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Ionic liquid phase synthesis (IoLiPS) of 2-aminothiazoles and imidazo[1,2-*a*]pyridines†

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An efficient and practical ionic liquid phase synthesis (IoLiPS) of aza-heterocycles has been developed through a 'catch-and-release' strategy using an ionic liquid-supported hypervalent iodine reagent. The hypervalent iodine played a dual role as a reagent and as a soluble support. This strategy provided a combinatorial approach for the synthesis of 2-aminothiazoles and imidazo[1,2-*a*]pyridines directly from substituted acetophenones in good to excellent yields. The use of an ionic liquid supported reagent offered better isolation of the products by simple extraction with organic solvents.

Introduction

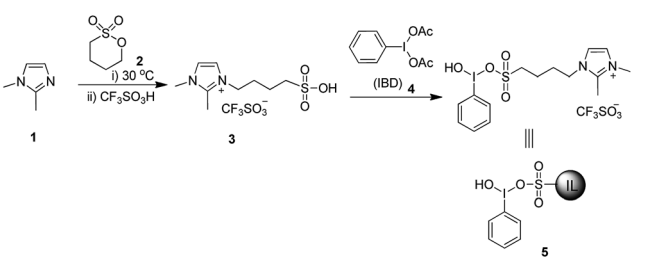
Finding novel and more expedient techniques that will facilitate the rapid production and purification of desired molecules is an area of continued creativity for organic chemists. Development of new linkers for tethering organic compounds to the supports is an area of active investigation in supported synthesis.[1] Choice of linker is a key consideration in planning a supported synthesis since the cleavage conditions often leads to extra or unwanted functional groups in the molecule and moreover, the liability of the linker limits the chemistry which may be carried out on it. In this context, catch-and-release strategies have been very useful and they have been explored in combinatorial chemistry for rapid production of library of organic compounds with adequate purity.[2] Although solid-phase catch-and-release methods enables the efficient generation of many pharmacological important compounds, difficulties in analyzing the intermediates, non linear kinetics and heterogeneous reaction conditions are major concerns in these methods.

To overcome the problems associated with solid-phase catch-and-release methods several new alternative approaches using soluble supports such as fluorous,[3] PEG and ionic liquid have been developed.[4] For example, Procter group developed an efficient fluorous cyclative-capture strategy for the synthesis of aza-heterocyles[5] and Galan and co-workers introduced ion supported catch-and-release strategy for the synthesis of β-(**1** → **6**) and β-(**1** → **2**)-linked oligosaccharides.[2c] Recently, we have developed a new ionic liquid-supported sulfonyl hydrazine linker and demonstrated its application in the synthesis of 1,2,3-thiadiazoles and 1,2,3-selenadiazoles *via* catch-and-release strategy.[6]

Nitrogen-containing heterocyclic compounds 2-aminothiazoles and imidazo[1,2-*a*]pyridines play significant role in the pharmaceutical and agrochemical industries.[7] Several synthetic methodologies have been developed for the synthesis of thiazoles[8] and imidazo[1,2-*a*]pyridines.[9] The most widely and practically used method for the synthesis of these aza-heterocycles is coupling reaction of α-tosyloxycarbonyls/α-halocarbonyls with thiourea and 2-aminopyridine.[10] However, this method requires isolation and purification of the intermediates and/or use of lachrymatory α-halocarbonyls and thus novel method that can address these issues are desired for the synthesis of these aza-heterocycles. Adding to our continuous interest and our ongoing research program on functionalized ionic liquids,[6,11] here in we report ionic liquid phase synthesis of 2-aminothiazoles and imidazo[1,2-*a*]pyridines *via* catch-and-release strategy using ionic liquid-supported hypervalent iodine reagent.

Results and discussion

Ionic liquid-supported hypervalent iodine reagent (**5**) has been synthesized in three steps starting from 1,2-dimethylimidazole



1 3 5

Scheme 1 Synthesis of ionic liquid-supported hypervalent iodine reagent.

