,[1] antitubercular,[2] antibacterial,[3] antifilarial,[3] HIV inhibiting,[4] HMG-CoA reductase inhibiting.[5] In addition to medicinal applications, quinoline derivatives are found to undergo hierarchical self-assembly into a variety of nano-structures and meso-structures with enhanced electronic and photonic functions.[6] In addition, quinolines have been employed in the study of bioorganic and bioorgano-metallic processes.[7] Considering the significant applications in the fields of medicinal, bioorganic, industrial and synthetic organic chemistry, there has been tremendous interest in developing efficient methods for the synthesis of quinolines, such as the Combes, Pfitzinger, Skraup and Friedlander methods.[8] Among them, the Friedlander annulation is still one of the most simple and straightforward approaches for the synthesis of polysubstituted quinolines. This method involves the acid or base catalyzed or thermal condensation between a 2-aminoaryl ketone and another carbonyl compound possessing an α-reactive methylene group followed by cyclodehydration. Recently, Lewis acids, such as $Ag_3PW_{12}O_{40}$,[9a] $SnCl_2$,[9b] $FeCl_3$,[9c] $Mg(ClO_4)_2$,[9d] $Nd(NO_3)_3$,[9e] $Y(OTf)_3$,[9f] $NiCl_2$,[9g] and others effective agents and methods, such as I_2/CAN,[9h] $NaHSO_4$–SiO_2,[9i] Amberlyst 15,[9j] dodecyl phosphoric acid,[9k] ionic liquids,[10] microwave,[11] urea,[12] poly(N-bromo-N-ethylbenzene-1,3-disulfonamide),[13] and KO*t*Bu[14] have been shown to be effective for the synthesis of quinolines.

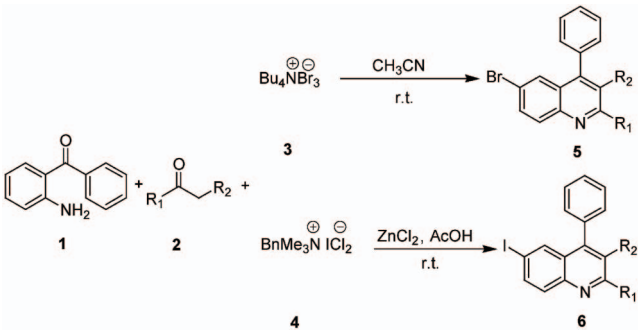
In continuation of our efforts to synthesis of bromoheterocyclic compounds using tetrabutylammonium tribromide (TBATB),[15] herein, we wish to report a modification of the Friedlander reaction for the synthesis of 6-bromoquinolines, which involves the formation *in situ* of the 2-amino-5-bromobenzophenone using TBATB as brominating agent. This latter reagent also serves as an *in situ* generator of HBr, which acts as a catalyst for the subsequent Friedlander condensation. During our study, we also observed the formation of 6-iodoquinolines in excellent yields by a three-component reaction 2-aminobenzophenone, α-methylene carbonyl compounds, and benzyltrimethyl ammonium dichloroiodate in the presence of $ZnCl_2$ (Scheme I).

RESULTS AND DISCUSSION

Previously, TABAB was used as a brominating agent. This solid reagent is considerably safe and convenient, and has a fine selectivity. It is well known that the bromination of amines having electron withdrawing groups in the aromatic ring with a calculated amount of TABAB can give the desired *p*-bromo-substituted products.[16] Thus, it is con-

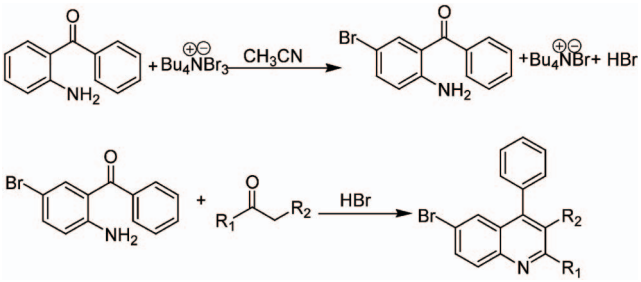
* Corresponding author. E-mail: wliq870@163.com

Scheme I



ceivable that the reaction involves the following two steps: (1) the 2-amino-5-bromobenzophenone is initially formed *in situ* using TBATB as brominating agent; (2) TBATB serves as an *in situ* generator of HBr, which acts as a catalyst for the the subsequent Friedlander condensation in the second step (see Scheme II).

