Tetrahedron 65 (2009) 8507–8512

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Recyclable catalytic synthesis of substituted quinolines: copper-catalyzed heterocyclization of 1-(2-aminoaryl)-2-yn-1-ols in ionic liquids

Bartolo Gabriele [a,*], Raffaella Mancuso [b], Elvira Lupinacci [b], Rosella Spina [b], Giuseppe Salerno [b], Lucia Veltri [b], Angela Dibenedetto [c]

[a] Dipartimento di Scienze Farmaceutiche, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy
[b] Dipartimento di Chimica, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy
[c] Dipartimento di Chimica, Università di Bari, 70126 Bari, Italy

ARTICLE INFO

Article history:
Received 22 May 2009
Received in revised form 22 July 2009
Accepted 7 August 2009
Available online 11 August 2009

ABSTRACT

A convenient and simple approach for the recyclable catalytic synthesis of substituted quinolines is presented. The method is based on $CuCl_2$-catalyzed heterocyclization of readily available 1-(2-aminoaryl)-2-yn-1-ols in $BmimBF_4$ as the solvent at 100 °C for 15–24 h. The solvent–catalyst system could be successfully recycled up to six times without significant loss of activity.

1. Introduction

Ionic liquids (ILs) are now a well-established class of non-conventional reaction media, which present several useful characteristics: they are stable, non-flammable, non-volatile, recyclable, and in several cases may even promote organic reactions.[1,2] Another attractive facet of these solvents is related to the possibility to easily separate the products from the reaction mixture (by simple extraction procedures) and, in catalytic reactions, to recycle the solvent–catalytic system several times.[1,2]

We have very recently reported that 1-(2-aminoaryl)-2-yn-1-ols **2**, easily obtained by the Grignard reaction between the appropriate alkynylmagnesium bromide and 2-aminoaryl ketones **1**, can undergo a selective Cu- or Pd-catalyzed 6-*endo*-*dig* dehydrative heterocyclization to give substituted quinolines **3** in good yields, according to Scheme 1.[3,4] The crude substrates **2** could be used without further purification for the subsequent step. Heterocyclizations were typically carried out in MeOH or 1,2-dimethoxyethane (DME) as the solvent at 100 °C in the presence of $CuCl_2$ (2 mol %) or PdX_2 (2 mol %) in conjunction with an excess of KX (X=Cl, I) as the catalyst.

We have now found that this reaction can also effectively take place in ionic liquids as the reaction media, using 1–2 mol % of $CuCl_2$, and that the solvent–catalyst system can be conveniently recycled several times without appreciable loss of catalytic activity.

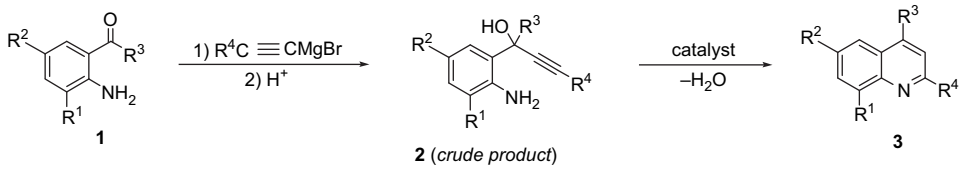
2. Results and discussion

The first experiments were carried out using 2-(2-aminophenyl)oct-3-yn-2-ol **2aa** (R^1=R^2=H, R^3=Me, R^4=Bu) as the substrate. The reaction of **2aa**, carried out in $BmimBF_4$ (1-butyl-3-methylimidazolium tetrafluoroborate) as the solvent in the presence of $CuCl_2$ (2 mol %) at 100 °C for 15 h, led to the formation of 2-butyl-4-methylquinoline **3aa** in 71% isolated yield based on starting 2-aminoacetophenone **1a** (Table 1, Entry 1, Run 1).[5] This result was very promising, since showed that the heterocyclodehydration reaction could indeed occur in an ionic liquid as the solvent. We then verified the possibility to recycle the solvent–catalyst: the reaction crude was extracted several times with Et_2O, in order to separate the product, while freshly prepared **2aa** was added to the ionic liquid phase, and the resulting mixture let to react again under the above-mentioned conditions (see the Experimental Section for details). As can be seen from the results shown in Table 1, Entry 1, Runs 2–7, no significant decrease of activity was observed, even after the sixth recycle.