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† Electronic supplementary information (ESI) available: Experimental procedure, ^{1}H and ^{13}C NMR data of compounds **7a–g**, **9a–g** and **11a–g**, copies of NMR spectra for compounds **5**, **7a–g**, **9a–g** and **11a–g**. See DOI: 10.1039/c4ra08009b

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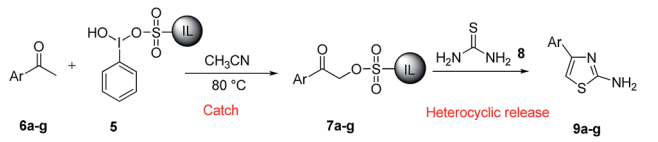
(**1**) (Scheme 1).[11b] *N*-Alkylation of **1** with 1,4-butanesultone (**2**) and acidification with trifluoromethanesulfonic acid gave ionic liquid-supported sulfonic acid **3** in 98% yield.[11e] Homogeneous solution of **3** was added to the hot solution of iodobenzene diacetate (**4**) in CH_3CN and the resulting reaction mixture was reserved at room temperature for one week to obtain **5**.

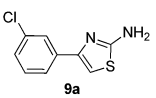
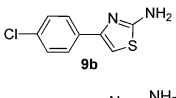
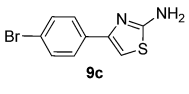
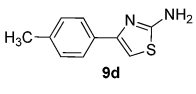
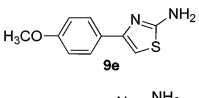
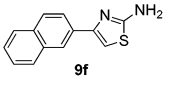
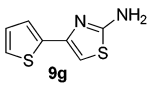
Reagent **5** was further studied for the capturing of 3-chloroacetopheone (**6a**). Of the various conditions that were studied, it was found that **6a** was completely captured by using 2 equiv. of **5** in CH_3CN under reflux conditions for 12 h. After completion of the reaction, resulting ionic liquid-supported substituted α-sulfonyloxy-acetophenone **7a** was purified by passing through a short silica column using dichloromethane : methanol mixture (95 : 5 v/v) as eluent. We want to probe whether **7a** would have same reactivity that of conventional α-tosyloxy ketones. The reaction of **7a** with thiourea afforded 4-(3-chlorophenyl)thiazol-2-amine (**9a**) in good yield. Being confident that our ionic liquid-supported α-sulfonyloxy-acetophenone **7a** was emulating its counterpart α-tosyloxy ketones, we then focused our attention to develop a simple and straight forward, chromatographic free protocol for the synthesis of thiazoles from acetophenones.

The synthetic procedure for 2-aminothiazoles **9** started by the reaction of **6a** with **5** in CH_3CN at 80 °C for 12 h in the presence of anhydrous Na_2SO_4 followed by reaction with thiourea. After complete 'capture' of **6a** by **5**, the reaction mixture was filtered to remove Na_2SO_4 and CH_3CN was evaporated under reduced pressure and the residue containing **7a** was washed with diethyl ether to remove excess iodobenzene. Next, **7a** was allowed to react with thiourea under solvent free conditions at 40 °C for 4 h to 'release' **9a**. Use of the ionic liquid-linked reagent facilitated easy product isolation by simple phase separation. After completion of reaction, the product **9a** was isolated by extracting with hexane–ethyl acetate (2 : 8 v/v) mixture. In order to ascertain the scope of the reagent **5** in combinatorial synthesis a library of 2-aminothiazoles **9a–g** were prepared from acetophenones bearing both electron-donating and electron-withdrawing substituents. The yield of all the 2-aminothiazoles **9a–g** is given in Table 1. It is worthy to mention that the 2-aminothiazoles were of pure enough and no further purification was required.

With our interest in the synthesis of imidazo[1,2-*a*]pyridines[9a,12] we further extended this catch-and-release method for the synthesis of imidazo[1,2-*a*]pyridine ring systems. Initial attempt showed that the capture of **6a** with **5**, followed by

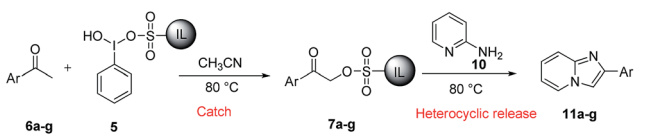
Table 1 Synthesis of 2-aminothiazoles **9a–g** using **5**[a]