Scheme II

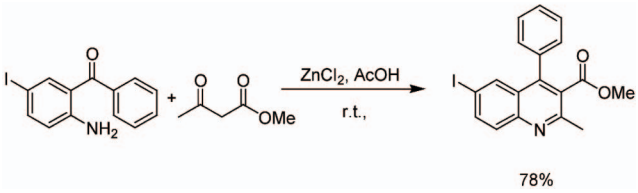


In a typical example, to a stirred solution of the 2-aminobenzophenone (1 mmol) and methyl acetoacetate (1 mmol) in CH_3CN (10 mL) at room temperature in a 50-mL reactor, TBATB (1 mmol) was added in a single portion. The vessel was sealed immediately and stirred at room temperature for 10 h. After completion of the reaction (TLC), the mixture was filtered and then poured into 50 mL saturated $NaHCO_3$ solution, extracted with 50 mL diethyl ether, dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to column chromatography over silica gel using EtOAc (8%) in hexane to obtain pure methyl 6-bromo-2-methyl-4-phenylquinoline-3-carboxylate **5a**, in 83% yield, mp 118-119 °C (Table 1, entry 1).

Similarly, various 1,3-diketones such as 2,4-pentanedione, 5,5-dimethylcyclohexandione, 2*H*-indene-1,3-dione, 1,3-cyclohexanedione, 2-hydroxynaphthalene-1,4-dione; cyclic ketones such as cyclopentanone and cyclohexanone; acyclic ketones including 2-pentanone and 2-oenanthone efficiently reacted with 2-aminobenzophenone and TBATB to produce the corresponding 6-bromoquinolines (Table 1).

Encouraged by these results, we hoped that the present protocol could safely be extended to the condensation reaction of 2-aminobenzophenone, α-methylene carbonyl compounds, and benzyltrimethylammonium dichloroiodate in same condition. Unfortunately, 6-iodoquinolines were obtained in low yields. BTMA ICl_2 is insoluble in CH_3CN or AcOH at room temperature, but the addition of $ZnCl_2$ increases its solubility, allowing the iodination of aromatic amines to proceed smothly under mild conditions.[17] In addition, we also noticed the introduction of $ZnCl_2$ could promote the subsequent Friedlander condensation in the reaction, which is demonstrated by Scheme III. Therefore, we executed the reaction in AcOH in the presence of $ZnCl_2$. 6-Iodoquinolines were obtained in excellent yields (Table 2).

Scheme III

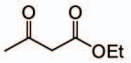
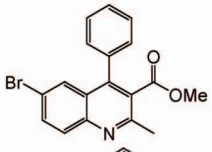
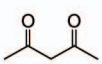
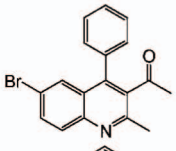
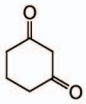
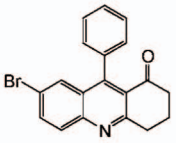
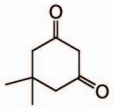
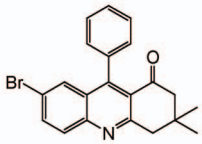
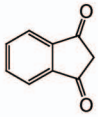
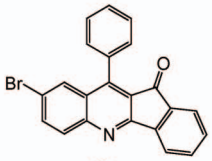
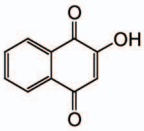
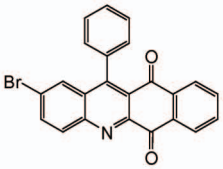
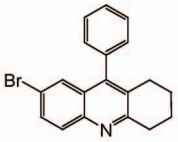
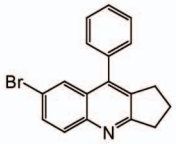
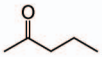
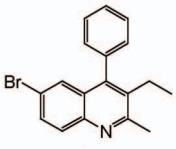
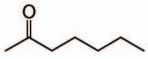
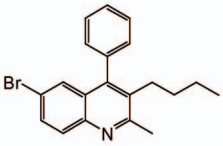


