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Metal-free, ionic liquid-mediated synthesis of functionalized quinolines

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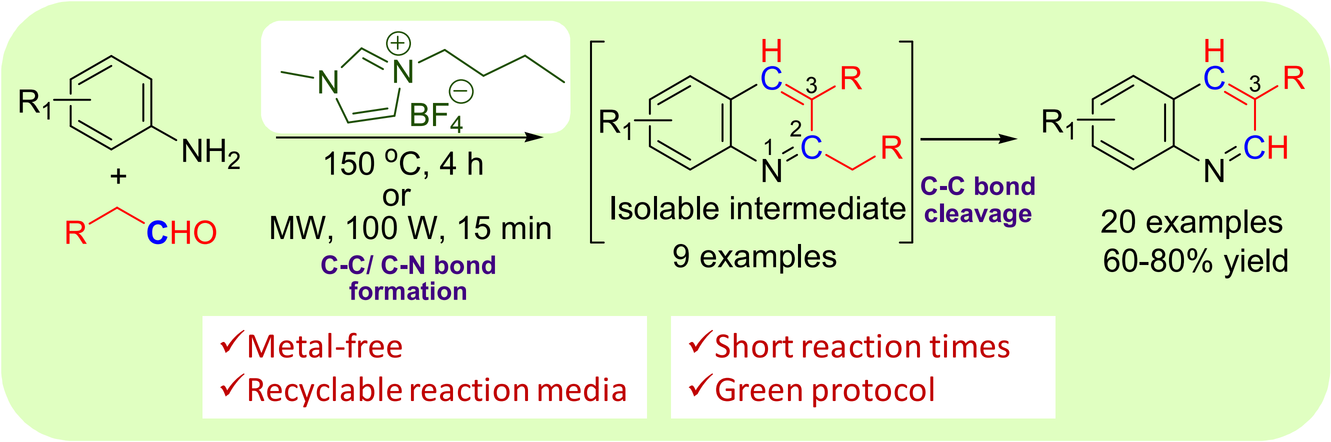
TOC Graphic.



ABSTRACT:

An expedient and metal-free synthetic protocol for construction of substituted quinolines has been developed from anilines and phenylacetaldehydes using imidazolium cation-based ionic liquids as the reaction medium. Mechanistic analysis indicated that the reaction occurs through C-C and C-N bond formation to produce isolable 2,3-disubstituted quinoline intermediates, which undergo C-C bond cleavage to produce 3-substituted quinolines. The reaction proceeds smoothly with a range of functionalities in good to excellent yields. Advantages of this protocol include metal-free, environmentally friendly, recyclable reaction media, higher yields and shorter reaction times, and thus is promising for the efficient combinatorial synthesis of structurally diverse 2,3-disubstituted and 3-substituted quinolines.

KEYWORDS.

Ionic liquids,

metal-free,

quinolines,

heterocycle synthesis,

green chemistry

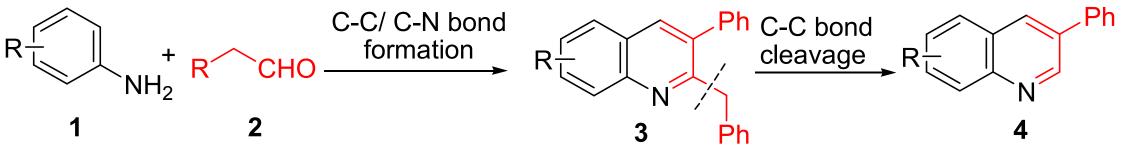
INTRODUCTION

Metal-free synthetic protocols can diminish adverse environmental consequences of many organic reactions.[1-4] Many efforts to establish metal-free reaction conditions uses polar solvents and ionic liquids (ILs), the latter area focusing largely on water-soluble imidazolium cation-based systems.[5-8] ILs have been considered as green solvents due to their properties of high thermal stability, non-flammable nature, immiscibility with a number of organic solvents, negligible vapor pressure, and recyclability.[9, 10] Furthermore, ILs are known to play roles both as solvent and catalyst.[11] For example, 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim]BF_4) has been used in a wide variety of reactions, including synthesis of vic-diamines,[12] Michael reaction,[13] synthesis of 1,4- dihydropyridines,[14] cleavage of ethers,[15] Stille coupling,[16] halogenation of alkenes,[17] olefin metathesis,[18] and Suzuki-Miyaura cross-coupling.[19] The ILs are also widely used in the synthesis of heterocyclic compounds[5, 20, 21] and inorganic materials.[22]

Quinoline is one of the most widely occurring heterocyclic scaffolds in drugs and natural products, possessing a diverse range of pharmacological activities and therefore attracting the continued attention of medicinal and synthetic chemists. Apart from conventional approaches,[23-28] several new methods have been discovered for quinoline synthesis.[29-32] Among these, the condensation of anilines and phenylacetaldehydes provides an elegant approach to substituted quinolines, for which two methods are reported in the literature (Table 1): (a) sulfamic acid catalyzed synthesis of 2,3-disubstituted quinolines (**3**)[33] and (b) $CuBr/CF_3SO_3H$ catalyzed synthesis of 3-substituted quinolines (**4**).[34] In addition to these two reports, there exists another similar approach for synthesis of 3-substituted quinolines **4**, which involves $FeCl_3$-catalyzed condensation of anilines and styrene oxides.[35]

In the present paper, we report a green, facile and efficient metal-free synthesis of 2,3-disubstituted **3** and 3-substituted quinolines **4** through sequential one-pot C-C/C-N bond formation and C-C bond cleavage (entries 3-5, Table 1). The advantages of present protocol include: (a) both 2,3-disubstituted **3** as well as 3-substituted quinolines **4** can be prepared using this reaction; (b) metal-free reaction condition; and (c) recyclable and eco-friendly ionic liquid reaction media.