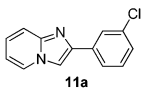
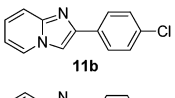
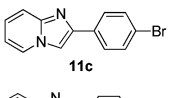
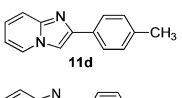
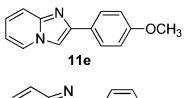
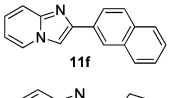
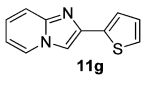


S. No.	Ar	Product	Yield[b] (%) (purity)[c]
1	3-ClC_6H_4	 **9a**	84 (>98)
2	4-ClC_6H_4	 **9b**	83 [63][d] (>99)
3	4-BrC_6H_4	 **9c**	80 (99)
4	4-$CH_3C_6H_4$	 **9d**	71 [58][d] (99)
5	4-$OCH_3C_6H_4$	 **9e**	71 (97)
6	$C_{10}H_7$	 **9f**	81 (>89)
7	C_4H_3S	 **9g**	77 (94)

[a] Reaction conditions: **6** (0.5 mmol), **5** (1 mmol), Na_2SO_4 (0.25 mmol), CH_3CN (3 mL), 80 °C, 12 h, followed by **8**, 40 °C, 4 h (0.5 mmol). [b] Isolated yields. [c] Purity determined by HPLC. [d] Isolated yields of **9b** and **9d** when α-tosyloxycarbonyls were used in acetonitrile.

Table 2 Synthesis of imidazo[1,2-*a*]pyridines **11a–g** using **5**[a]



S. No.	Ar	Product	Yield[b] (%) (purity)[c]
1	3-ClC_6H_5	 **11a**	84 (82)
2	4-ClC_6H_4	 **11b**	83 [68][d] (>98)
3	4-BrC_6H_4	 **11c**	80 (>99)
4	4-$CH_3C_6H_4$	 **11d**	71 [57][d] (>99)
5	4-$OCH_3C_6H_4$	 **11e**	58 (99)
6	$C_{10}H_7$	 **11f**	63 (99)
7	C_4H_3S	 **11g**	66 (>99)

[a] Reaction conditions: **6** (0.5 mmol), **5** (1 mmol), Na_2SO_4 (0.25 mmol), CH_3CN (3 mL), 80 °C, 12 h, followed by **10** (0.5 mmol), 80 °C, 5 h. [b] Isolated yields. [c] Purity determined by HPLC. [d] Isolated yields of **11b** and **11d** when α-tosyloxycarbonyls were used in acetonitrile.

reaction with 2-aminopyridine did not gave desired imidazo[1,2-*a*]pyridines at 40 °C. Heating the reaction mixture at elevated temperature (80 °C) was fruitful and the desired imidazo[1,2-*a*]pyridine **11a** was obtained in 84% yield. Under the optimized reaction conditions, various acetophenones were found to be suitable substrates to provide the desired imidazo[1,2-*a*]pyridines (Table 2). The results demonstrated that both electron donating and electron withdrawing groups on the aryl group of acetophenones were well tolerated to give corresponding imidazo[1,2-*a*]pyridines in moderate to good yields. Moreover, heteroaryl substituted imidazo[1,2-*a*]pyridines (Table 2, **11g**) can also be synthesized using this method.

Conclusions

In summary, a new approach have been developed for the synthesis of 2-aminothiazoles and imidazo[1,2-*a*]pyridines by the combination of ionic liquid phase synthesis and 'catch-and-release' strategy. The method developed for the synthesis of aza-heterocycles using ionic liquid-supported hypervalent iodine reagent provided good to excellent yield of aza-heterocycles and allows easy monitoring of the reaction progress. This combinatorial approach could be a good alternative for the synthesis of 2-aminothiazoles and imidazo[1,2-*a*]pyridines and can also be extended to other heterocyclic compounds.

Experimental section

General information

The NMR spectra were recorded on 300 MHz, 400 MHz and 500 MHz spectrometers using $CDCl_3$, DMSO-d_6 and CD_3OD as solvents. The chemical shifts were expressed in ppm. Reactions were monitored by thin-layer chromatography (TLC) carried out on silica-coated aluminium plates (60F-254) using UV light as visualizing agent. High resolution mass spectra (HRMS) were recorded on a mass spectrometer using electrospray ionization-time of flight (ESI-TOF). All the chemicals and reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated.