In summary, we have developed a simple and efficient methodology to synthesize 6-bromoquinolines using TBATB as a selective brominating agent and an efficient generator of HBr in Friedlander reaction. In addition, a novel and highly efficient method for the synthesis of 6-iodoquinolines from 2-aminobenzophenone, α-methylene carbonyl compounds, and benzyltrimethylammonium dichloroiodate in the presence of $ZnCl_2$ has been also developed. The methods are associated with the benefits derived from multicomponent reactions. We feel that this economically viable procedure will find practical utility for the one-pot synthesis of 6-bromoquinolines and 6-iodoquinolines.

EXPERIMENTAL

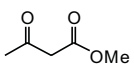
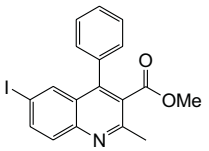
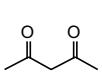
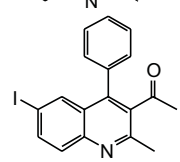
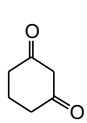
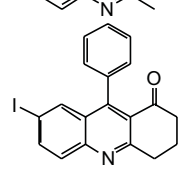
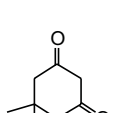
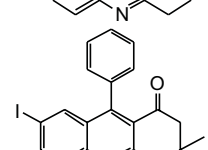
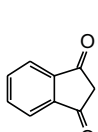
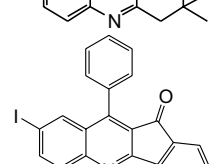
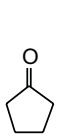
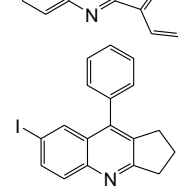
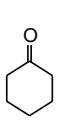
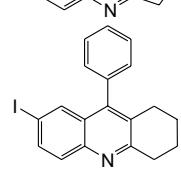
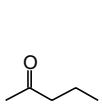
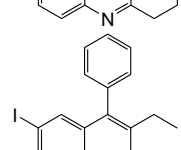
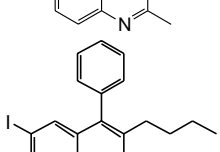
NMR spectra were determined on Bruker AV-400 spectrometer at room temperature using TMS as internal

Table 1. Synthesis of 6-bromoquinolines using TBATB[a]

Entry	Ketone **2**	6-Bromoquinolines **5**	Time (h)	Yield (%)
a			10	83
b			12	80
c			10	85
d			10	89
e			12	79
f			10	82
g			13	74
h			15	72
i			15	71
j			15	76

[a] 2-aminobenzophenone: α-methylene carbonyl compounds: TBATB = 1:1:1; reactions executed in a sealed vessel at room temperature.

Table 2. Synthesis of 6-iodoquinolines using BTMA ICl_2[a]

Entry	Ketone **2**	6-Iodoquinolines **6**	Time (h)	Yield (%)
a			8	88
b			10	82
c			8	81
d			8	91
e			10	76
f			10	75
g			12	74
h			12	70
i			12	78

[a] 2-aminobenzophenone: α-methylene carbonyl compounds: BTMA ICl_2: $ZnCl_2$ = 1:1:1:1; reactions executed in a sealed vessel at room temperature.

standard, coupling constants (*J*) were measured in Hz; Elemental analysis were performed by a Vario-III elemental

analyzer; Melting points were determined on a XT-4 binocular microscope and were uncorrected; Commercially available reagents were used throughout without further purification unless otherwise stated.