Table 1. Methods for quinoline synthesis from aniline and phenylacetaldehyde



Sr No	Group	Condition	% yield of **3/4**
1.	Zhang *et al.* (2012)[33]	NH_2SO_3H, 80 °C, 3-5 h	63-86/ 0[a]
2.	Yan *et al.* (2013)[34]	CuBr/ CF_3SO_3H, DMSO, 110 °C	0[b]/45-93
3.	This work	$[Bmim]BF_4$, 150 °C, 4 h	8/78[c]
4.	This work	$[Bmim]BF_4$, 120 °C, MW, 100 W, 15 min	8/ 80[c]
5.	This work	$[Bmim]BF_4$, 110 °C/ 0.5 h	35/50[c]

[a] only product **3** was formed; [b] only product **4** was formed; [c] yields are mentioned for products obtained from 2,3-dimethyl aniline.

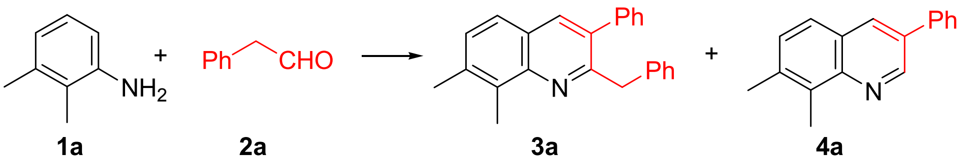
RESULTS AND DISCUSSION

To establish a metal-free protocol for the synthesis of substituted quinolines, we explored the reaction of 2,3-dimethylaniline (**1a**) with phenylacetaldehyde (**2a**) in presence of CuBr and 1-butyl-3-methylimidazolium tetrafluoroborate ionic liquid (as a replacement for CF_3SO_3H and DMSO in the published protocol[34]) at 110 °C (Table 2, entry 1). Gratifyingly, the desired 3-substituted quinoline **4a** was obtained in good yield (entry 1), which was comparable to the Yan method (entry 2).[34] Control reactions without addition of CF_3SO_3H (entry 3) or CuBr (entry 4) established the essential nature of these reagents in the absence of IL. The Lewis acid $FeCl_3$ was an effective replacement for CuBr (giving **4a** in 70% yield, entry 5), and the addition of ionic liquid gave a slightly better result (78% yield, entry 6). Most encouraging, however, was the formation of quinolines **3a** and **4a** in 12% and 70% yields, respectively in the presence of ionic liquid $[Bmim]BF_4$, without the addition of any catalyst or additive (entry 7). Exploration of reaction temperature (entries 7-11) indicated 150 °C as optimal, with no reaction occurring at room temperature. When the reaction time was reduced from 4 h to 30 min, the 2,3-disubstituted quinoline **3a** could be isolated in 35% yield (entry 10). A different ionic liquid, 1-ethyl-

3-methylimidazolium 1,1,2,2-tetrafluoroethane sulfonate ([emim][$CHF_2CF_2SO_3$]), was not successful (entry 12).

Since ILs have ability to absorb microwave energy and convert it into heat, microwave irradiation is an attractive alternative for thermally-driven reactions in these media. Accordingly, the above model reaction was subjected to microwave irradiation (100 W) at 120 °C for 5-15 min (entries 13 and 14), which produced desired product **4a** in 80% yield (entry 14). Thus, the entries 8 and 14 are considered as optimized reaction conditions under conventional heating and microwave irradiation, respectively.

Table 2. Optimization of reaction conditions[a]



Entry	Catalyst	Additive	Reaction medium	Temp. (°C)/ time	Yield[b] (%) **3a**/**4a**
1	CuBr	None	[Bmim]BF_4	110/ 4 h	5/80
2	CuBr	CF_3SO_3H	DMSO	110/ 4 h	5/74
3	CuBr	None	DMSO	110/ 4 h	0/0
4	None	CF_3SO_3H	DMSO	110/ 4 h	0/0
5	$FeCl_3$	None	CH_3CN	110/ 4 h	8/70
6	$FeCl_3$	None	[Bmim]BF_4	110/ 4 h	5/78
7	None	None	[Bmim]BF_4	110/ 4 h	12/70
8[c]	**None**	**None**	**[Bmim]BF_4**	**150/ 4 h**	**8/78**
9	None	None	[Bmim]BF_4	180/ 4 h	8/80
10	None	None	[Bmim]BF_4	110/ 30 min	35/50
11	None	None	[Bmim]BF_4	25/ 4 h	0/0
12	None	None	[Emim][$CHF_2CF_2SO_3$]	110/ 4 h	0/0
13	None	None	[Bmim]BF_4	120, MW, 100 W, 5 min	18/ 48
14[c]	**None**	**None**	**[Bmim]BF_4**	**120, MW, 100 W, 15 min**	**8/ 80**

MW, microwave irradiation; [a] **1a** (1.0 mmol), **2a** (2.0 mmol) and catalyst and/ or additive (wherever mentioned) and solvent; [b] Isolated yields after silica gel column chromatography; [c] bold entries indicates optimized reaction conditions for synthesis of 3-substituted quinolines **4**.