Synthesis of ionic liquid-supported sulfonic acid (3)

1,4-Butanesultone (6.0 g, 44.0 mmol) was added drop-wise to 1,2-dimethylimidazole (4.24 g, 44.0 mmol) at 30 °C and the resulting solution was then heated at 60 °C for 2 h and then cooled to room temperature to give a white solid. The solid was washed with toluene (3 × 15 mL) followed by diethyl ether (2 × 10 mL) to remove unreacted starting materials. Trifluoromethanesulfonic acid (47.0 mmol) was added drop-wise to the zwitter ion at 0 °C. The reaction mixture was warmed slowly and stirred at 60 °C for 1 h and a thick liquid was obtained. The thick liquid was washed with toluene (3 × 15 mL) to remove excess of triflic acid. The residue was dried under reduced pressure to give a pale yellow thick liquid of ionic liquid-supported sulfonic acid (**3**) in 98% yield.

Synthesis of ionic liquid-supported hypervalent iodine (5)

Ionic liquid supported-sulfonic acid (5 mmol) and IBD (5 mmol) were taken in different conical flasks and were dissolved in minimum amount of CH_3CN under heating conditions. The homogeneous mixture of ionic liquid-supported sulfonic acid was added to the clear solution of IBD under hot conditions. The resulting reaction mixture was kept aside at room temperature for one week. After completion of the reaction CH_3CN was evaporated and the reaction mixture was purified by washings with dry DCM (3 × 30 mL) to get yellow thick liquid (7.55 g, 96%).

5. ^{1}H NMR (300 MHz, DMSO-d_6, CD_3OD) δ 8.22 (s, 1H), 7.76 (d, J = 1.1 Hz, 1H), 7.73 (d, J = 1.1 Hz, 1H), 7.62 (d, J = 2.1 Hz, 1H), 7.58 (d, J = 2.0 Hz, 1H), 7.44–7.37 (m, 1H), 7.23–7.15 (m, 2H), 4.14 (t, J = 7.3 Hz, 2H), 3.76 (s, 3H), 2.64 (d, J = 7.5 Hz, 2H), 2.59 (s, 3H), 1.91–1.78 (m, 2H), 1.71–1.58 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 144.6, 137.5, 130.9, 128.0, 123.1, 122.6, 121.2, 121.0 (q, J_{C-F} = 320.25 Hz, OTf), 94.9, 50.7, 34.8, 28.4, 21.9, 9.2; HRMS (ESI-TOF) calcd for $C_{15}H_{22}IN_2O_4S^+$ 453.0339 found 453.0356 $[M - CF_3SO_3]^+$.

Procedure for the synthesis of ionic liquid-supported sulfonate (7a)

Acetophenone (**6a**, 0.5 mmol) and dry Na_2SO_4 (0.25 mmol) were added to the solution of **5** (1 mmol) in CH_3CN (5 mL) and the resulting reaction mixture was heated at reflux until **6a** was completely captured in the form of ionic liquid-supported sulfonates (as indicated by thin layer chromatography). The reaction mixture was filtered to remove Na_2SO_4 and CH_3CN was evaporated under reduced pressure. The resulting crude compound was purified by silica-gel column chromatography (dichloromethane–methanol 3 : 1 as eluent) to give the desired compound **7a**.

7a. Yield 50%; yellow liquid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.01–7.97 (m, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.80 (dd, J = 8.0, 1.1 Hz, 1H), 7.67–7.62 (m, 3H), 5.74 (s, 2H), 4.19 (t, J = 6.9 Hz, 2H), 3.76 (s, 3H), 3.59–3.52 (m, 2H), 2.60 (s, 3H), 1.94–1.76 (m, 4H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 189.2, 142.8, 142.6133.7, 132.2, 129.3, 126.0, 124.9, 120.7, 119.2, 119.0 (q, J_{C-F} = 320.25 Hz, OTf), 69.6, 47.2, 45.1, 33.0, 25.8, 18.3, 7.5; HRMS (ESI-TOF) calcd for $C_{17}H_{22}ClN_2O_4S^+$ 385.0983 found 385.1015 $[M - CF_3SO_3]^+$.