General Procedure for the synthesis of 6-bromoquinolines

To a stirred solution of the 2-aminobenzophenone (1 mmol) and α-methylene carbonyl compounds (1 mmol) in CH_3CN (10 mL) at room temperature in a 50-mL reactor, TBATB (1 mmol) was added in a single portion. The vessel was sealed immediately and stirred at room temperature for 10-15 h. After completion of the reaction (TLC), the mixture was filtered and then poured into 50 mL saturated $NaHCO_3$ solution, extracted with 50 mL diethyl ether, dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to column chromatography over silica gel using EtOAc (8%) in hexane to obtain pure 6-bromoquinolines.

Methyl 6-bromo-2-methyl-4-phenylquinoline-3-carboxylate (5a)

White solid; m.p. 118-119 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.94 (d, *J* = 8.8 Hz, 1H), 7.80-7.72 (m, 2H), 7.51 (m, 3H), 7.35 (m, 2H), 3.58 (s, 3H), 2.76 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.6, 155.0, 146.3, 145.4, 134.9, 133.7, 130.7, 129.1, 128.8, 128.5, 128.4, 128.0, 126.3, 120.5, 52.2, 23.8. Anal. calcd for $C_{18}H_{14}BrNO_2$: C 60.69, H 3.96, N 3.93; found: C 60.50, H 4.04, N 3.89.

1-(6-Bromo-2-methyl-4-phenylquinolin-3-yl)ethanone (5b)

White solid; m.p. 157-158 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.94 (d, *J* = 9.2 Hz, 1H), 7.80-7.74 (m, 2H), 7.54 (m, 3H), 7.34 (m, 2H), 2.67 (s, 3H), 1.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 154.1, 146.1, 143.0, 135.4, 134.4, 133.6, 130.6, 129.9, 129.2, 129.0, 128.2, 126.3, 120.6, 31.8, 23.9. Anal. calcd for $C_{18}H_{14}BrNO_2$: C 63.55, H 4.15, N 4.12; found: C 63.42, H 4.20, N 4.18.

7-Bromo-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (5c)

Pallide-flavens solid; m.p. 195-196 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.93 (d, *J* = 8.8 Hz, 1H), 7.83 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.60 (d, *J* = 2.0, 1H), 7.53 (m, 3H), 7.17 (m, 2H), 3.76-3.34 (m, 2H), 2.73-2.70 (m, 2H), 2.29-2.24 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 197.7, 162.7, 150.4, 147.2, 136.8, 135.1, 130.3, 130.1, 128.7, 128.3, 127.9, 124.4, 120.6, 40.6, 34.6, 21.2. Anal. calcd for $C_{19}H_{14}BrNO$: C 64.79, H 4.01, N 3.98; found: C 64.85, H 3.96, N 4.10.

7-Bromo-3,3-dimethyl-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (5d)

Pallide-flavens solid; m.p. 207-208 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.94 (d, *J* = 8.8 Hz, 1H), 7.83 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.61 (d, *J* = 2.0, 1H), 7.53 (m, 3H), 7.19-7.16 (m, 2H), 3.26 (s, 2H), 2.58 (m, 2H), 1.17 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 197.7, 161.6, 150.0, 147.6, 136.7, 135.0, 130.3, 130.1, 128.7, 128.3, 128.0, 127.9, 123.3, 120.6, 54.2, 48.3, 32.2, 28.3. Anal. calcd for $C_{21}H_{18}BrNO$: C 66.33, H 4.77, N 3.68; found: C 66.45, H 4.62, N 3.62.

8-Bromo-10-phenyl-11*H*-indeno[1,2-*b*]quinolin-11-one (5e)

Pallide-flavens solid; m.p. 250-251 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.12 (d, *J* = 7.6 Hz, 1H), 8.02 (dd, *J* = 3.2, 6.0 Hz, 1H), 7.83 (m, 2H), 7.73-7.69 (m, 2H), 7.61 (t, *J* = 6.0 Hz, 3H), 7.52 (t, *J* = 14.8 Hz, 1H), 7.44 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 162.3, 149.0; 147.0, 143.0, 137.4, 135.5, 135.0, 132.1, 131.8, 131.4, 130.6, 129.3, 129.2, 129.1, 128.4, 124.0, 123.3, 121.7, 121.2. Anal. calcd for $C_{22}H_{12}BrNO$: C 68.41, H 3.13, N 3.63; found: C 68.52, H 3.06, N 3.75.

