ACS Combinatorial Science

Research Article

pubs.acs.org/acscombsci

# New Pyridinium-Based Ionic Liquid as an Excellent Solvent–Catalyst System for the One-Pot Three-Component Synthesis of 2,3-Disubstituted Quinolines

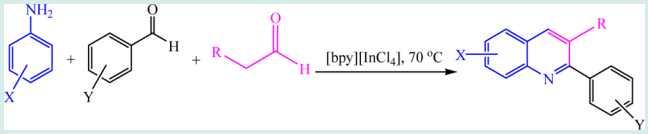
Salma Anvar,[†] Iraj Mohammadpoor-Baltork,*[,†] Shahram Tangestaninejad,*[,†] Majid Moghadam,[†] Valiollah Mirkhani,[†] Ahmad Reza Khosropour,[†] Amir Landarani Isfahani,[†] and Reza Kia[‡]

[†]Catalysis Division, Department of Chemistry, University of Isfahan, Isfahan 81746-73441, Iran

[‡]Chemistry Department, Sharif University of Technology, P.O. Box 11155-3516, Tehran, Iran

Supporting Information

**ABSTRACT:** The synthesis of a variety of 2,3-disubstituted quinolines has been achieved successfully via a one-pot three-component reaction of arylamines, arylaldehydes and aliphatic aldehydes in the presence of butylpyridinium tetrachloroindate-(III), [bpy][$InCl_4$], ionic liquid as a green catalyst and solvent. Mild conditions with excellent conversions, and simple product isolation procedure are noteworthy advantages of this method. The recyclability of the ionic liquid makes this protocol environmentally benign.



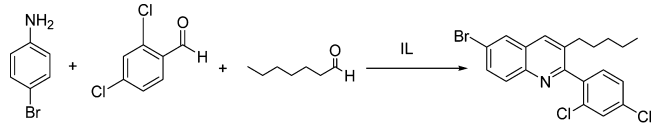

**KEYWORDS:** *aldehydes, anilines, quinolines, ionic liquid, three-component reaction*

## INTRODUCTION

Ionic liquids (ILs) have recently appeared as the main subject of many studies aiming at not only understanding the nature of these solvents but also finding their physicochemical and photochemical properties in different applications such as sensors, fuel cells, batteries, capacitors, thermal fluids, plasticizers, lubricants, ion gels, extractants, and solvents in analysis, synthesis, catalysis, and separation.[1−6] Other new applications of the ILs are their use as energetic compounds as well as in pharmaceutical industry. ILs can be considered as more than just alternative "green" solvents. They differ from molecular solvents by their unique ionic character, as well as their "structure and organization", which can lead to specific effects, making them tunable and multipurpose materials.[7−10] In addition, the combinatorial synthesis of some fine chemicals, such as sulfonamides and carboxamides,[11] 3-arylideneaminoquinazolin-4(1H)-one derivatives,[12] spirooxindoles,[13] and fused pyridine derivatives[14] in the presence of ionic liquids, provides a greener means for the preparation of these compounds.

Multicomponent reactions (MCRs) provide an opportunity for the coupling of three or more simple and flexible building blocks in a one-pot operation, producing complex structures by simultaneous formation of two or more bonds, according to the domino principle.[15] Environmentally friendly operation via reducing the number of synthetic steps, the energy consumption, and the waste production are among the advantages of MCRs. Additionally, during the past decade, industrial and academic researchers have transformed this beneficial technology into one of the most efficient and economic approaches for combinatorial and parallel synthesis, as evidenced by the increase in the literature focusing on this research field.[16−22]

**Table 1. Optimization of Reaction Parameters for the Synthesis of 4{*1,1,1*}[a]**




1{1} 2{1} 3{1} 4{1,1,1}

| entry | catalyst (mmol) | *T* (°C) | time (min) | yield (%)[b] |
|---|---|---|---|---|
| 1 | no catalyst | 70 | 120 | 0 |
| 2 | [bpy]Cl (1) | 70 | 30 | 70 |
| 3 | [bpy][$FeCl_4$] (1) | 70 | 30 | 91 |
| 4 | [bpy][$ZnCl_3$] (1) | 70 | 30 | 80 |
| 5 | [bmim]OTf (1) | 70 | 30 | 80 |
| 6 | [bmim]Cl (1) | 70 | 30 | 70 |
| 7 | [bmim]Br (1) | 70 | 30 | 65 |
| 8 | [bmim]$NO_3$ (1) | 70 | 30 | 75 |
| 9 | [bmim]$BF_4$ (1) | 70 | 30 | 75 |
| 10 | [bpy][$InCl_4$] (1) | 70 | 30 | 96 |
| 11 | [bpy][$InCl_4$] (1.1) | 70 | 30 | 96 |
| 12 | [bpy][$InCl_4$] (0.8) | 70 | 30 | 88 |
| 13 | [bpy][$InCl_4$] (1) | 90 | 30 | 96 |
| 14 | [bpy][$InCl_4$] (1) | 50 | 30 | 70 |

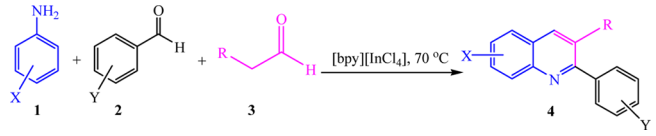
[a]4-Bromoaniline (1 mmol), 2,4-dichlorobenzaldehyde (1 mmol), and heptanal (1 mmol). [b]Isolated yield.