The reaction carried out with 1 mol % of catalyst, led, after 15 h, to a mixture of **3aa** (66% yield) and the enynic derivative **4aa** (7%), deriving from dehydration of the alcoholic function of the substrate (Table 1, Entry 2, Run 1). Similar results were obtained after 4 recycles (Table 1, Entry 2, Runs 2–5). We have verified that **4aa** can be a possible intermediate in the formation of **3aa**: in fact, when pure **4aa** was let to react under the same reaction conditions as those reported in Table 1 (Entry 2), **3aa** was obtained in 95% isolated yield. In agreement with this result, when the reaction of Entry 2 was carried out for 24 h rather than 15 h, no formation of **4aa** was observed, and the yield of **3aa** increased to 76% (Table 1, Entry 3, Run 1). It is worth noting that the yield obtained under these conditions is

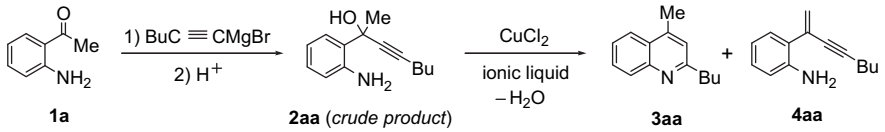
* Corresponding author.
E-mail address: b.gabriele@unical.it (B. Gabriele).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.08.017



Scheme 1. Heterocyclodehydration of 1-(2-aminoaryl)-2-yn-1-ols **2** (crude products obtained by alkynylation of 2-aminoaryl ketones **1**) leading to quinolines **3**.

Table 1
Reactions of 2-(2-aminophenyl)oct-3-yn-2-ol **2aa** in different ionic liquids (ILs) in the presence of $CuCl_2$ as the catalyst[a]

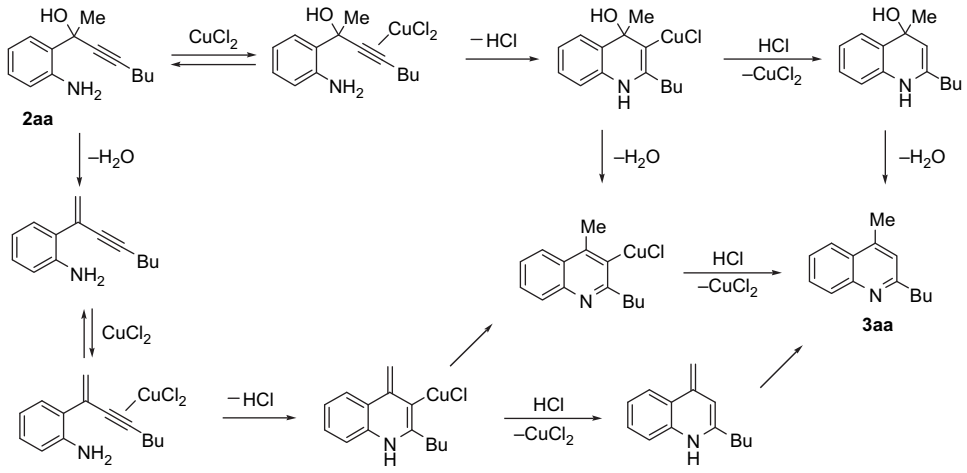


Entry	Solvent	Mol % of $CuCl_2$[b]	Time (h)	Run[c]	Yield of **3aa** (%)[d]	Yield of **4aa** (%)[d]
1	$BmimBF_4$	2	15	1	71	
				2	74	
				3	70	
				4	69	
				5	70	
				6	71	
				7	70	
2	$BmimBF_4$	1	15	1	66	7
				2	65	5
				3	63	5
				4	64	5
				5	66	4
3	$BmimBF_4$	1	24	1	76	
				2	70	
				3	71	
				4	69	
				5	68	
				6	72	
				7	68	
4	$BmimNTf_2$	1	24	1	65	
				2	62	
				3	61	
				4	61	
				5	55	
				6	50	
				7	49	
5	BmimOTf	1	24	1	51	
				2	48	
				3	54	
				4	53	
				5	58	
				6	56	
				7	55	
6	BmimCl	1	24	1	48	17
				2	40	16
				3	38	15
				4	42	18
				5	43	20
7	$BmimPF_6$	1	24	1	82	
				2	76	
				3	67	6
				4	59	10
				5	60	11
				6	56	11
				7	48	18

[a] All reactions were carried out at 100 °C in the given ionic liquid as the solvent (0.22 mmol of starting 2-aminoacetophenone **1a** per mL of solvent, 1 mmol scale based on **1a**). Conversion of **2aa** was quantitative in all cases.
[b] Mol % of $CuCl_2$ with respect to starting **1a**.
[c] Run 1 corresponds to the first experiment, the next runs to recycles. See text for details.
[d] Isolated yield based on starting **1a**.

similar to that observed in MeOH as the solvent (80%), which, however, was obtained using 2 mol % of $CuCl_2$.