2-Bromo-12-phenylbenzo[*b*]acridine-6,11-dione (5f)

Yellow solid; m.p. 317-318 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.46 (dd, *J* = 1.2, 7.6 Hz, 1H), 8.39 (d, *J* = 9.2 Hz, 1H), 8.18 (m, 1H), 7.99 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.85-7.81 (m, 2H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.64 (t, *J* = 6.0 Hz, 3H), 7.28 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 182.4, 181.6, 151.9, 148.5, 147.9, 136.3, 136.2, 134.8, 134.7, 134.3, 133.5, 133.0, 130.9, 130.1, 128.6, 128.4, 127.8, 127.7, 127.6, 124.6, 124.5. Anal. calcd for $C_{23}H_{12}BrNO_2$: C 66.69, H 2.92, N 3.38; found: C 66.75, H 3.06, N 3.24.

2-Bromo-9-phenyl-5,6,7,8-tetrahydroacridine (5g)

White solid, m.p. 102-103 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.89 (d, *J* = 8.8 Hz, 1H), 7.70 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.57-7.46 (m, 4H), 7.22 (d, *J* = 7.2 Hz, 2H), 3.19-3.16 (m, 2H), 2.61-2.58 (m, 2H), 2.00-1.94 (m, 2H), 1.82-1.76 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.6, 145.6, 144.8, 136.3, 131.8, 130.2, 129.4, 129.0, 128.8, 128.0, 127.9, 127.8, 119.4, 34.2, 28.1, 22.9, 22.8. Anal. calcd for $C_{19}H_{16}BrN$: C 67.47, H 4.77, N 4.14; found: C 67.31, H 4.82, N 4.05.

7-Bromo-9-phenyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline (5h)

White solid; m.p. 118-119 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.93 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 1.6 Hz, 1H),

7.70-7.67 (m, 1H), 7.56-7.47 (m, 3H), 7.35 (m, 2H), 3.24-3.20 (m, 2H), 2.92-2.89 (m, 2H), 2.21-2.13 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.0, 146.6, 141.8, 135.9, 134.7, 131.6, 130.5, 129.2, 128.7, 128.3, 127.8, 127.5, 119.5, 35.2, 30.4, 23.4. Anal. calcd for $C_{18}H_{14}BrN$: C 66.68, H 4.35, N 4.32; found: C 66.74, H 4.50, N 4.20.

6-Bromo-3-ethyl-2-methyl-4-phenylquinoline (5i)

White solid, m.p. 155-156 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.89 (d, *J* = 8.8 Hz, 1H), 7.67 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.56-7.48 (m, 3H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.24 (m, 2H), 2.81 (s, 3H), 2.62-2.56 (m, 2H), 1.07-1.04 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.0, 145.4, 144.6, 136.6, 134.4, 131.7, 130.2, 129.2, 128.6, 128.4, 128.2, 128.0, 119.5, 23.8, 23.5, 14.4. Anal. calcd for $C_{18}H_{16}BrN$: C 66.27, H 4.94, N 4.29; found: C 66.41, H 5.05, N 4.19.

6-Bromo-3-butyl-2-methyl-4-phenylquinoline (5j)

White solid; m.p. 141-142 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.89 (d, *J* = 8.8 Hz, 1H), 7.67 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.55-7.50 (m, 3H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.23 (m, 2H), 2.80 (s, 3H), 2.55-2.51 (m, 2H), 1.40-1.38 (m, 2H), 1.26-1.22 (m, 2H), 0.79-0.76 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.1, 145.6, 144.6, 136.6, 133.3, 131.6, 130.2, 129.2, 128.5, 128.4, 128.2, 128.0, 119.4, 32.2, 30.0, 23.9, 22.9, 13.5. Anal. calcd for $C_{20}H_{20}BrN$: C 67.80, H 5.69, N 3.95; found: C 67.87, H 5.56, N 4.02.