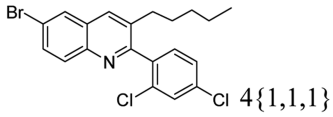
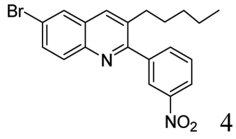
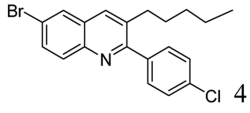
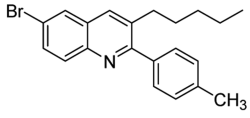
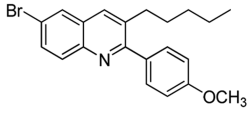
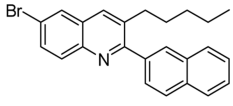
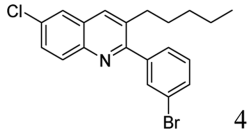
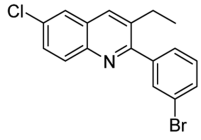
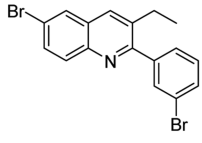
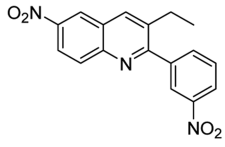
Among nitrogen-containing heterocycles, quinolines have received special attention because of their abundance in a variety

**Received:** March 16, 2013
**Revised:** February 9, 2014
**Published:** February 12, 2014

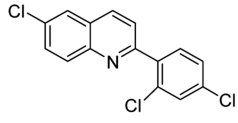
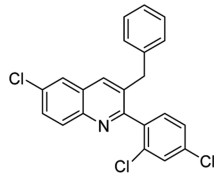
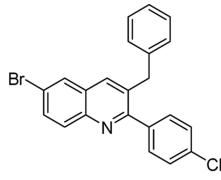
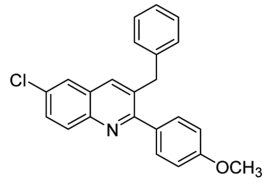
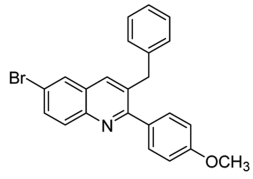
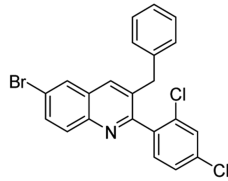
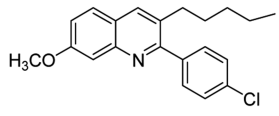
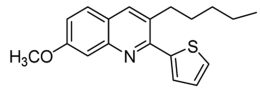
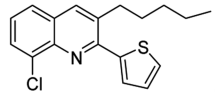
**Table 2. One-Pot Three-Component Synthesis of 2,3-Disubstituted Quinolines 4 Catalyzed by [bpy][$InCl_4$][a]**




| Entry | Product | Time (min) | Yield (%)[b] |
|---|---|---|---|
| 1 |  4{1,1,1} | 30 (45[c]) | 96 (42[c]) |
| 2 |  4{1,2,1} | 35 | 90 |
| 3 |  4{1,3,1} | 30 (45[c]) | 95 (49[c]) |
| 4 |  4{1,4,1} | 35 | 92 |
| 5 |  4{1,5,1} | 30 (45[c]) | 93 (47[c]) |
| 6 |  4{1,6,1} | 45 | 85 |
| 7 |  4{2,7,1} | 30 | 97 |
| 8 |  4{2,7,2} | 30 | 90 |
| 9 |  4{1,7,2} | 30 | 90 |
| 10 |  4{3,2,2} | 30 | 95 |


dx.doi.org/10.1021/co400144b | ACS Comb. Sci. 2014, 16, 93−100

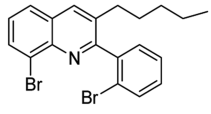
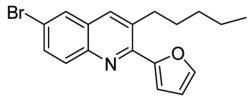
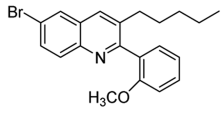
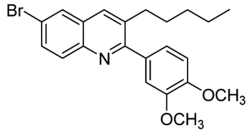
**Table 2. continued**

| Entry | Product | Time (min) | Yield (%)[b] |
|---|---|---|---|
| 11 |  4{2,1,3} | 35 | 90 |
| 12 |  4{2,1,4} | 30 (45[c]) | 92 (40[c]) |
| 13 |  4{1,3,4} | 35 | 90 |
| 14 |  4{2,5,4} | 40 | 95 |
| 15 |  4{1,5,4} | 40 | 97 |
| 16 |  4{1,1,4} | 35 | 93 |
| 17 |  4{4,3,1} | 30 | 95 |
| 18 |  4{4,9,1} | 35 | 93 |
| 19 |  4{5,9,1} | 40 | 85 |



dx.doi.org/10.1021/co400144b | *ACS Comb. Sci.* 2014, 16, 93−100

**Table 2. continued**

| Entry | Product | Time (min) | Yield (%)[b] |
|---|---|---|---|
| 20 |  4{6,8,1} | 40 | 83 |
| 21 |  4{1,10,1} | 30 | 92 |
| 22 |  4{1,11,1} | 40 | 86 |
| 23 |  4{1,12,1} | 30 | 93 |

[a]Arylamine (1 mmol), arylaldehyde (1 mmol), aliphatic aldehyde (1 mmol), IL (1 mmol), 70 °C. [b]Isolated yield. [c]Reaction was carried out in the presence of iodine.

of naturally occurring products and medicinally active compounds.[23] A great number of quinoline based compounds exhibit a broad range of physiological and biological properties such as antituberculosis,[24] antimalarial,[25] antiasthmatic,[26] antidiabetic,[27] and antibacterial[28] activities. Because of the importance of different quinoline derivatives, various procedures have been developed for the synthesis of this heterocyclic compound.[29−32]

In continuation of our interest in the development of useful synthetic methodologies for the preparation of fine chemicals;[33] herein, we report a convenient and efficient one-pot three-component protocol for the synthesis of 2,3-disubstituted quinolines starting directly from arylamines, arylaldehydes and aliphatic aldehydes in the presence of [bpy][$InCl_4$] ionic liquid as the catalyst and solvent. The preparation of quinolines from the reaction of 2-aminoaryl ketones with $\beta$-ketoesters/ketones, by three-component reaction of aldehydes, alkynes, and amines, or from the reaction of 2-aminoaryl ketones with phenylacetylenes has been previously reported in the presence of ionic liquids,[34] but to the best of our knowledge, this is the first report on the synthesis of quinolines via a one-pot three-component reaction of arylamines, arylaldehydes and aliphatic aldehydes in the presence of [bpy][$InCl_4$] ionic liquid.