An exploration of aniline and phenylacetaldehyde scope using the conventional optimized reaction conditions (entry 8, Table 2) gave the results shown in Figure 1. Anilines substituted with electron-donating groups (**4a-4e**, **4g-4l**) and electron-withdrawing groups (**4m-4o** and **4s**) each participated well in this reaction. Similarly, non-substituted (**4a-4o**) as well as substituted (**4p-4s**) phenylacetaldehydes produced corresponding quinoline products in good yields. For the latter examples, the corresponding phenylacetaldehydes were prepared from phenyl epoxides by treatment with Zeolite in methylene chloride.[36] The phenylacetaldehydes obtained by evaporation of the solvent were treated directly with anilines and ionic liquid in the same pot to produce the desired quinolines **4p-4s** (Figure 1). In contrast to anilines, cyclohexylamine did not produce the desired product.

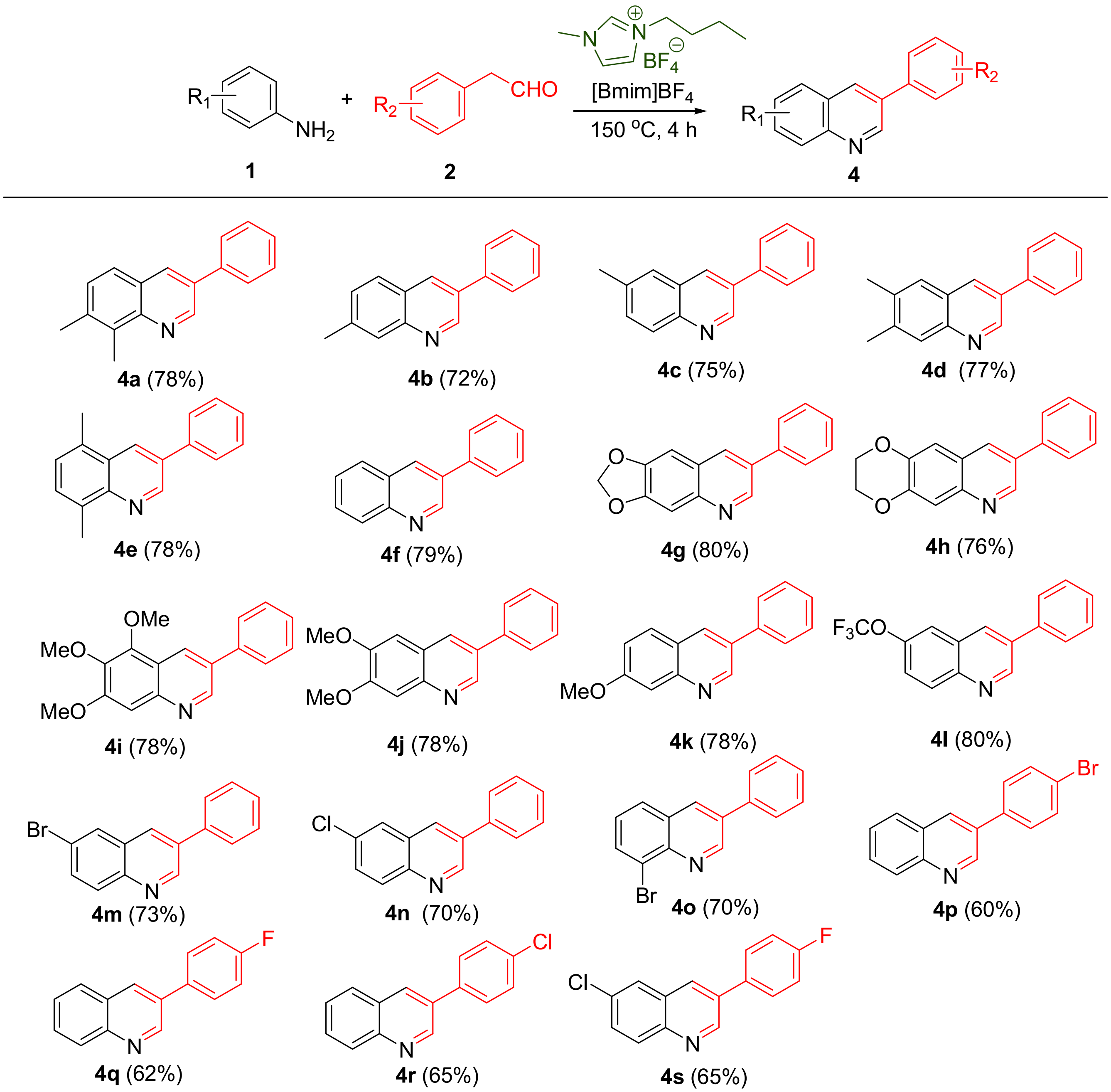


Figure 1. Metal-free synthesis of 3-substituted quinolines in ionic liquid under conventional heating.