General procedure for the preparation of 6-iodo-quinolines

To a stirred solution of the 2-aminobenzophenone (1 mmol, α-methylene carbonyl compounds (1 mmol), and $ZnCl_2$ (1 mmol) in AcOH (10 mL) at room temperature in a 50-mL reactor, BTMA ICl_2 (1 mmol) was added in a single portion. The vessel was sealed immediately and stirred at room temperature for 8-12 h. After completion of the reaction (TLC), the mixture was filtered and then poured into 50 mL saturated $NaHCO_3$ solution, extracted with 50 mL diethyl ether, dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to column chromatography over silica gel using EtOAc (8%) in hexane to obtain pure 6-iodoquinolines.

Methyl 6-iodo-2-methyl-4-phenylquinoline-3-carboxylate (6a)

White solid, m.p. 129-130 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.97-7.95 (m, 2H), 7.79 (d, *J* = 9.2 Hz, 1H), 7.51 (m, 3H), 7.34 (m, 2H), 2.67 (s, 3H), 1.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 205.20, 154.24, 146.43, 142.47, 138.82, 135.29, 134.75, 134.37, 130.58, 129.93, 129.22, 128.93, 126.79, 92.33, 31.81, 23.93; Anal. calcd for $C_{18}H_{14}INO_2$: C 53.62, H 3.50, N 3.47; found: C 53.48, H 3.55, N 3.59.

1-(6-Iodo-2-methyl-4-phenylquinolin-3-yl)ethanone (6b)

White solid, m.p. 155-156 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.98-7.93 (m, 2H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.54-7.50 (m, 3H), 7.34 (m, 2H), 3.58 (s, 3H), 2.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.57, 155.22, 146.68, 145.18, 139.05, 135.11, 134.84, 130.59, 129.13, 128.81, 128.49, 127.86, 126.82, 92.23, 52.28, 23.84; Anal. calcd for $C_{18}H_{14}INO$: C 55.83, H 3.64, N 3.62; found: C 55.78, H 3.58, N 3.70.

7-Iodo-9-phenyl-3,4-dihydroacridin-1(2H)-one (6c)

White solid, m.p. 189-190 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.00 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.81-7.78 (m, 2H), 7.54-7.50 (m, 3H), 7.17 (m, 2H), 3.37-3.34 (m, 2H), 2.73-2.70 (m, 2H), 2.29-2.06 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 162.82, 150.15, 147.53, 140.34, 136.73, 136.70, 130.18, 129.20, 128.31, 127.98, 40.57, 34.58, 21.21; Anal. calcd for $C_{19}H_{14}INO$: C 57.16, H 3.53, N 3.51; found: C 57.26, H 3.49, N 3.48.

7-Iodo-3,3-dimethyl-9-phenyl-3,4-dihydroacridin-1(2H)-one (6d)

White solid, m.p. 218-219 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.00 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.83-7.78 (m, 2H), 7.56-7.51 (m, 3H), 7.17 (m, 2H), 3.25 (s, 2H), 2.58 (s, 2H), 1.16 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.74, 149.78, 147.88, 140.29, 136.78, 136.65, 130.18, 129.15, 128.33, 128.00, 127.90, 123.13, 92.24, 54.15, 48.34, 32.22, 28.31; Anal. calcd for $C_{21}H_{18}INO_2$: C 59.03, H 4.25, N 3.28; found: C 59.01, H 4.32, N 3.32.

8-Iodo-10-phenyl-11H-indeno[1,2-b]quinolin-11-one (6e)

Yellow solid, m.p. 258-259 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.13 (d, *J* = 7.6 Hz, 1H), 8.03-7.99 (m, 2H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.74-7.69 (m, 2H), 7.61 (m, 3H), 7.54-7.50 (m, 1H), 7.43 (m, 2H), ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 189.75, 162.31, 149.40, 146.76, 142.95, 140.35, 137.51, 137.06, 135.42, 132.07, 131.82, 131.40, 129.45, 129.34, 129.27, 129.13, 128.34, 123.93, 123.16, 121.76, 92.83; Anal. calcd for $C_{22}H_{12}INO_2$: C 60.99, H 2.79, N 3.23; found: C 61.06, H 2.68, N 3.32.