## RESULTS AND DISCUSSION

First, the model reaction of 4-bromoaniline, 2,4-dichlorobenzaldehyde, and heptanal was performed in the presence of different ILs (Table 1). It was observed that all of the investigated ILs were capable of catalyzing the synthesis of desired quinoline **4**{*1,1,1*}. However, the yield of the corresponding quinoline was higher in the presence of [bpy][$InCl_4$] (Table 1, entry 10). Then, different reaction conditions such as the amount of IL, temperature, and reaction time were checked (Table 1). The results revealed that the best yield of the desired quinoline was obtained by carrying out the reaction with 1:1:1:1 molar ratios of 4-bromoaniline, 2,4-dichlorobenzaldehyde, heptanal and [bpy][$InCl_4$] at 70 °C for 30 min (Table 1, entry 10).

The substrate scope of [bpy][$InCl_4$]-catalyzed system was then examined under the optimized reaction condition. As shown in Table 2, a wide variety of arylaldehydes containing electron-withdrawing and electron-donating groups at the para or meta position were reacted with anilines containing para or meta electron-withdrawing substituents and aliphatic aldehydes (Figure 1) to afford the corresponding 2,3-disubstituted quinolines in excellent yields. It is noteworthy that the ortho-substituted aldehydes 2-bromobenzaldehyde and 2-methoxybenzaldehyde, and the ortho-substituted anilines 2-chloroaniline and 2-bromoaniline were efficiently converted into the desired 2,3-disubstituted quinolines under the same reaction conditions. The heterocyclic aldehydes thiophene-2-carbaldehyde and furfural took part in the reaction smoothly affording the expected products in excellent yields. The results show that [bpy][$InCl_4$] is an efficient catalyst for the preparation of a large spectrum of 2,3-disubstituted quinolines in good yields (Table 2). It was also found that anilines with electron-donating groups ((4-MeO, 4-Me) did not take part in the reaction to give the corresponding quinolines.

It is important to note that some of these reactions were also carried out in the presence of iodine as a catalyst[32] (Table 2, entries 1, 3, 5 and 12). Under these conditions, the desired quinolines were obtained in only 40−49% yields. These results clearly show that the present IL catalyst is more efficient and convenient for the synthesis of quinolines.

To prepare the quinolines with alkyl substituents at 2- and 3-positions, the reaction of 4-bromoaniline (1 mmol) with heptanal (2 mmol) or butanal (2 mmol) was examined in the presence of [bpy][$InCl_4$] (1 mmol). As shown in Scheme 1, the desired quinolines were not obtained under these conditions. Consequently, the present method could be used only for the synthesis of quinolines containing aryl and alkyl substituents at 2- and 3-positions, respectively, in excellent yields.

The recovery and reusability of the catalyst, which is very important for industrial purposes and is highly recommended