We then tested the effect of the nature of the ionic liquid on reactivity. The results using $BmimNTf_2$, BmimOTf, BmimCl, and $BmimPF_6$ are shown in Table 1, Entries 4–7. As can be seen, among the LIs tested, $BmimBF_4$ led to the most satisfactory results: in particular, $BmimNTf_2$ and BmimOTf consistently led to lower yields of quinoline **3aa** with respect to that achieved with $BmimBF_4$ (compare Entries 4 and 5 with Entry 3). In the case of BmimCl, the main product **3aa** was obtained in a mixture with **4aa** (Entry 6). With $BmimPF_6$, the yields



Scheme 2. Proposed reaction mechanism for the conversion of 2-(2-aminophenyl)oct-3-yn-2-ol **2aa** and 2-(1-methylenehept-2-ynyl)aniline **4aa** into 2-butyl-4-methylquinoline **3aa**.

in the first two runs (Table 1, Entry 7, Runs 1–2) were higher with respect to those observed with $BmimBF_4$ (Table 1, Entry 3, Runs 1–2). However, starting from the third recycle, the reaction led to a mixture of **3aa** and **4aa** (Table 1, Entry 7, Runs 3–7).

A plausible reaction mechanism for the formation of **3aa** from **2aa** or **4aa** is shown in Scheme 2. The key steps of the mechanism involve the 6-*endo*-*dig* nucleophilic attack of the amino group to the triple bond of **2aa** or **4aa** coordinated to $CuCl_2$, followed by protonolysis and aromatization or vice versa.

The next experiments, aimed at generalizing the process to the use of variously substituted 1-(2-aminoaryl)-2-yn-1-ols, were therefore carried out using $BmimBF_4$ as the solvent, under the same conditions as those of Entry 3, Table 1. The results obtained with substrates bearing different substituents on the triple bond, at the benzylic position, and on the phenyl ring are shown in Table 2. As can be seen, the corresponding quinolines were consistently obtained in good yields, and in all cases the ionic liquid containing the catalyst could be recycled and reused up to six times without significant loss of activity. In some cases, the reaction led to better results working with 2 mol % of $CuCl_2$ rather than 1 mol % (Entries 9, 14, and 15). In the case of 2-(2-aminophenyl)-4-trimethylsylanylbut-3-yn-2-ol **2ac** (R^1=R^2=H, R^3=Me, R^4=TMS), as we already observed in the process carried out in DME,[3] the TMS group was lost in the course of the process (Entries 13–14).

3. Conclusion

In conclusion, we have shown that the $CuCl_2$-catalyzed heterocyclodehydration of 1-(2-aminoaryl)-2-yn-1-ols may efficiently take place in an ionic liquid, such as $BmimBF_4$, as the reaction medium. The yields obtained in $BmimBF_4$ are similar to those obtained under the 'classical' conditions (in MeOH or DME as the solvent)[3]; however, the use of the ionic liquid has allowed to recycle the solvent–catalytic system several times, without appreciable loss of activity. The present recyclable catalytic method for synthesis of substituted quinolines thus represents a simple and convenient approach for the production of a very interesting class of heterocyclic compounds, whose importance in various fields of Science is well known.[6–9]

4. Experimental section

4.1. General

Melting points were determined with a Reichert Thermovar apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Bruker DPX Avance 300 spectrometer in $CDCl_3$ solutions at 300 MHz and 75 MHz, respectively, with Me_4Si as internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. IR spectra were taken with a Jasco FT-IR 4200 spectrometer. Mass spectra were obtained using a Shimadzu QP-2010 GC–MS apparatus at 70 eV ionization voltage. Microanalyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. All reactions were analyzed by TLC on silica gel 60 F254 and by GLC using a Shimadzu GC-2010 gas chromatograph and capillary columns with polymethylsilicone+5% phenylsilicone as the stationary phase (HP-5). Column chromatography was performed on silica gel 60 (Merck, 70–230 mesh).

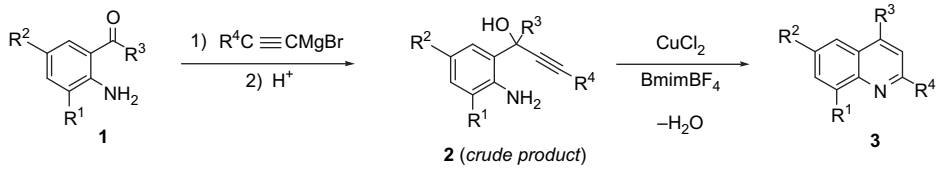
4.2. Preparation of substrates and ionic liquids

2-Aminoacetophenone **1a** and 2-aminobenzophenone **1d** were commercially available (Aldrich, Fluka) and were used as received. 2-Amino-3-methoxyacetophenone **1b** and 2-amino-5-chloroacetophenone **1c** were prepared as we already reported.[3] Ionic liquids $BmimNTf_2$,[10] BmimOTf[11] were prepared according to literature procedures. All the other ionic liquids were prepared as described below.