7-Iodo-9-phenyl-2,3-dihydro-1H-cyclopenta[b]quinoline (6f)

White solid, m.p. 156-157 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.97 (d, *J* = 1.6 Hz, 1H), 7.86 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.57-7.47 (m, 3H), 7.35-7.32

(m, 2H), 3.23-3.19 (m, 2H), 2.91-2.88 (m, 2H), 2.20-2.13 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.07, 147.00, 141.54, 136.90, 135.97, 134.45, 134.33, 130.61, 129.14, 128.68, 128.24, 128.07, 91.05, 35.18, 30.36, 23.35; Anal. calcd for $C_{18}H_{14}IN$: C 58.24, H 3.80, N 3.77; found: C 58.31, H 3.75, N 3.82.

2-Iodo-9-phenyl-5,6,7,8-tetrahydroacridine (6g)

White solid, m.p. 146-147 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.84 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.57-7.48 (m, 3H), 7.22 (m, 2H), 3.19-3.16 (m, 2H), 2.60-2.57 (m, 2H), 2.00-1.94 (m, 2H), 1.82-1.76 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.79, 145.30, 137.03, 136.26, 134.47, 130.22, 129.23, 129.00, 128.76, 128.44, 128.01; Anal. calcd for $C_{19}H_{16}IN$: C 59.24, H 4.19, N 3.64; found: C 58.98, H 4.25, N 3.60.

3-Ethyl-6-iodo-2-methyl-4-phenylquinoline (6h)

White solid, m.p. 186-187 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.85 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.58-7.49 (m, 4H), 7.24 (m, 2H), 2.81 (s, 3H), 2.58 (m, 2H), 1.07-1.04 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.19, 145.27, 144.87, 137.05, 136.51, 134.88, 134.28, 130.15, 129.17, 128.99, 128.55, 128.02, 91.21, 23.73, 23.46, 14.40; Anal. calcd for $C_{18}H_{16}IN$: C 57.92, H 4.32, N 3.75; found: C 58.01, H 4.37, N 3.69.

3-Butyl-6-iodo-2-methyl-4-phenylquinoline (6i)

White solid, m.p. 125-126 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.85 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 1.6 Hz, 1H), 7.56-7.48 (m, 3H), 7.24-7.21 (m, 2H), 2.81 (s, 3H), 2.55-2.51 (m, 2H), 1.39 (m, 2H), 1.25-1.22 (m, 2H), 0.79-0.75 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 259.25, 137.11, 136.45, 134.89, 133.26, 129.98, 129.22, 128.96, 128.51, 128.04, 91.26, 32.14, 29.97, 23.76, 22.91, 13.51; Anal. calcd for $C_{20}H_{20}IN$: C 59.86, H 5.02, N 3.49; found: C 59.90, H 5.11, N 3.52.

ACKNOWLEDGEMENTS

We are pleased to acknowledge the financial support from Xinxiang Medical University.

Received April 26, 2010.