General procedure for synthesis of 2-aminothiazoles (9a–g)

Substituted acetophenone derivative (**6**) (0.5 mmol), Na_2SO_4 (0.25 mmol) and **5** (1 mmol) were added to the round bottom flask containing CH_3CN (5 mL) and the resulting reaction mixture was heated at 40 °C until the acetophenone is completely consumed (TLC). After completion of the reaction, the reaction mixture was cooled and Na_2SO_4 was separated by filtration and the CH_3CN was evaporated under reduced pressure. The residue was washed with ether (3 × 10 mL) and ionic liquid-supported sulfonates (**7**) obtained was treated with thiourea (0.5 mmol) under vigorous stirring at room temperature under solvent free conditions. Progress of the reaction was monitored by TLC. After completion of the reaction, the product

was extracted with hexane–ethyl acetate mixture (3 × 10 mL, 2 : 8 v/v). The combined organic layers were washed with water, dried with anhydrous sodium sulfate, and evaporated under reduced pressure to give the pure 2-aminothiazoles (**9**) without chromatographic purification.

4-(3-Chlorophenyl)-1,3-thiazol-2-amine (9a). Yield 84%; off white solid; mp 132–133 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.64 (d, J = 7.2 Hz, 2H), 7.36–7.19 (m, 2H), 6.74 (s, 1H), 5.18 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 149.9, 136.4, 134.9, 129.83, 127.7, 126.2, 124.0, 103.9.

4-(4-Chlorophenyl)-1,3-thiazol-2-amine (9b). Yield 83%; colorless solid; mp 163–165 °C (lit.[10a] 163–164 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 2H), 7.36 (d, J = 6.8 Hz, 2H), 6.73 (s, 1H), 5.10 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.33, 135.42, 133.52, 133.19, 128.80, 127.34, 103.29.

4-(4-Bromophenyl)-1,3-thiazol-2-amine (9c). Yield 80%; yellow solid; mp 178–180 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.75 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 7.10 (s, 2H), 7.08 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.8, 149.1, 134.5, 131.8, 128.0, 120.5, 102.8.

4-(4-Methylphenyl)-1,3-thiazol-2-amine (9d). Yield 71%; off white solid; mp 130–131 °C (lit.[10a] 125–126 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 6.4 Hz, 2H), 7.18 (d, J = 6.1 Hz, 2H), 6.65 (s, 1H), 5.26 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 151.4, 137.5, 132.0, 129.3, 125.9, 102.0, 21.2.

4-(4-Methoxyphenyl)-1,3-thiazol-2-amine (9e). Yield 71%; off white solid; mp 200–203 °C (lit.[13] 204–207 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 7.5 Hz, 2H), 6.91 (d, J = 7.5 Hz, 2H), 6.58 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 159.3, 150.4, 127.4, 127.2, 113.9, 100.5, 55.2.

4-(Naphthalen-6-yl)thiazol-2-amine (9f). Yield 81%; solid; mp 152–154 °C (lit.[13] 152–153 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.30 (s, 1H), 7.89 (dd, J = 37.4, 4.3 Hz, 4H), 7.47 (s, 2H), 7.15 (s, 1H), 7.09 (s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.7, 150.2, 133.6, 132.8, 132.7, 128.5, 128.3, 128.0, 126.8, 126.2, 124.5, 124.4, 102.8.

4-Thiophen-2-yl-thiazol-2-ylamine (9g). Yield 77%; off white solid; mp 135–136 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.42–7.36 (m, 2H), 7.14 (s, 2H), 7.04 (dd, J = 5.0, 3.7 Hz, 1H), 6.84 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.7, 144.9, 139.7, 128.2, 125.1, 123.2, 100.2.