dx.doi.org/10.1021/co400144b | ACS Comb. Sci. 2014, 16, 93−100

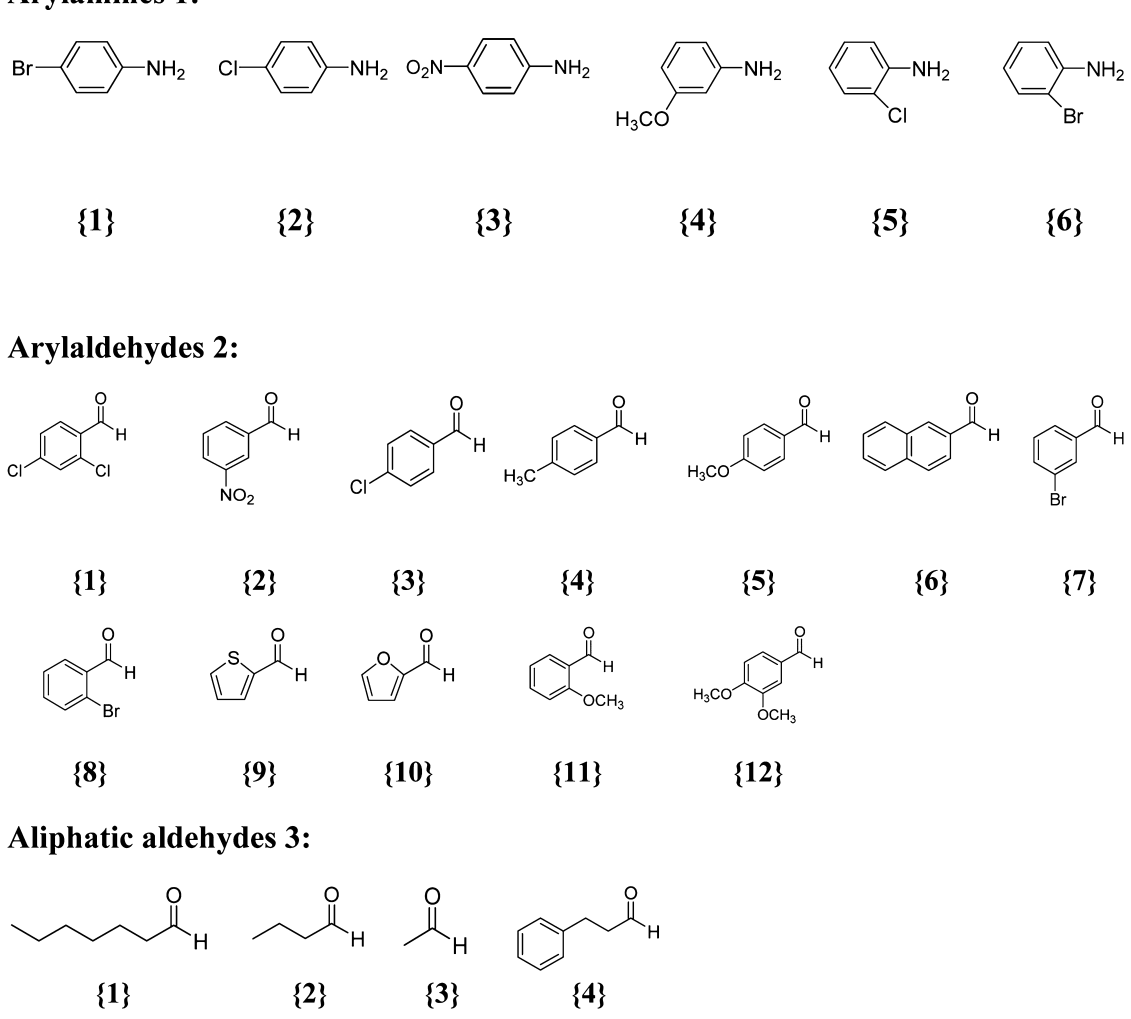
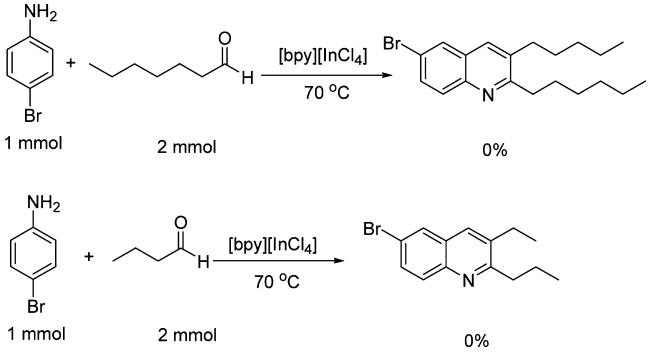



**Figure 1.** Diversity of reagents.

**Scheme 1. Reaction of Arylamine with Aliphatic Aldehydes**




for green processes, was also explored in the model reaction. To test the reusability of the catalyst, after completion of the reaction, the mixture was diluted with 5 mL of water and 5 mL of EtOAc and shaken vigorously. The organic layer was separated from the IL. The aqueous layer was evaporated and the ionic liquid was dried at 60−70 °C under vacuum and then reused. The results showed that the [bpy][$InCl_4$] catalyst could be used at least six times without any significant loss in the yield of the product (Table 3).

It is evident from the literature that ILs containing chloroindate(III) exhibit Lewis acid properties in various

**Table 3. Recycling of the IL in the Synthesis of 4{*1,1,1*}[a]**

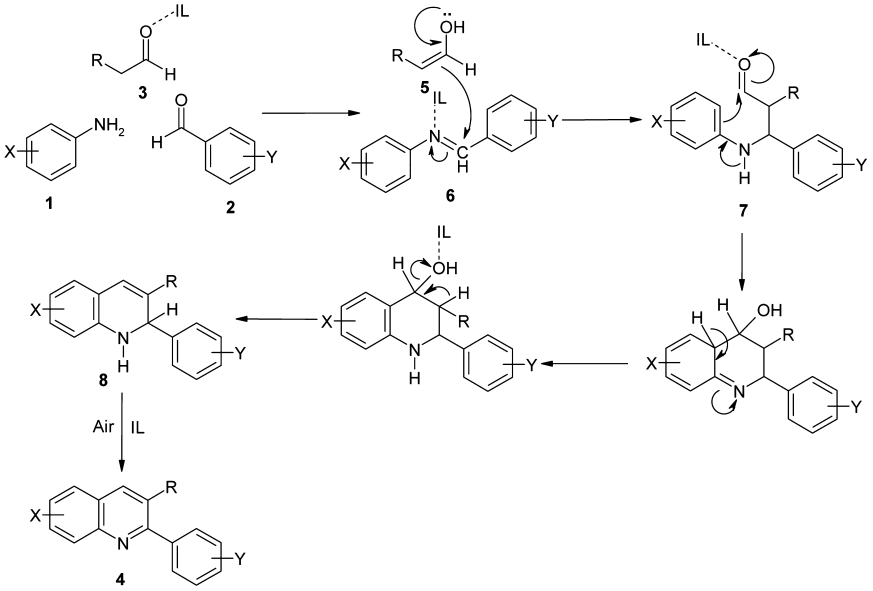
| run | yield (%)[b] |
|---|---|
| 1 | 96 |
| 2 | 95 |
| 3 | 95 |
| 4 | 93 |
| 5 | 90 |
| 6 | 90 |

[a]4-Bromoaniline (1 mmol), 2,4-dichlorobenzaldehyde(1 mmol), heptanal (1 mmol), 70 °C, and 30 min. [b]Isolated yield.

organic transformations.[35−37] Accordingly, a plausible mechanism for this IL catalyzed three-component synthesis of 2,3-disubstituted quinolines is proposed in Scheme 2. First, the [bpy][$InCl_4$] IL catalyzes the keto−enol tautomerization of aliphatic aldehyde and also activates the imine to give **5** and **6**, respectively. The in situ formed enol attacks the activated imine to give **7**, which upon intramolecular Friedel−Crafts reaction and subsequent dehydration in the presence of IL produces dihydroquinoline **8** and releases the catalyst (IL) for the next catalytic cycle. Finally, aromatization of dihydroquinoline **8** under air atmosphere affords the desired product **4**. As we mentioned, anilines with electron-donating groups did not take part in the reaction to give the corresponding quinolines. It seems that


dx.doi.org/10.1021/co400144b | ACS Comb. Sci. 2014, 16, 93−100

**Scheme 2. Proposed Mechanism for [bpy][$InCl_4$] Catalyzed Three-Component Synthesis of 2,3-Disubstituted Quinolones 4**