Representative aliphatic aldehydes (n-butyraldehyde and phenylpropanal) also proved to be interesting (Figure 2). The 3-substituted quinoline product **4t** was obtained from the reaction of 2-bromoaniline with n-butyraldehyde, which was not possible using Yan and coworkers[34] protocol. However in other cases, 2,3-disubstituted quinolines **3u-x** were obtained. As with CuBr/CF_3SO_3H,[34] the reaction of 3-phenylpropanal **2w** with aniline **1b** using our optimized reaction conditions led to formation of only 2,3-

disubstituted product 3-benzyl-2-phenethylquinoline **3w** (Figure 2). Performing the reaction at 110 °C for 30 min gave both 2,3-disubstituted and 3-mono-substituted products (Table 3). The 2,3-disubstituted quinolines **3a**, **3g-3k** were obtained in 18-45% yields, along with 3-substituted quinolines **4a**, **4g-k** (38-50%).

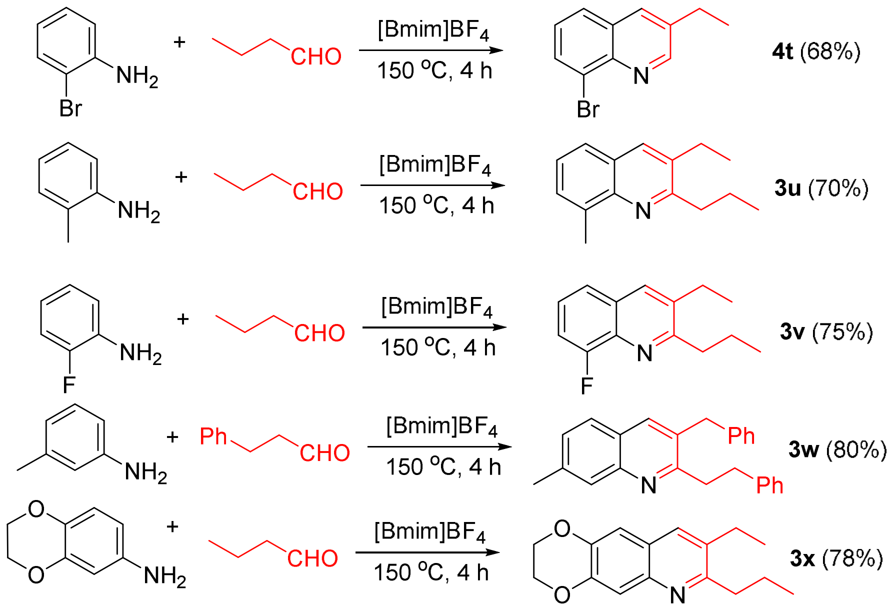
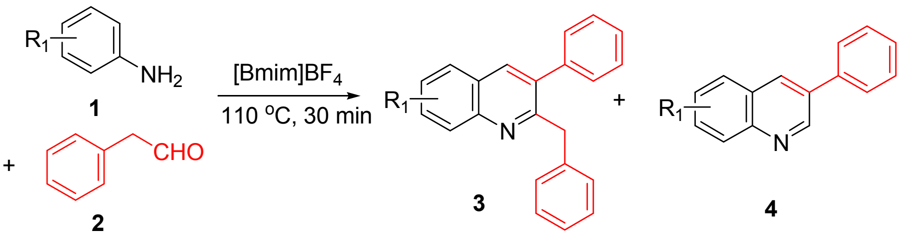
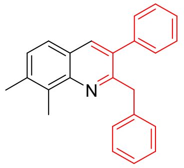
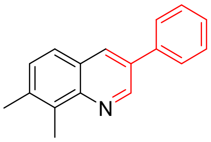
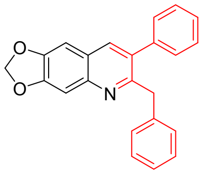
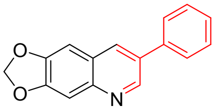
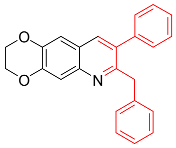
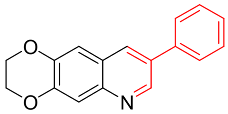
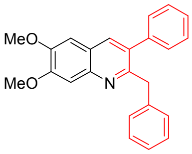
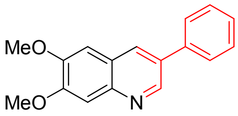
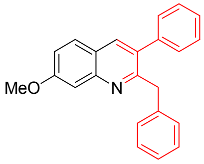
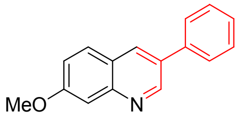


Figure 2. Metal-free synthesis of 3-substituted and 3,4-disubstituted quinolines in ionic liquid

Table 3. Synthesis of mono- and disubstituted quinolines[a]



Entry	Product 3		Product 4	
	Structure	%Yield[b]	Structure	%Yield[b]
1	 **3a**	35	 **4a**	50
2	 **3g**	28	 **4g**	42

3	 **3h**	30	 **4h**	45
4	 **3j**	18	 **4j**	38
5	 **3k**	26	 **4k**	40

[a] aniline **1** (1.0 mmol), phenylacetaldehyde **2** (2.0 mmol) and ionic liquid was heated to reflux at 110 °C for 30 min; [b] Isolated yields after silica gel column chromatography.