4.3. Preparation of BmimCl

A mixture of 1-methylimidazole (40 mL, 41.2 g, 502 mmol) and toluene (50 mL) maintained at 0 °C under nitrogen was stirred for 10 min. 1-Chlorobutane (58 mL, 51.4 g, 555 mmol) was quickly added at 0 °C and the resulting mixture was vigorously stirred for 15 min at the same temperature. The solution was allowed to warm up to room temperature and then heated at 110 °C for 24 h with stirring. After cooling to room temperature, the mixture was refrigerated (−20 °C) and allowed to stand for 24 h. After this time, two phases separated; toluene was removed by decantation, while the residue was taken up with MeCN. The solvent was removed under vacuum and MeCN (ca. 30 mL) and THF (ca. 30 mL) were added. The resulting mixture was cooled with the aid of an ice-water bath, to give, on standing, BmimCl as a whitish solid. The mixture was then cooled at −20 °C overnight. After decantation and removal of the solvent, the residue was washed with cold THF and eventually dried in vacuo to give pure BmimCl as a whitish solid, which was stored at −20 °C under nitrogen (77.6 g, 89%).

Table 2
Synthesis of quinolines **3** by heterocyclization $CuCl_2$-catalyzed of 1-(2-aminoaryl)-2-yn-1-ols **2** in $BmimBF_4$[a]



Entry	1	R^1	R^2	R^3	R^4	2	Mol % of $CuCl_2$[b]	3	Run[c]	Yield of 3 (%)[d]
8	**1b**	OMe	H	Me	Bu	**2ba**	1	**3ba**	1	46[e]
9	**1b**	OMe	H	Me	Bu	**2ba**	2	**3ba**	1	73
									2	66
									3	68
									4	66
									5	65
									6	66
									7	66
10	**1c**	H	Cl	Me	Bu	**2ca**	1	**3ca**	1	71
									2	69
									3	66
									4	65
									5	66
									6	65
									7	65
11[f]	**1d**	H	H	Ph	Bu	**2da**	1	**3da**	1	81
									2	81
									3	75
									4	83
									5	79
									6	76
									7	75
12	**1a**	H	H	Me	*t*-Bu	**2ab**	1	**3ab**	1	70
									2	68
									3	62
									4	60
									5	63
									6	61
									7	61
13	**1a**	H	H	Me	TMS	**2ac**	1	**3ac**[g]	1	57[h]
14	**1a**	H	H	Me	TMS	**2ac**	2	**3ac**[g]	1	61
									2	59
									3	60
									4	58
									5	60
									6	61
									7	61
15	**1d**	H	H	Ph	Ph	**2dd**	2	**3dd**	1	60
									2	58
									3	57
									4	55
									5	51
									6	50
									7	52

[a] Unless otherwise noted, all reactions were carried out at 100 °C for 24 h in $BmimBF_4$ as the solvent (0.22 mmol of starting 2-aminoaryl ketones **1** per mL of solvent, 1 mmol scale based on **1**). Conversion of **2** was quantitative in all cases.
[b] Mol % of $CuCl_2$ with respect to starting **1**.
[c] Run 1 corresponds to the first experiment, the next runs to recycles. See text for details.
[d] Isolated yield based on starting **1**.
[e] The reaction also led to the formation of 2-methoxy-6-(1-methylenehept-2-ynyl)aniline **4ba** in 9% isolated yield.
[f] Reaction time was 15 h.
[g] R^4=H in the final quinoline **3ac**.
[h] The reaction also led to the formation of 2-(1-methylene-3-trimethylsilanylprop-2-ynyl)aniline **4ac** in 18% isolated yield.

4.4. Preparation of $BmimBF_4$

$NaBF_4$ (5.7 g, 51.9 mmol) was added to 9.0 g (51.8 mmol) of BmimCl maintained at 80 °C under vigorous stirring. The mixture was allowed to stir at 80 °C for 8 h and then at room temperature for 15 h. CH_2Cl_2 (ca. 30 mL) was added with stirring, and the solution was cooled to −20 °C and allowed to stand at this temperature overnight. The precipitate (NaCl) was removed by filtration, and the solvent was removed under vacuum to give pure $BmimBF_4$, which was stored under nitrogen at room temperature (9.3 g, 80%).

4.5. Preparation of $BmimPF_6$

KPF_6 (9.5 g, 51.6 mmol) was added to 9.0 g (51.8 mmol) of BmimCl maintained at 80 °C under vigorous stirring. The mixture was allowed to stir at 80 °C for 8 h and then at room temperature for 15 h. CH_2Cl_2 (ca. 30 mL) was added with stirring, and the solution was cooled to −20 °C and allowed to stand at this temperature overnight. The precipitate (KCl) was removed by filtration, and the solvent was removed under vacuum to give pure $BmimPF_6$, which was stored under nitrogen at room temperature (11.8 g, 81%).