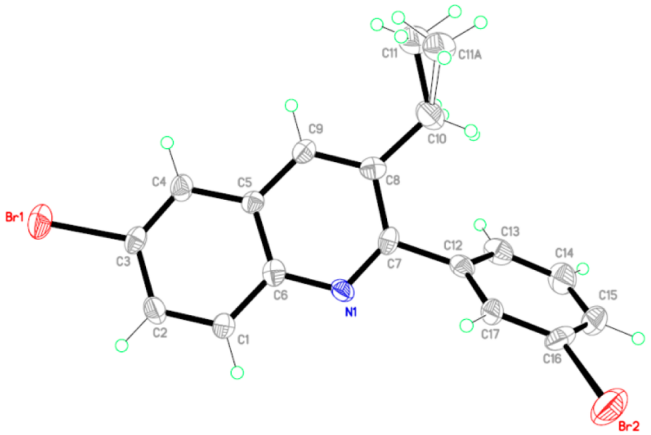




**Figure 2.** X-ray Crystallography structure of compound **4**{*1,7,2*}. The methyl segment shows disorder and the minor fragment is shown as open line.

electron-donating substituent increases the electron density on the nitrogen in aniline, so, an acid–base complex is rapidly formed between amino group and the catalyst, which prevents further reaction leading to the desired quinoline.

The structures of the products were characterized by IR, $^1H$ and $^{13}C$ NMR spectroscopy, mass spectrometry and elemental analysis. The structure of the product **4**{*1,7,2*} was additionally confirmed by X-ray crystal structure analysis (Figure 2, CCDC-851671).

## CONCLUSION

We have developed a novel and facile protocol for the synthesis of 2,3-disubstituted quinolines through a one-pot three-component reaction of arylamines, arylaldehydes, and aliphatic aldehydes using [bpy][$InCl_4$] as a green catalyst and solvent. The waste-free process combined with recovery and reusability of the catalyst make this method economic and benign for the synthesis of quinolines. In addition, excellent yields, short reaction times, mild conditions, avoiding hazardous organic solvents, and simple experimental procedure are other advantages of the present method.

## EXPERIMENTAL PROCEDURES

**General Information.** Melting points were determined using a Stuart Scientific SMP2 apparatus without correction. FT-IR spectra were obtained as KBr pellets using a Jasco 6300 instrument in the range of 400–4000 $cm^{-1}$. $^1H$ and $^{13}C$ NMR (500 and 125 MHz) spectra were recorded on a Bruker-AC 500 spectrometer in $CDCl_3$ solution. Mass spectra were recorded on a Platform II spectrometer from Micromass; EI mode at 70 eV. Elemental analysis was carried out on a LECO, CHNS-932 instrument.

**Preparation of [bpy][$InCl_4$].** A mixture of pyridine (0.096 g, 1.2 mmol) and 1-chlorobutane (0.105 g, 1.1 mmol) was stirred under reflux conditions for 72 h in dark. The reaction mixture was cooled and the resulting solid was recrystallized from MeCN/EtOAc (1:1), filtered under vacuum and washed with EtOAc. The excess solvent was then removed under vacuum at 70 °C. The IL was prepared by stirring [bpy]Cl (0.171 g, 1 mmol,) with $InCl_3$ (0.219 g, 1 mmol) at room temperature for 10 min. mp: 68–70 °C. IR (KBr): $\nu_{max}$ = 3130, 3085, 2963, 2935, 2877, 1633, 1487, 1466, 1178, 769, 681 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 0.76 (t, $J$ = 7.2 Hz, 3H), 1.16–1.22 (m, 2H), 1.80–1.86 (m, 2H), 4.45 (t, $J$ = 7.6 Hz, 2H), 7.89 (t, $J$ = 7.2 Hz, 2H), 8.37 (t, $J$ = 7.6 Hz, 1H), 7.68 (d, $J$ = 5.6 Hz, 2H). $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 12.57, 18.63, 32.49, 61.66, 128.09, 144.12, 145.37. Anal. Calcd for $C_9H_{14}Cl_4InN$: C, 27.52; H, 3.59; N, 3.57. Found: C, 27.60; H, 3.54; N, 3.65.

**Typical Procedure for the Synthesis of 6-Bromo-2-(2,4-dichlorophenyl)-3-pentylquinoline 4{*1,1,1*}.** To a mixture of 4-bromoaniline (0.172 g, 1 mmol), 2,4-dichlorobenzaldehyde (0.174 g, 1 mmol), and hexanal (0.114 g, 1 mmol), was added [bpy][$InCl_4$] (0.390 g, 1 mmol). The reaction mixture was stirred at 70 °C for 30 min. The progress of the reaction was monitored by TLC (eluent = *n*-hexane/EtOAc = 9/1). After completion of the reaction, the mixture was diluted with water (5 mL) and EtOAc (5 mL) and shaken vigorously. The organic layer was separated from the IL. The IL was dried at 60–70 °C under vacuum to remove water and reused. The organic layer was dried over $Na_2SO_4$ and evaporated. The crude product was purified by recrystallization from EtOH to obtain the pure