The repeated reuse of the ionic liquid reaction medium was investigated using the model reaction between 2,3-dimethyl aniline **1a** and phenylacetaldehyde **2a**. After completion of the reaction, products were extracted with diethyl ether and remaining ionic liquid after drying under reduced pressure was reused for next reaction. The desired product **4a** was obtained in 70, 68, 65 and 62% yield over four cycles, indicating good recyclability of the ionic liquid over several cycles.

Since ILs are known to activate carbonyl groups through hydrogen – bonding, we suggest that [Bmim]BF_4 activates the aldehyde electrophile by interaction with the carbonyl oxygen as illustrated in Figure 3 for the representative reaction of **1a**+**2a**. The ionic liquid [Bmim]BF_4 may also enhance the nucleophilicity of the amine through interaction of tetrafluoroborate with N-H bond. The resulting imine intermediate undergoes self-condensation to generate **3a$_1$** as a key intermediate. This is supported by monitoring of the reaction by LC-ESI-MS at intermittent reaction time (30 min). As shown in Figure 4, 2,3-disubstituted quinoline intermediates **3a$_1$** and **3a$_2$** were observed along with product **4a**. At 4 h reaction time, the ratio of **4a**: **3a$_2$** changed from 37:35 to 70:0, suggesting that **3a$_2$** is a key intermediate in the formation of **4a** (S3 of Supporting Information).

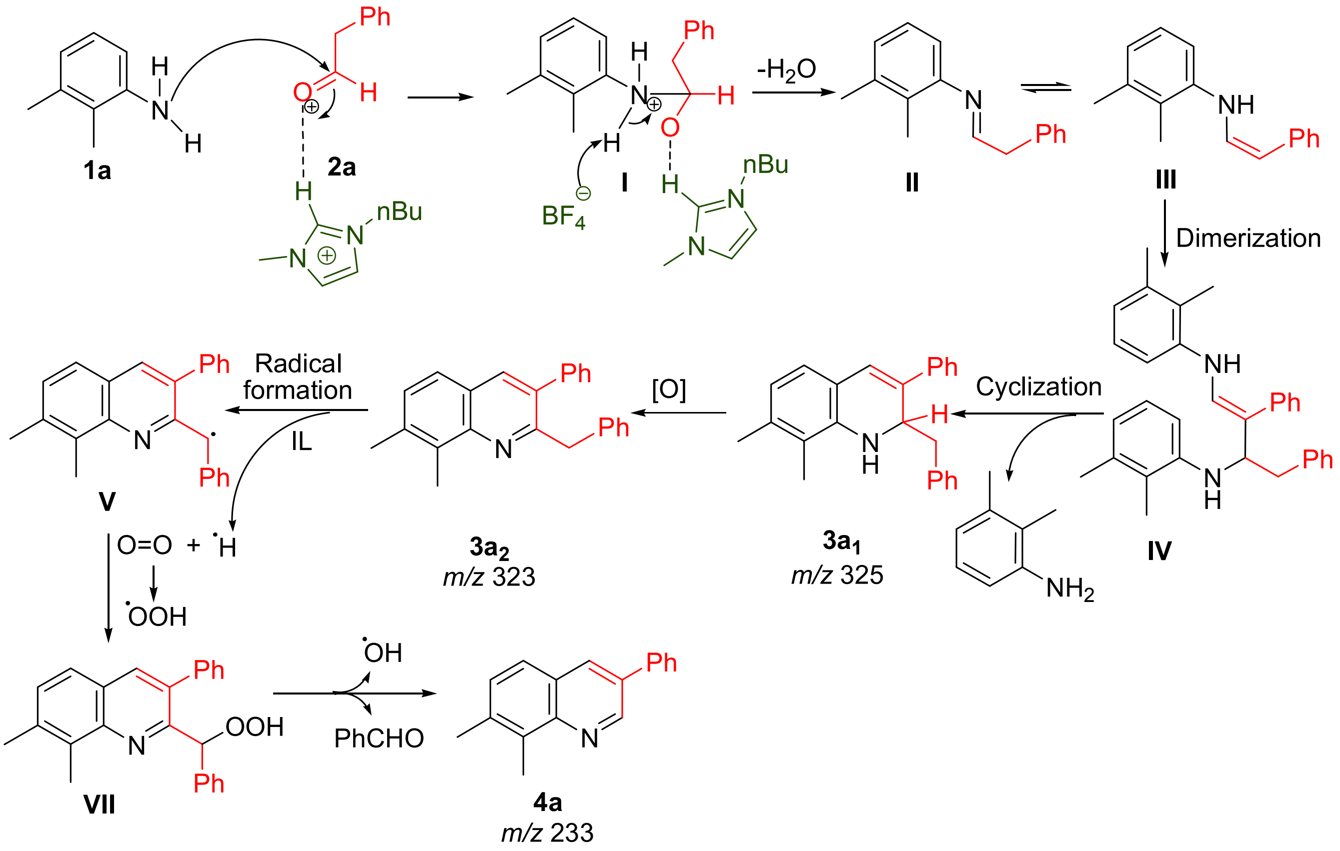


Figure 3. Plausible reaction mechanism showing formation of **3a$_1$** and **3a$_2$** as key intermediates during synthesis of 3-substituted quinoline **4a**.