4.6. General procedure for the synthesis of quinolines 3 in ionic liquids (Tables 1 and 2)

To a suspension of Mg turnings (700.0 mg, 28.8 mmol) in anhydrous THF (2.0 mL), maintained under nitrogen and under reflux, was added pure EtBr (0.5 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise (ca. 20 min) in THF solution (1.5 mL of EtBr in 15.0 mL of THF; total amount of EtBr added: 2.92 g, 26.8 mmol). The mixture was then allowed to reflux for additional 20 min. After cooling, the solution of EtMgBr thus obtained was transferred under nitrogen to a dropping funnel and was added dropwise to a solution of the 1-alkyne (26.8 mmol) in anhydrous THF (7.0 mL) at 0 °C with stirring. After additional stirring at 0 °C for 15 min, the mixture was allowed to warm up to room temperature, maintained at 50 °C for 2 h, and then used as such for the next step. 2-Amino ketone **1** (8.9 mmol) was dissolved under nitrogen in anhydrous THF (7.0 mL) and then added dropwise to the solution of the alkynylmagnesium bromide in THF (prepared as described above) at 50 °C under nitrogen. After stirring at 50 °C for 1 h (R^1=R^2=H, R^3=Me, R^4=Bu; R^1=OMe, R^2=H, R^3=Me, R^4=Bu; R^1=H, R^2=Cl, R^3=Me, R^4=Bu), 2 h (R^1=R^2=H, R^3=Me, R^4=*t*-Bu; R^1=R^2=H, R^3=Me, R^4=TMS), or 3 h (R^1=R^2=H, R^3=Ph, R^4=Bu; R^1=R^2=H, R^3=R^4=Ph), the mixture was cooled to room temperature. Saturated NH_4Cl was added with stirring to achieve a weakly acidic pH. After additional stirring at room temperature for 15 min, AcOEt (ca. 20 mL) was added and phases were separated. The aqueous phase was extracted with AcOEt (3×30 mL), and the collected organic layers were washed with brine to neutral pH and eventually dried over Na_2SO_4. After filtration, the solvent was evaporated and crude products **2** were diluted with Et_2O and transferred into a volumetric flask (50 mL). 6.2 mL of the solution (formally deriving from 1.10 mmol of **1**) were transferred under nitrogen to a Schlenk flask containing the ionic liquid (5.0 mL) and $CuCl_2$ (1.5 mg, 1.1×10^{-2} mmol, Tables 1 and 2, Entries 2–8, 10–13, or 3.0 mg, 2.2×10^{-2} mmol, Tables 1 and 2, Entries 1, 9, 14, 15). Et_2O was removed under vacuum, and the resulting mixture was heated at 100 °C for 15 h (Entry 1, 2, 11) or 24 h (3–10, 12–15). After cooling, the product was extracted with Et_2O (6×4 mL), and the residue (still containing the catalyst dissolved in the ionic liquid) was used as such for the next recycle (see below). The collected ethereal phases were concentrated and the product purified by column chromatography (SiO_2, hexane/AcOEt from 99:1 to 95:5) to give pure quinolines **3**. In the case of the reactions also leading to the formation of enynes **4** (Entry 2, 6–8, 13), the order of elution was **4**, **3**. The isolated yields obtained in each experiment are reported in Tables 1and 2.

4.7. Recycling procedure (Tables 1 and 2)

To the residue obtained as described above, still containing the catalyst dissolved in the ionic liquid, were added 6.2 mL of the ethereal solution containing crude **2**. Et_2O was removed under vacuum, and then the same procedure described above was followed.

4.8. Conversion of 2-(1-methylenehept-2-ynyl)aniline 4aa into 2-butyl-4-methylquinoline 3aa

A solution of pure **4aa** (297.0 mg, 1.49 mmol) in Et_2O (3.0 mL) was transferred under nitrogen to a Schlenk flask containing $BmimBF_4$ (6.8 mL) and $CuCl_2$ (2.0 mg, 1.5×10^{-2} mmol). Et_2O was removed under vacuum, and the resulting mixture was heated at 100 °C for 15 h. After cooling, the product was extracted with Et_2O (6×4 mL). The collected ethereal phases were concentrated, and the residue was purified by column chromatography (SiO_2, 95:5 hexane/AcOEt) to give 281.7 mg of quinoline **3aa** (95%).

4.9. Characterization of products

All quinolines **3** were characterized by comparison with literature data.[3] Enynic derivatives **4** were fully characterized by elemental analysis, MS spectrometry, and IR, ^{1}H NMR, and ^{13}C NMR spectroscopies, as reported below.