dx.doi.org/10.1021/co400144b | ACS Comb. Sci. 2014, 16, 93–100

product 4{*1,1,1*}. mp: 133−134 °C. IR (KBr): $\nu_{max}$ = 2923, 2854, 1593, 1468, 1376, 1344, 1099, 817, 644 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 0.75 (t, $J$ = 6.8 Hz, 3H), 1.14−1.16 (m, 4H), 1.47−1.46 (m, 2H), 2.44−2.60 (m, 2H), 7.27 (d, $J$ = 8.0 Hz, 1H), 7.33 (dd, $^1J$ = 8.0 Hz, $^2J$ = 2.0 Hz, 1H), 7.47 (d, $J$ = 2.0 Hz, 1H), 7.69 (dd, $^1J$ = 9.2 Hz, $^2J$ = 2.0 Hz, 1H), 7.93−7.95 (m, 3H). $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 13.86, 18.36, 22.29, 29.59, 31.34, 120.85, 127.33, 129.11, 129.15, 129.47, 130.84, 131.23, 132.53, 133.65, 134.44, 134.96, 135.70, 137.72, 144.72, 158.00. MS: $m/z$ = 423.17 ($[M]^+$, 94.20), 422.04 (62.80), 388.04 (64.73), 330.94 (65.70), 250.00 (77.78), 113.87 (91.79), 77.89 (5.28), 55.92 (32.37). Anal. Calcd for $C_{20}H_{18}BrCl_2N$: C, 56.76; H, 4.29; N, 3.31. Found: C, 56.87; H, 4.22; N, 3.21.

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1H$ and $^{13}C$ NMR spectra for all products and crystallographic data for compound 4{*1,7,2*}. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Authors

*Fax: +98(311)6689732. Phone: +98(311)7932705. E-mail: imbaltork@sci.ui.ac.ir

*Fax: +98(311)6689732. Phone: +98(311)7932705. E-mail: stanges@sci.ui.ac.ir.

### Funding

The authors are grateful to the Center of Excellence of Chemistry and Research Council of the University of Isfahan for financial support of this work.

### Notes

The authors declare no competing financial interest.

## ■ REFERENCES

(1) Liu, X. D.; Ma, J. M.; Peng, P.; Zheng, W. J. One-Pot Hydrothermal Synthesis of Znse Hollow Nanospheres from an Ionic Liquid Precursor. *Langmuir* **2010**, *26*, 9968−9973.

(2) Hubbard, C. D.; Illner, P.; Van Eldik, R. Understanding Chemical Reaction Mechanisms in Ionic Liquids: Successes and Challenges. *Chem. Soc. Rev.* **2011**, *40*, 272−290.

(3) Olivier-Bourbigou, H.; Magna, L.; Morvan, D. Ionic Liquids and Catalysis: Recent Progress from Knowledge to Applications. *Appl. Catal., A* **2010**, *373*, 1−56.

(4) Gupta, A. K.; Kumari, K.; Singh, N.; Raghuvanshi, D. S.; Singh, K. N. An Eco-Safe Approach to Benzopyranopyrimidines and 4*H*-Chromenes in Ionic Liquid at Room Temperature. *Tetrahedron Lett.* **2012**, *53*, 650−653.

(5) Chatel, G.; Goux-Henry, C.; Kardos, N.; Suptil, J.; Andrioletti, B.; Draye, M. Ultrasound and Ionic Liquid: An Efficient Combination to Tune the Mechanism of Alkenes Epoxidation. *Ultrason. Sonochem.* **2012**, *19*, 390−394.

(6) Ma, Y.; Zhan, G.; Ma, M.; Wang, X.; Li, C. Direct Electron Transfer of Hemoglobin in a Biocompatible Electrochemical System Based on Zirconium Dioxide Nanotubes and Ionic Liquid. *Bioelectrochemistry* **2012**, *84*, 6−10.

(7) Liu, C. Z.; Wang, F.; Stiles, A. R.; Guo, C. Ionic Liquids for Biofuel Production: Opportunities and Challenges. *Appl. Energy* **2012**, *92*, 406−414.

(8) Xue, L.; Li, Y.; Zou, F.; Lu, L.; Zhao, Y.; Huang, X.; Qu, Y. The Catalytic Efficiency of Lipase in a Novel Water-in-[Bmim][$PF_6$] Microemulsion Stabilized by Both AOT and Triton X-100. *Colloids Surf., B* **2012**, *92*, 360−366.

(9) Liao, X.; Wang, S.-G.; Xiang, X.; Zhu, Y.; She, X.; Li, Y. $SO_3H$-Functionalized Ionic Liquids as Efficient Catalysts for the Synthesis of Bioadditives. *Fuel Process. Technol.* **2012**, *96*, 74−79.

(10) Kakibe, T.; Hishii, J.-Y.; Yoshimoto, N.; Egashira, M.; Morita, M. Binary Ionic Liquid Electrolytes Containing Organo-Magnesium Complex for Rechargeable Magnesium Batteries. *J. Power Sources* **2012**, *203*, 195−200.

(11) Muthayala, M. K.; Chhikara, B. S.; Parang, K.; Kumar, A. Ionic Liquid-Supported Synthesis of Sulfonamides and Carboxamides. *ACS Comb. Sci.* **2012**, *14*, 60−65.

(12) Wang, X.-S.; Sheng, J.; Lu, L.; Yang, K.; Li, Y.-L. Combinatorial Synthesis of 3-Arylideneaminoquinazolin-4(1*H*)-one Derivatives Catalyzed by Iodine in Ionic Liquids. *ACS Comb. Sci.* **2011**, *13*, 196−199.

(13) Khalafi-Nezhad, A.; Mohammadi, S. Magnetic, Acidic, Ionic Liquid-Catalyzed One-Pot Synthesis of Spirooxindoles. *ACS Comb. Sci.* **2013**, *15*, 512−518.

(14) Huang, Z.; Hu, Y.; Zhou, Y.; Shi, D. Efficient One-Pot Three-Component Synthesis of Fused Pyridine Derivatives in Ionic Liquid. *ACS Comb. Sci.* **2011**, *13*, 45−49.