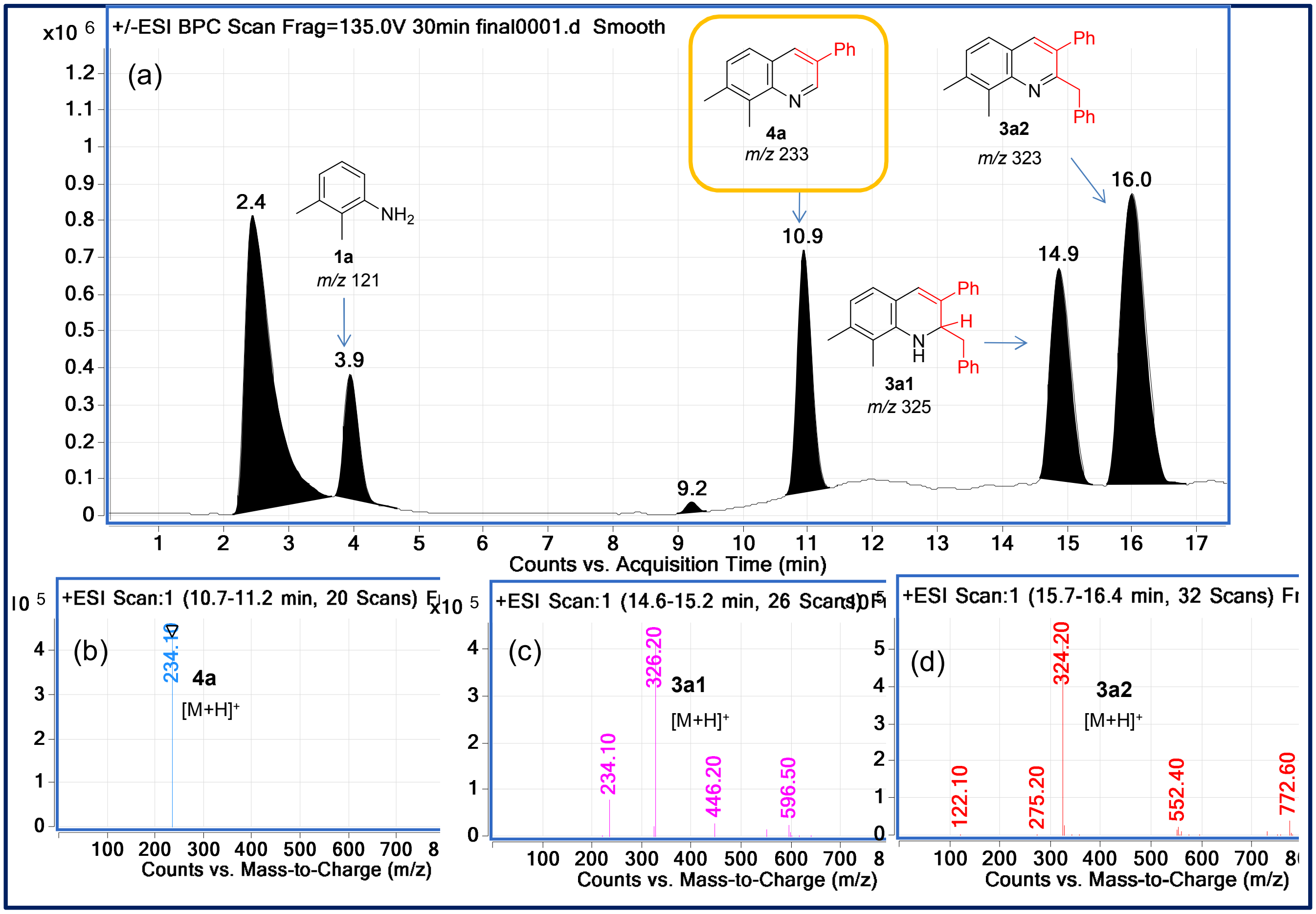


Figure 4. LC-ESI-MS analysis of reaction mixture after 30 min. (a) LCMS chromatogram showing product **4a** and intermediates **3a$_1$** and **3a$_2$**; (b-d). MS chromatograms of peaks appearing at t_R 10.9, 14.9 and 16.0 min, respectively.

The cleavage process that takes **3** to **4** was found to be inhibited by a radical quencher: the reaction of **1a**+**2a** performed in the presence of TEMPO produced **3a$_1$** as the major product with **4a** formed only in trace amounts. In the absence of TEMPO, the cleavage event generates benzaldehyde as a byproduct (seen in TLC). These observations are consistent with the presumed formation of a benzylic radical **V** and hydroperoxide **VII** (Figure 3). Based on the literature precedence,[37, 38] we presume that IL plays a role in generating benzylic radical **V** from intermediate **3a$_2$**; however, the exact mechanism of radical generation is not clearly understood.

In summary, we have found that an ionic solvent allows for the direct synthesis of substituted quinolines without metal catalyst or additive, presumably by functioning both as a Lewis acid and Lewis base. The method is operationally simple and can be used to access both 2,3-disubstituted and 3-substituted quinolines. The ionic liquid [Bmim]BF_4 provides a recyclable and non-volatile medium, simple work-up, and high product yield, and therefore a useful alternative to existing processes for quinoline synthesis.