*4.9.1. 2-(1-Methylenehept-2-ynyl)aniline (**4aa**).* Pale yellow oil. IR (film): 3462 (m, br), 3375 (m, br), 2957 (m), 2931 (m), 2871 (w), 2220 (w), 1618 (s), 1494 (m), 1455 (m), 1308 (m), 904 (m), 748 (s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17 (1H, dd, *J*=7.8, 1.6 Hz, H-3), 7.12–7.05 (1H, m, H-5), 6.72 (1H, td, *J*=7.5, 1.2 Hz, H-4), 6.65 (1H, dd, *J*=7.7, 1.2 Hz, H-6), 5.67 (1H, d, *J*=2.0 Hz, =C*H*H), 5.56 (1H, d, *J*=2.0 Hz, =CH*H*), 4.15 (1H, s, br, NH_2), 2.34 (2H, t, *J*=7.1 Hz, $\equiv CCH_2$), 1.60–1.34 (4H, m, $CH_2CH_2CH_3$), 0.91 (3H, t, *J*=7.3 Hz, Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.7, 129.7, 129.4, 128.9, 125.2, 124.3, 118.3, 116.0, 92.1, 79.9, 30.7, 22.1, 19.1, 13.6. MS (70 eV, EI): *m*/*z* (%): 199 (64) [M^+], 184 (9), 170 (35), 157 (100), 156 (85), 155 (27), 154 (40), 144 (16), 130 (38), 129 (43), 128 (44), 127 (20), 115 (20), 89 (13), 77 (28). Anal. Calcd for $C_{14}H_{17}N$ (199.29): C, 84.37; H, 8.60; N, 7.03. Found: C, 84.45; H, 8.56; N, 7.01.

*4.9.2. 2-Methoxy-6-(1-methylenehept-2-ynyl)aniline (**4ba**).* Pale yellow oil. IR (film): 3471 (m, br), 3378 (m, br), 2957 (s), 2932 (s), 2864 (w), 2231 (w), 1614 (m), 1562 (m), 1475 (s), 1287 (m), 1211 (m), 1048 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.84 (1H, distorted dd, *J*=7.3, 1.6 Hz, H-3), 6.78–6.65 (1H, m, H-4+H-5), 5.68 (1H, distorted d, *J*=2.0 Hz, =C*H*H), 5.59 (1H, distorted d, *J*=2.0 Hz, =CH*H*), 4.36 (2H, s, br, NH_2), 3.85 (3H, s, OMe), 2.35 (2H, t, *J*=7.1 Hz, $\equiv CCH_2$), 1.60–1.35 (4H, m, $CH_2CH_2CH_3$), 0.91 (3H, t, *J*=7.3 Hz, Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.1, 133.9, 129.5, 124.9, 124.2, 121.4, 117.2, 109.6, 92.0, 79.9, 55.7, 30.7, 22.1, 19.1, 13.6. MS (70 eV, EI): *m*/*z* (%): 229 (100) [M^+], 214 (14), 200 (19), 187 (51), 186 (40), 172 (54), 171 (27), 170 (27), 154 (25), 144 (17), 127 (15), 115 (22). Anal. Calcd for $C_{15}H_{19}NO$ (229.32): C, 78.56; H, 8.35; N, 6.11. Found: C, 78.65; H, 8.33; N, 6.10.

*4.9.3. 2-(1-Methylene-3-trimethylsilanylprop-2-ynyl)aniline (**4ac**).* Pale yellow oil. IR (film): 3466 (m, br), 3378 (m, br), 2960 (m), 2144 (m), 1620 (s), 1495 (m), 1455 (m), 1250 (s), 957 (m), 842 (vs), 759 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16 (1H, distorted ddd, *J*=7.5, 1.6, 0.3 Hz, H-3), 7.09 (1H, distorted ddd, *J*=8.0, 7.5, 1.6 Hz, H-5), 6.72 (1H, td, *J*=7.5, 1.1 Hz, H-4), 6.64 (1H, distorted ddd, *J*=8.0, 1.1, 0.3 Hz, H-6), 5.79 (1H, d, *J*=1.8 Hz, =C*H*H), 5.67 (1H, d, *J*=1.8 Hz, =CH*H*), 4.17 (2H, s, br, NH_2), 0.20 (9H, s, TMS). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.2, 129.8, 129.7, 129.5, 126.8, 124.4, 118.7, 116.4, 104.3, 96.3, 0.2. MS (70 eV, EI): *m*/*z* (%): 215 (100) [M^+], 200 (97), 198 (33), 184 (44), 174 (16), 170 (15), 160 (56), 100 (14). Anal. Calcd for $C_{13}H_{17}NSi$ (215.37): C, 72.50; H, 7.96; N 6.50. Found: C, 72.64; H, 7.99; N, 4.47.