General procedure for synthesis of imidazo[1,2-*a*]pyridine (11a–g)

To a stirred solution of substituted acetophenone derivative (**6**, 0.5 mmol) and Na_2SO_4 (0.25 mmol) in CH_3CN (3 mL), **5** (1 mmol) was added and the resulting reaction mixture was heated at 80 °C until the acetophenone is completely consumed. After completion of the reaction (as indicated by TLC), reaction mixture was filtered and the CH_3CN was evaporated under reduced pressure. The resulting residue was washed with ether (3 × 10 mL) and subsequently treated with 2-aminopyridine (0.5 mmol) and stirred vigorously at 80 °C temperature under solvent free conditions. After completion of the reaction, the product was extracted with hexane–ethyl acetate mixture (3 × 10 mL, 2 : 8 v/v) and washed with water. The combined organic layers were dried with anhydrous sodium sulfate, and evaporated under reduced pressure to give the desired products in pure form without chromatographic purification.

4-(3-Chlorophenyl)*H*-imidazo[1,2-*a*]pyridine (11a). Yield 84%; yellow solid; mp 105–107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (d, J = 4.7 Hz, 1H), 7.96 (s, 1H), 7.84 (s, 2H), 7.63 (d, J = 6.4 Hz, 1H), 7.42–7.23 (m, 2H), 7.19 (d, J = 5.6 Hz, 1H), 6.79 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.7, 144.4, 135.6, 134.7, 130.0, 127.9, 126.1, 125.7, 125.0, 124.1, 117.6, 112.7, 108.5.

4-(4-Chlorophenyl)*H*-imidazo[1,2-*a*]pyridine (11b). Yield 83%; yellow solid; mp 199–201 °C (lit.[14] 201–202 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 6.8 Hz, 1H), 7.79 (d, J = 8.5 Hz, 2H), 7.72 (s, 1H), 7.53 (d, J = 9.1 Hz, 1H), 7.31 (d, J = 8.5 Hz, 2H), 7.09 (dd, J = 11.4, 4.4 Hz, 1H), 6.69 (t, J = 6.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 143.6, 132.6, 131.3, 127.9, 126.2, 124.6, 123.9, 116.50, 111.6, 107.2.

4-(4-Bromophenyl)*H*-imidazo[1,2-*a*]pyridine (11c). Yield 80%; yellow solid; mp 196–198 °C (lit.[9a] 201–203 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.83 (s, 3H), 7.59 (d, J = 16.6 Hz, 3H), 7.19 (s, 1H), 6.79 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.7, 144.6, 132.7, 131.8, 127.6, 125.6, 125.1, 121.9, 117.5, 112.7, 108.3.

4-(4-Methylphenyl)*H*-imidazo[1,2-*a*]pyridine (11d). Yield 71%; off white solid; mp 142–144 °C (lit.[15] 144–145 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 6.0 Hz, 1H), 7.84 (d, J = 7.5 Hz, 2H), 7.79 (s, 1H), 7.61 (d, J = 8.7 Hz, 1H), 7.24 (d, J = 7.5 Hz, 2H), 7.18–7.06 (m, 1H), 6.79–6.67 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 145.6, 137.8, 130.9, 129.4, 126, 125.5, 124.5, 117.4, 112.3, 107.7, 21.3.

4-(4-Methoxyphenyl)*H*-imidazo[1,2-*a*]pyridine (11e). Yield 58%; colorless solid; mp 142–144 °C (lit.[15] 137–138 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 6.7 Hz, 1H), 7.89 (d, J = 8.8 Hz, 2H), 7.76 (s, 1H), 7.60 (d, J = 9.1 Hz, 1H), 7.14 (ddd, J = 9.0, 6.8, 1.1 Hz, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.74 (t, J = 6.7 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 145.7, 145.6, 127.3, 126.5, 125.4, 124.4, 117.3, 114.3, 112.2, 107.2, 55.3.

2-(Naphthalen-1-yl)imidazo[1,2-*a*]pyridine (11f). Yield 63%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.11 (d, J = 6.0 Hz, 1H), 8.06–7.78 (m, 5H), 7.67 (d, J = 8.6 Hz, 1H), 7.47 (s, 2H), 7.20 (dd, J = 19.1, 12.1 Hz, 1H), 6.77 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.8, 145.8, 133.8, 133.2, 131.1, 128.4, 128.3, 127.7, 126.3, 126.0, 125.6, 124.8, 124.8, 124.2, 117.6, 112.5, 108.6.