EXPERIMENTAL PROCEDURES

General optimized procedure for synthesis of 3-substituted quinolines 4a-t. The ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate used in the present study was purchased from Sigma-Aldrich. Although this IL is commercially available, it can be prepared starting from N-methylimidazole.[39] The mixture of aniline (**1**, 1.0 mmol) and phenylacetaldehyde (**2**, 2.0 mmol) in ionic liquid [Bmim]BF_4 (1 mL) was stirred at 150 °C in an oil bath in an open-air atmosphere for 4 h. After completion of the reaction, products were extracted with diethyl ether (50 ml x 3). The remaining ionic liquid was further washed with diethyl ether and dried at 80 °C under reduced pressure, for its reuse. The combined organic layer was evaporated under reduced pressure to give the crude product. Purification by silica gel column chromatography (mesh 100-200) using hexane-EtOAc as eluent gave quinolines **4a-4t** as major products in 60-80% yield. The spectral data for all synthesized quinolines **4a-4t** and **3a-x** is provided in the supporting information.

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Notes

The authors declare no competing financial interest.

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SUPPORTING INFORMATION.

Experimental procedures and NMR spectra of all compounds. This information is available free of charge via the Internet at http://pubs.acs.org/

REFERENCES

(1) Roscales, S.; Csákÿ, A. G. Transition-metal-free C-C bond forming reactions of aryl, alkenyl and alkynylboronic acids and their derivatives. *Chem. Soc. Rev.* **2014**, DOI: 10.1039/C4CS00195H.

(2) van Berkel, S. S.; van Delft, F. L. Metal-free bioconjugation reactions. *Drug Discov. Today Technol.* **2013,** 10, e45-51.

(3) Melone, L.; Punta, C. Metal-free aerobic oxidations mediated by N-hydroxyphthalimide. A concise review. *Beilstein J. Org. Chem.* **2013,** 9, 1296-1310.

(4) Rawling, M. J.; Tomkinson, N. C. Metal-free syn-dioxygenation of alkenes. *Org. Biomol. Chem.* **2013,** 11, 1434-1440.

(5) Isambert, N.; Sanchez Duque Mdel, M.; Plaquevent, J. C.; Genisson, Y.; Rodriguez, J.; Constantieux, T. Multicomponent reactions and ionic liquids: a perfect synergy for eco-compatible heterocyclic synthesis. *Chem. Soc. Rev.* **2011,** 40, 1347-1357.

(6) Allen, C. L.; Williams, J. M. J. Metal-catalysed approaches to amide bond formation. *Chem. Soc. Rev.* **2011,** 40, 3405–3415.

(7) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. Ionic liquid (molten salt) phase organometallic catalysis. *Chem. Rev.* **2002,** 102, 3667-3692.

(8) Lee, S.-g. Functionalized imidazolium salts for task-specific ionic liquids and their applications. *Chem. Commun.* **2006**, 1049-1063.

(9) Hubbard, C. D.; Illner, P.; Eldik, R. v. Understanding chemical reaction mechanisms in ionic liquids: successes and challenges. *Chem. Soc. Rev.* **2011,** 40, 272–290.

(10) Petkovic, M.; Seddon, K. R.; Rebelo, L. P. N.; Pereira, C. S. Ionic liquids: a pathway to environmental acceptability. *Chem. Soc. Rev.* **2011,** 40, 1383–1403.

(11) Boon, J. A.; Levisky, J. A.; Pflug, J. L.; Wilkes, J. S. Friedel-Crafts reactions in ambient-temperature molten salts. *J. Org. Chem.* **1986,** 51, 480-483.

(12) Yadav, J. S.; Reddy, B. V. S.; Premalatha, K. 1-Butyl-3-methylimidazolium tetrafluoroborate ([Bmim]BF4) ionic liquid: A novel and recyclable reaction medium for the synthesis of vic-diamines. *Adv. Synth. Catal.* **2003,** 345, 948-952.

(13) Dell'Anna, M. M.; Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Romanazzi, G.; Suranna, G. P. Metal catalysed Michael additions in ionic liquids. *Chem. Commun.* **2002**, 434-435.

(14) Yadav, J. S.; Reddy, B. V. S.; Basak, A. K.; Narsaiah, A. V. Three-component coupling reactions in ionic liquids: an improved protocol for the synthesis of 1,4-dihydropyridines. *Green Chem.* **2003,** 5, 60–63.

(15) Boovanahalli, S. K.; Kim, D. W.; Chi, D. Y. Application of ionic liquid halide nucleophilicity for the cleavage of ethers: A green protocol for the regeneration of phenols from ethers. *J. Org. Chem.* **2004,** 69, 3340-3344.

(16) Handy, S. T.; Zhang, X. Organic synthesis in ionic liquids: The Stille coupling. *Org. Lett.* **2001,** 3, 233-236.

(17) Chiappe, C.; Capraro, D.; Conte, V.; Pieraccini, D. Stereoselective halogenations of alkenes and alkynes in ionic liquids. *Org. Lett.* **2001,** 3, 1061-1063.

(18) Mayo, K. G.; Nearhoof, E. H.; Kiddle, J. J. Microwave-accelerated ruthenium-catalyzed olefin metathesis. *Org. Lett.* **2002,** 4, 1567-1570.