(15) Ruijter, E.; Scheffelaar, R.; Orru, R. V. A. Multicomponent Reaction Design in the Quest for Molecular Complexity and Diversity. *Angew. Chem., Int. Ed.* **2011**, *50*, 6234−6246.

(16) Bala, B. D.; Balamurugan, K.; Perumal, S. Facile, Four-Component, Domino Reactions for the Regioselective Synthesis of Tetrahydrobenzo[g]quinolines. *Tetrahedron Lett.* **2012**, *52*, 4562−4566.

(17) Pericherla, K.; Khungar, B.; Kumar, A. One-Pot, Three-Component Synthesis of 1-Amidomethyl-imidazo[1,2-*a*]pyridines Catalyzed by Ytterbium Triflate. *Tetrahedron Lett.* **2012**, *53*, 1253−1257.

(18) Sharma, R. K.; Rawat, D.; Gaba, G. Inorganic−Organic Hybrid Silica Based Tin(II) Catalyst: Synthesis, Characterization and Application in One-Pot Three-Component Mannich Reaction. *Catal. Commun.* **2012**, *19*, 31−36.

(19) Muthusaravanan, S.; Perumal, S.; Almansour, A. I. Facile Catalyst-Free Pseudo-Five-Component Domino Reactions in the Expedient Synthesis of 5-Aroyl-1,3-diarylhexahydropyrimidines. *Tetrahedron Lett.* **2012**, *53*, 1144−1148.

(20) Baghernejad, B.; Heravi, M. M.; Oskooie, H. A.; Poormohammad, N.; Khorshidi, M.; Beheshtiha, Y. S. A Novel and Facile Synthesis of *N*-Cyclohexylbenzofurans by One-Pot Three-Component Reaction. *Mol. Diversity* **2011**, *15*, 245−248.

(21) Xu, Z.; Shaw, A. Y.; Nichol, G. S.; Cappelli, A. P.; Hulme, C. Applications of *ortho*-Phenylisonitrile and *ortho*-*N*-BocAniline for the Two-Step Preparation of Novel Bis-Heterocyclic Chemotypes. *Mol. Diversity* **2012**, *16*, 607−612.

(22) Gunawan, S.; Keck, K.; Laetsch, A.; Hulme, C. Synthesis of Peptidomimetics, $\delta$- and $\varepsilon$-Lactam Tetrazoles. *Mol. Diversity* **2012**, *16*, 601−606.

(23) Michael, J. P. Quinoline, Quinazoline and Acridone Alkaloids. *Nat. Prod. Rep.* **2008**, *25*, 166−187.

(24) Balamurugan, K.; Jeyachandran, V.; Perumal, S.; Manjashetty, T. H.; Yogeeswari, P.; Sriram, D. A Microwave-Assisted, Facile, Regioselective Friedländer Synthesis and Antitubercular Evaluation of 2,9-Diaryl-2,3-dihydrothieno-[3,2-*b*]quinolones. *Eur. J. Med. Chem.* **2010**, *45*, 682−688.

(25) Solomon, V. R.; Hag, W.; Srivastava, K.; Puri, S. K.; Katti, S. B. Synthesis and Antimalarial Activity of Side Chain Modified 4-Aminoquinoline Derivatives. *J. Med. Chem.* **2007**, *50*, 394−398.

(26) Doube, D.; Blouin, M.; Brideau, C.; Chan, C.; Desmarais, C.; Ethier, D.; Falgueyret, J. P.; Friesen, R. W.; Girard, M.; Girard, Y.; Guay, J.; Tagari, P.; Young, R. N. Quinolines as Potent 5-Lipoxygenase Inhibitors: Synthesis and Biological Profile of L-746,530. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1255−1260.

(27) Edmont, D.; Rocher, R.; Plisson, C.; Chenault, J. Synthesis and Evaluation of Quinoline Carboxyguanidines as Antidiabetic Agents. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1831−1834.

(28) Kidwai, M.; Bhushan, K. R.; Sapra, P.; Saxena, P. K.; Gupta, R. Alumina-Supported Synthesis of Antibacterial Quinolines Using Microwaves. *Bioorg. Med. Chem.* **2000**, *8*, 69−72.

(29) (a) Kulkarni, A.; Török, B. Microwave-Assisted Multicomponent Domino Cyclization−Aromatization: An Efficient Approach for the Synthesis of Substituted Quinolines. *Green Chem.* **2010**, *12*, 875−878. (b) Lekhok, K. C.; Bhuyan, D.; Prajapati, D.; Boruah, R. C. Zinc Triflate: A Highly Efficient Reusable Catalyst in the Synthesis of Functionalized Quinolines via Friedländer Annulations. *Mol. Diversity* **2010**, *14*, 841−846. (c) Sheykhan, M.; Mámani, L.; Ebrahimi, A.; Heydari, A. Sulfamic Acid Heterogenized on Hydroxyapatite-Encapsulated $\gamma$-$Fe_2O_3$ Nanoparticles as a Magnetic Green Interphase Catalyst. *J. Mol. Catal. A: Chem.* **2011**, *335*, 253−261.

(30) (a) Wang, X.-S.; Jie Zhou, J.; Yin, M.-Y.; Yang, K.; Tu, S.-J. Efficient and Highly Selective Method for the Synthesis of Benzo(naphtho)quinoline Derivatives Catalyzed by Iodine. *J. Comb. Chem.* **2010**, *12*, 266−269. (b) Xiao, F.; Chen, Y.; Liu, Y.; Wang, J. Sequential Catalytic Process: Synthesis of Quinoline Derivatives by $AuCl_3$/CuBr-Catalyzed Three-Component Reaction of Aldehydes, Amines, and Alkynes. *Tetrahedron* **2008**, *64*, 2755−2761.