Acknowledgements

This work was supported by the Ministero dell'Università e della Ricerca (Progetto di Ricerca di Interesse Nazionale PRIN 2006031888, Roma, Italy).

References and notes

1. For some recent books and reviews, see: (a) *Ionic Liquids*; Seddon, K. R., Rogers, R. D., Eds.; John Wiley & Sons: New York, NY, 2009; (b) Wu, B.; Liu, W.; Zhang, Y.; Wang, H. *Chem.—Eur. J.* **2009**, *15*, 1804; (c) Winkel, A.; Reddy, P. V. G.; Wilhelm, R. *Synthesis* **2008**, 999; (d) Domínguez de Maria, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 6960; (e) Plechkova, N. V.; Seddon, K. R. *Chem. Soc. Rev.* **2008**, *37*, 123; (f) Ledź, P. Ś; Mauduit, M.; Grela, K. *Chem. Soc. Rev.* **2008**, *37*, 2433; (g) Greaves, T. L.; Drummond, C. J. *Chem. Rev.* **2008**, *108*, 206; (h) Haumann, M.; Riisager, A. *Chem. Rev.* **2008**, *108*, 1474; (i) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. *Chem. Rev.* **2008**, *108*, 2015; (j) Plaquevent, J.-C.; Levillain, J.; Guillen, F.; Malhiac, C.; Gaumont, A.-C. *Chem. Rev.* **2008**, *108*, 5035; (k) Šebesta, R.; Kmentová, I.; Toma, S. *Green. Chem.* **2008**, *10*, 484; (l) *Ionic Liquids in Synthesis*;

Wasserscheid, P., Welton, T., Eds.; Wiley-VCH: Weinheim, 2007; (m) Ueki, T.; Watanabe, M. *Macromolecules* **2008**, *41*, 3739; (n) Prvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615; (o) van Rantwijk, F.; Sheldon, R. A. *Chem. Rev.* **2007**, *107*, 2757; (p) Zhang, Z. C. *Adv. Synth. Catal.* **2006**, *49*, 153; (q) Muzart, J. *Adv. Synth. Catal.* **2006**, *348*, 275; (r) Calò, V.; Nacci, A.; Monopoli, A. *Eur. J. Org. Chem.* **2006**, 3791; (s) Toma, Š.; Mečiarová, M.; Šebesta, R. *Eur. J. Org. Chem.* **2006**, 3791; (t) Jain, N.; Kumar, A.; Chaudan, S.; Chaudan, S. M. S. *Tetrahedron* **2005**, *61*, 1015; (u) Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459; (v) Welton, T.; Smith, P. J. *Adv. Organomet. Chem.* **2004**, *51*, 251; (w) Gu, Y. L.; Peng, J. J.; Qiao, K.; Yang, H. Z.; Shi, F.; Deng, Y. Q. *Prog. Chem.* **2003**, *15*, 222; (x) Dupont, J.; De Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667; (y) Zhao, H.; Malhotra, S. V. *Aldrichimica Acta* **2002**, *35*, 75; (z) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157.