(19) Revell, J. D.; Ganesan, A. Ionic liquid acceleration of solid-phase Suzuki-Miyaura cross-coupling reactions. *Org. Lett.* **2002,** 4, 3071-3073.

(20) Martins, M. A.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. Ionic liquids in heterocyclic synthesis. *Chem. Rev.* **2008,** 108, 2015-50.

(21) Zakrzewska, M. E.; Bogel-Łukasik, E.; Bogel-Łukasik, R. Ionic liquid-mediated formation of 5-hydroxymethylfurfurals: A Promising biomass-derived building block. *Chem. Rev.* **2011,** 111, 397–417.

(22) Hasan, M.; Kozhevnikov, I. V.; Siddiqui, M. R.; Femoni, C.; Steiner, A.; Winterton, N. N,N'-dialkylimidazolium chloroplatinate(II), chloroplatinate(IV), and chloroiridate(IV) salts and an N-heterocyclic carbene complex of platinum(II): synthesis in ionic liquids and crystal structures. *Inorg. Chem.* **2001,** 40, 795-800.

(23) Knorr, L. Synthetische versuche mit dem acetessigester. *Eur. J. Org. Chem.* **1886,** 236, 69-115.

(24) Jia, C.-S.; Zhang, Z.; Tu, S.-J.; Wang, G.-W. Rapid and efficient synthesis of poly-substituted quinolines assisted by p-toluene sulphonic acid under solvent-free conditions: comparative study of microwave irradiation versus conventional heating. *Org. Biomol. Chem.* **2006,** 4, 104-110.

(25) Staskun, B. The conversion of benzoylacetanilides into 2- and 4-hydroxyquinolines. *J. Org. Chem.* **1964,** 29, 1153–1157.

(26) Born, J. L. Mechanism of formation of benzo[g]quinolones via the Combes reaction. *J. Org. Chem.* **1972,** 37, 3952–3953.

(27) Doebner, O.; Miller, W. v. Ueber eine dem chinolin homologe base. *Ber.* **1881,** 14, 2812–2817.

(28) Denmark, S. E.; Venkatraman, S. On the mechanism of the Skraup−Doebner−Von Miller quinoline synthesis. *J. Org. Chem.* **2006,** 71, 1668–1676.

(29) Bharate, J. B.; Wani, A.; Sharma, S.; Reja, S. I.; Kumar, M.; Vishwakarma, R. A.; Kumar, A.; Bharate, S. B. Synthesis, antioxidant, neuroprotective and p-glycoprotein induction activity of 4-arylquinoline-2-carboxylates. *Org. Biomol. Chem.* **2014,** 12, 6267-6277.

(30) Ali, S.; Zhu, H.-T.; Xia, X.-F.; Ji, K.-G.; Yang, Y.-F.; Song, X.-R.; Liang, Y.-M. Electrophile-driven regioselective synthesis of functionalized quinolines. *Org. Lett.* **2011,** 13, 2598–2601.

(31) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Moreno-Manas, M.; Vallribera, A. The [(E,E,E)-1,6,11-tris(p-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) complex in the hydroarylation of alkynes in ionic liquids. An approach to quinolines. *Tetrahedron Lett.* **2002,** 43, 5537–5540.

(32) Khong, S.; Kwon, O. One-pot phosphine-catalyzed syntheses of quinolines. *J. Org. Chem.* **2012,** 77, 8257-8267.

(33) Zhang, M.; Xiong, B.; Yang, W.; Kumar, D. N. T.; Ding, Y.-Q. Facile one-pot synthesis of polysubstituted quinolines under solvent-free conditions using sulfamic acid as a reusable catalyst. *Monatsh Chem.* **2012,** 143, 471–478.

(34) Yan, R.; Liu, X.; Pan, C.; Zhou, X.; Li, X.; Kang, X.; Huang, G. Aerobic synthesis of substituted quinoline from aldehyde and aniline: copper-catalyzed intermolecular C-H active and C-C formative cyclization. *Org. Lett.* **2013,** 15, 4876-4879.

(35) Zhang, Y.; Wang, M.; Li, P.; Wang, L. Iron-promoted tandem reaction of anilines with styrene oxides via C-C cleavage for the synthesis of quinolines. *Org. Lett.* **2012,** 14, 2206–2209.

(36) Smith, K.; El-Hiti, G. A.; Al-Shamali, M. Rearrangement of epoxides to carbonyl compounds in the presence of reusable acidic zeolite catalysts under mild conditions. *Catal. Lett.* **2006,** 109, 77-82.

(37) Marcinek, A.; Zielonka, J.; Geübicki, J.; Gordon, C. M.; Dunkin, I. R. Ionic liquids: Novel media for characterization of radical ions. *J. Phys. Chem. A* **2001,** 105, 9305-9309.

(38) Ernst, S.; Norman, S. E.; Hardacre, C.; Compton, R. G. The electrochemical reduction of 1-bromo-4-nitrobenzene at zinc electrodes in a room temperature ionic liquid: a facile route for the formation of arylzinc compounds. *Phys. Chem. Chem. Phys.* **2014,** 16, 4478-4482.

(39) Dupont, J.; Consorti, C. S.; Suarez, P. A. Z.; de Souza, R. F. Preparation of 1-butyl-3-methyl imidazolium-based room temperature ionic liquids. *Org. Synth.* **2002,** 79, 236.