(31) (a) Xie, H.; Zhu, J.; Chen, Z.; Li, S.; Wu, Y. Synthesis of 2-Trifluoromethyl Quinoline by the Reaction of Fluorinated Imine with Alkyne catalyzed by Indium(III) Triflate. *Synlett* **2010**, 2659−2663. (b) Paolis, O. D.; Teixeira, L.; Török, B. Synthesis of Quinolines by a Solid Acid-Catalyzed Microwave-Assisted Domino Cyclization−Aromatization Approach. *Tetrahedron Lett.* **2009**, *50*, 2939−2942. (c) Cho, C. S.; Ren, W. X.; Yoon, N. S. A Recyclable Copper Catalysis in Modified Friedländer Quinoline Synthesis. *J. Mol. Catal. A: Chem.* **2009**, *299*, 117−120. (d) Bose, D. S.; Idrees, M.; Jakka, N. M.; Rao, J. V. Diversity-Oriented Synthesis of Quinolines via Friedländer Annulation Reaction under Mild Catalytic Conditions. *J. Comb. Chem.* **2010**, *12*, 100−110.

(32) (a) Lin, X.-F.; Cui, S.-L.; Wang, Y.-G. Molecular Iodine-Catalyzed One-Pot Synthesis of Substituted Quinolines from Imines and Aldehydes. *Tetrahedron Lett.* **2006**, *47*, 3127−3130. (b) Wang, X.-S.; Li, Q.; Zhang, M.-M.; Yao, C.-S.; Tu, S.-J. $I_2$-Catalyzed Reactions of Schiff Base and Alkyl Aldehyde towards Benzo[*f*]quinoline Derivatives. *J. Heterocycl. Chem.* **2008**, *45*, 1027−1031.

(33) (a) Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Soltani, M.; Mirjafari, A. One-Pot Synthesis of 2,3-Disubstituted-2,3-dihydroquinazolin-4(1*H*)-ones Using [Hmim][$NO_3$]: An Eco-Friendly Protocol. *J. Heterocycl. Chem.* **2011**, *48*, 1419−1427. (b) Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Anvar, S.; Mirjafari, A. Microwave-Promoted Alkynylation Cyclization of 2-Aminoaryl Ketones: A Green Strategy for the Synthesis of 2,4-Disubstituted Quinolines. *Synlett* **2010**, 3104−3112. (c) Safaei, S.; Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Khavasi, H. R. One-Pot Three-Component Synthesis of Pyrano[3,2-*b*]pyrazolo[4,3-*e*]pyridin-8(1*H*)-ones. *ACS Comb. Sci.* **2013**, *15*, 141−146. (d) Mohammadpoor-Baltork, I.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Mohammadiannejad-Abbasabadi, K.; Khavasi, H. R. $H_3PW_{12}O_{40}$-Catalyzed Alkylation of Arenes and Diveratrylmethanes: Convenient Access to Triarylmethanes, Symmetrical and Unsymmetrical 9,10-Diaryl-2,3,6,7-tetramethoxyanthracenes. *Eur. J. Org. Chem.* **2011**, 1357−1366. (e) Ghanbaripour, R.; Mohammadpoor-Baltork, I.; Moghadam, M.; Khosropour, A. R.; Tangestaninejad, S.; Mirkhani, V. Microwave-Promoted Efficient Conversion of Acetophenones to 1,3,5-Triarylbenzenes Catalyzed by $H_3PW_{12}O_{40}$ and Nano-Silica Supported $H_3PW_{12}O_{40}$ as Reusable Catalysts. *Polyhedron* **2012**, *31*, 721−728.

(34) (a) Akbari, J.; Heydari, A.; Kalhor, H. R.; Azizian Kohan, S. Sulfonic Acid Functionalized Ionic Liquid in Combinatorial Approach, A Recyclable and Water Tolerant-Acidic Catalyst for One-Pot Friedländer Quinoline Synthesis. *J. Comb. Chem.* **2010**, *12*, 137−140. (b) Kumar, A.; Rao, V. K. Microwave-Assisted and $Yb(OTf)_3$-Promoted One-Pot Multicomponent Synthesis of Substituted Quinolines in Ionic Liquid. *Synlett* **2011**, 2157−2162. (c) Abdollahi-Alibeik, M.; Pouriayevali, M. Nanosized MCM-41 Supported Protic Ionic Liquid as an Efficient Novel Catalytic System for Friedländer Synthesis of Quinolines. *Catal. Commun.* **2012**, *22*, 13−18. (d) Sarma, R.; Prajapati, D. Ionic Liquid—An Efficient Recyclable System for the Synthesis of 2,4-Disubstituted Quinolines via Meyer−Schuster Rearrangement. *Synlett* **2008**, 3001−3005.

(35) Kim, Y. J.; Varma, R. S. Microwave-Assisted Preparation of Imidazolium-Based Tetrachloroindate(III) and Their Application in the Tetrahydropyranylation of Alcohols. *Tetrahedron Lett.* **2005**, *46*, 1467−1469.

(36) Earle, M. J.; Hakala, U.; Hardacre, C.; Karkkainen, J.; McAuley, B. J.; Rooney, D. W.; Seddon, K. R.; Thompson, J. M.; Wähälä, K. Chloroindate(III) Ionic Liquids: Recyclable Media for Friedel−Crafts Acylation Reactions. *Chem. Commun.* **2005**, 903−905.

(37) Mirjafari, A.; Mohammadpoor-Baltork, I.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Khosropour, A. R. Microwave-Promoted, One-Pot Conversion of Alkoxymethylated Protected Alcohols into Their Corresponding Nitriles, Bromides, and Iodides using [bmim][$InCl_4$] as a Green Catalyst. *Tetrahedron Lett.* **2010**, *51*, 3274−3276.