REFERENCES

1. Muscia, G. C.; Bollini, M.; Carnevale, J. P.; Bruno, A. M.; Asis, S. E. *Tetrahedron Lett.* **2006**, *47*, 8811.
2. Desai, P. K.; Desai, P.; Machhi, D.; Desai, C. M.; Patel, D. *Indian J. Chem. Sect. B* **1996**, *35*(B), 871.
3. Srivastava, S. K.; Chauhan, P. M. S.; Bhaduri, A. P.; Fatima, N.; Chatterjee, R. *J. Med. Chem*. **2000**, *43*, 2275.
4. Kirsch, R.; Kleim, J. P.; Ries, G.; Rosenstock, B.; Roesner, M.; Winkler, I. DE Patent 19,613,591, 1997.
5. Suzuki, M.; Iwasaki, H.; Fujikawa, Y.; Kitahara, M.; Sakashita, M.; Sakoda, R. *Bioorg. Med. Chem.* **2001**, *9*, 2727.
6. (a) Agarwal, A. K.; Jenekhe, S. A. *Macromolecules* **1991**, *24*, 6806. (b) Zhang, X.; Shetty, A. S.; Jenekhe, S. A. *Macromolecules* **1999**, *32*, 7422. (c) Zhang, X.; Shetty, A. S.; Jenekhe, S. A. *Macromolecules* **2000**, *33*, 2069. (d) Jenekhe, S. A.; Lu, L.; Alam, M. M. *Macromolecules* **2001**, *34*, 7315.
7. (a) Saito, I.; Sando, S.; Nakatani, K. *Bioorg. Med. Chem.* **2001**, *9*, 2381. (b) He, C.; Lippard, S. J. *J. Am. Chem. Soc.* **2001**, *40*, 1414.
8. (a) Combes, A. *Bull. Soc. Chim. Fr.* **1888**, *49*, 89. (b) Buu-Hoi, N. P.; Nuong, N. D.; Jacquhnos, P. *J. Org. Chem.* **1953**, *18*, 1209. (c) Skraup, Z. H. *Ber. Dtsch. Chem. Ges.* **1880**, *13*, 2086. (d) Friedlander, P. *Ber. Dtsch. Chem. Ges.* **1882**, *15*, 2572.
9. (a) Yadav, J. S.; Reddy, B. V. S.; Sreedhar, P.; Rao, R. S.; Nagaiah, K. *Synthesis* **2004**, *14*, 2381. (b) Arumugam, P.; Karthikeyan, G.; Atchudan, R.; Murlidharan, D.; Perumal, P. T. *Chem. Lett.* **2005**, *34*, 314. (c) Wu, J.; Zhang, L.; Diao, T. N. *Synlett* **2005**, 2653. (d) Varala, R.; Enugala, R.; Adapa, S. R. *Synthesis* **2006**, 3825. (e) De, S. K.; Gibbs, R. A. *Tetrahedron Lett.* **2005**, *46*, 1647. (f) Dabiri, M.; Baghbanzadeh, M.; Arzroomchilar, E. *Heterocycles* **2008**, *75*, 397. (g) Wu, J.; Xia, H. G.; Gao, K. *Org. Biomol. Chem.* **2006**, *4*, 26. (h) Likhar, P. R.; Subhas, M. S.; Roy, S.; Kantam, M. L.; Sridhar, B.; Seth, R. K.; Biswas, S. *Org. Biomol. Chem.* **2009**, *7*, 85. (i) Dabiri, M.; Azimi, S. C.; Bazgir, A. *Monatsh. Chem.* **2007**, *138*, 659. (j) Das, B.; Damodar, K.; Chowdhury, N.; Kumar, R. A. *J. Mol. Catal. A Chem.* **2007**, *274*, 148. (k) Ghassamipour, S.; Sardarian, A. R. *Tetrahedron Lett.* **2009**, *50*, 514.
10. Palimkar, S. S.; Siddiqui, S. A.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *J. Org. Chem.* **2003**, *68*, 9371.
11. Szatmari, I.; Fulop, F. *Synthesis* **2009**, *5*, 775.
12. Qi, C.; Zheng, Q.; Hua, R. *Tetrahedron* **2009**, *65*, 1316.
13. Ghorbani-Vaghei, R.; Akbari-Dadamahaleh, S. *Tetrahedron Lett.* **2009**, *50*, 1055.
14. Mierde, H. V.; Voort, P. V. D.; Verpoort, F. *Tetrahedron Lett.* **2009**, *50*, 201.
15. Wu, L.-Q.; Yang, C.-G.; Wu, Y.-F.; Yang, L.-M. *J. Chin. Chem. Soc.* **2009**, *56*, 606.
16. Berthelot, J.; Guette, C.; Essayegh, M.; Desbene, P. L.; Basselier, J. J. *Synth. Commun.* **1986**, *16*, 164.
17. Kajigaeshi, S.; Kakinami, T.; Watanabe, F.; Okamoto, T. *Bull. Chem. Soc. Jpn*. **1989**, *62*, 1349.