2. (a) Sheldon, R. *Chem. Commun.* **2001**, 2399; (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3773; (c) Welton, T. *Chem. Rev.* **1999**, *99*, 2071.
3. Gabriele, B.; Mancuso, R.; Salerno, G.; Ruffolo, G.; Plastina, P. *J. Org. Chem.* **2007**, *72*, 6873.
4. We have recently reported several examples of metal-catalyzed heterocyclization reactions leading to heterocyclic derivatives: (a) Gabriele, B.; Mancuso, R.; Salerno, G. *J. Org. Chem.* **2008**, *73*, 7336; (b) Gabriele, B.; Salerno, G.; Costa, M. *Synlett* **2004**, 2468; (c) Gabriele, B.; Salerno, G.; Fazio, A. *J. Org. Chem.* **2003**, *68*, 7853; (d) Gabriele, B.; Salerno, G.; Fazio, A.; Pittelli, R. *Tetrahedron* **2003**, *59*, 6251; (e) Gabriele, B.; Salerno, G.; Fazio, A.; Bossio, M. R. *Tetrahedron Lett.* **2001**, *42*, 1339; (f) Gabriele, B.; Salerno, G.; Fazio, A. *Org. Lett.* **2000**, *2*, 351; (g) Gabriele, B.; Salerno, G.; De Pascali, F.; Costa, M.; Chiusoli, G. P. *J. Organomet. Chem.* **2000**, *594*, 409; (h) Gabriele, B.; Salerno, G.; Lauria, E. *J. Org. Chem.* **1999**, *64*, 7687; (i) Gabriele, B.; Salerno, G. *Chem. Commun.* **1997**, 1083.
5. The formation of unidentified heavy products accounted for substrate conversion (100%)
6. For reviews on recent advances in the synthesis of quinoline derivatives, see: (a) Madapa, S.; Tusi, Z.; Batra, S. *Curr. Org. Chem.* **2008**, *12*, 1116; (b) Kouznetsov, V. V.; Mendez, L. Y. V.; Gomez, C. M. M. *Curr. Org. Chem.* **2005**, *9*, 141.
7. For very recently reported approaches for the synthesis of substituted quinoline by heteroannulation of acyclic precursors, see: (a) Szatmari, I.; Fulop, F. *Synthesis* **2009**, 775; (b) Chen, S.; Chen, R.; He, M.; Pang, R.; Tan, Z.; Yang, M. *Bioorg. Med. Chem.* **2009**, *17*, 1948; (c) Juribasic, M.; Stella, L.; Marinic, Z.; Vinkovic, M.; Traldi, P.; Tusek-Bosic, L. *Lett. Org. Chem.* **2009**, *6*, 11; (d) Ghorbani-Vaghei, R.; Akbari-Dadamahaleh, S. *Tetrahedron Lett.* **2009**, *50*, 1055; (e) Hanna-Elias, A.; Manallack, D. T.; Berque-Bestel, I.; Irving, H. R.; Coupar, I. N.; Iskander, M. N. *Aust. J. Chem.* **2009**, *62*, 150; (f) Mierde, H. V.; van der Voort, P.; Verpoort, F. *Tetrahedron Lett.* **2009**, *50*, 201; (g) Ghassamipour, S.; Sardarian, A. R. *Tetrahedron Lett.* **2009**, *50*, 514; (h) Qi, C. M.; Zheng, Q. W.; Hua, R. M. *Tetrahedron* **2009**, *65*, 1316; (i) Cho, C. S.; Ren, W. X.; Yoon, N. S. *J. Mol. Catal. A: Chem.* **2009**, *299*, 177; (j) Likhar, P. R.; Subhas, M. S.; Roy, S.; Kantam, M. L.; Sridhar, B.; Seth, R. K.; Biswas, S. *Org. Biomol. Chem.* **2009**, *7*, 85.
8. For alternative approaches for the synthesis of quinolines in ionic liquids, mainly based on the Friedlander reaction, see: (a) Wang, H.-M.; Hou, R.-S.; Cheng, H.-T.; Chen, L.-C. *Heterocycles* **2009**, *78*, 487; (b) Heravi, M. R. P. *Ultrason. Sonochem.* **2009**, *16*, 361; (c) Sarma, R.; Prajapati, D. *Synlett* **2008**, 3001; (d) Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Nikcheh, M. S. *Tetrahedron Lett.* **2008**, *49*, 5366; (e) Zhou, T.; Lin, J. L.; Chen, Z. C. *Lett. Org. Chem.* **2008**, *5*, 47; (f) Wang, X. S.; Zhang, M.-M.; Jiang, H.; Yao, C.-S.; Tu, S.-J. *Tetrahedron* **2007**, *63*, 4439; (g) Karthikeyan, G.; Perumal, P. T. *J. Heterocycl. Chem.* **2004**, *41*, 1039; (h) Wang, J.; Fan, x.; Zhang, H.; Han, L. *Can. J. Chem.* **2004**, *82*, 1192; (i) Palimkar, S. S.; Siddiqui, S. A.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *J. Org. Chem.* **2003**, *68*, 9371; (j) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Moreno-Mañas, M.; Vallribera, A. *Tetrahedron Lett.* **2002**, *43*, 5537.
9. For recent reviews on the importance and applications of quinoline derivatives, see: (a) Henry, M.; Alibert, S.; Rogier, C.; Barbe, J.; Pradines, B. *Curr. Top. Med. Chem.* **2008**, *8*, 563; (b) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166; (c) Kimyonok, A.; Wang, X. Y.; Weck, M. *Polym. Rev.* **2006**, *46*, 47; (d) Mahamoud, A.; Chevalier, J.; Davin-Regli, A.; Barbe, J.; Pages, J. M. *Curr. Drug Targets* **2006**, *7*, 843; (e) Fitch, C. D. *Life Sci.* **2004**, *74*, 1957.
10. Huddleston, J. G.; Visser, A. E.; Reichert, W. M.; Willauer, H. D.; Broker, G. A.; Rogers, R. D. *Green. Chem.* **2001**, 156.
11. Crosthwaite, J. M.; Aki, S. N. V. K.; Maginn, E. J.; Brennecke, J. F. *J. Phys. Chem. B* **2004**, *108*, 5113.