2-(Thiophen-2-yl)*H*-imidazo[1,2-*a*]pyridine (11g). Yield 66%; off white solid; mp 134–137 °C (lit. 137–139 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 6.7 Hz, 1H), 7.73 (s, 1H), 7.59 (d, J = 9.1 Hz, 1H), 7.49–7.42 (m, 1H), 7.29 (dd, J = 4.9, 0.9 Hz, 1H), 7.16–7.10 (m, 1H), 7.08 (dd, J = 4.9, 3.6 Hz, 1H), 6.74 (dd, J = 9.7, 3.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4, 140.8, 137.5, 127.7, 125.4, 125.0, 124.8, 123.7, 117.3, 112.5, 107.4.

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Notes and references

1 (*a*) S. Bräse and S. Dahmen, in *Handbook of Combinatorial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, 2005, pp. 59–169; (*b*) W. Zhang, *Chem. Rev.*, 2009, **109**, 749; (*c*) E. Åkerblom, *Mol. Diversity*, 1998, **4**, 53; (*d*) K. Gordon and S. Balasubramanian, *J. Chem. Technol. Biotechnol.*, 1999, **74**, 835.

2 (*a*) A. Solinas and M. Taddei, *Synthesis*, 2007, 2409; (*b*) L. De Luca, G. Giacomelli and A. Porcheddu, *J. Comb. Chem.*, 2005, **7**, 905; (*c*) I. Sittel, A.-T. Tran, D. Benito-Alifonso and M. C. Galan, *Chem. Commun.*, 2013, **49**, 4217; (*d*) G. A. Strohmeier and C. O. Kappe, *Angew. Chem.*, 2004, **116**, 631.

3 W. Zhang, *Curr. Opin. Drug Discovery Dev.*, 2004, **7**, 784.

4 H. Hakkou, J. J. Vanden Eynde, J. Hamelin and J. P. Bazureau, *Tetrahedron*, 2004, **60**, 3745.

5 L. A. McAllister, R. A. McCormick, K. M. James, S. Brand, N. Willetts and D. J. Procter, *Chem.–Eur. J.*, 2007, **13**, 1032.

6 A. Kumar, M. K. Muthyala, S. Choudhary, R. K. Tiwari and K. Parang, *J. Org. Chem.*, 2012, **77**, 9391.

7 (*a*) Z. Jin, *Nat. Prod. Rep.*, 2006, **23**, 464; (*b*) E.-G. Cecile and G. Alain, *Mini-Rev. Med. Chem.*, 2007, **7**, 888.

8 (*a*) M. K. Muthyala and A. Kumar, *J. Heterocycl. Chem.*, 2012, **49**, 959; (*b*) P. Wipf and S. Venkatraman, *J. Org. Chem.*, 1996, **61**, 8004.

9 (*a*) K. Pericherla, P. Kaswan, P. Khedar, B. Khungar, K. Parang and A. Kumar, *RSC Adv.*, 2013, **3**, 18923; (*b*) C. He, J. Hao, H. Xu, Y. Mo, H. Liu, J. Han and A. Lei, *Chem. Commun.*, 2012, **48**, 11073; (*c*) J. Yu, Y. Jin, H. Zhang, X. Yang and H. Fu, *Chem.–Eur. J.*, 2013, **19**, 16804.

10 (*a*) T. M. Potewar, S. A. Ingale and K. V. Srinivasan, *Tetrahedron*, 2007, **63**, 11066; (*b*) Y.-Y. Xie, Z.-C. Chen and Q.-G. Zheng, *Synthesis*, 2002, 1505.

11 (*a*) M. K. Muthyala, S. Choudhary, K. Pandey, G. M. Shelke, M. Jha and A. Kumar, *Eur. J. Org. Chem.*, 2014, 2365; (*b*) M. K. Muthyala, S. Choudhary and A. Kumar, *RSC Adv.*, 2014, **4**, 14297; (*c*) M. K. Muthayala and A. Kumar, *ACS Comb. Sci.*, 2011, **14**, 5; (*d*) M. K. Muthayala, B. S. Chhikara, K. Parang and A. Kumar, *ACS Comb. Sci.*, 2011, **14**, 60; (*e*) M. K. Muthyala, S. Choudhary and A. Kumar, *J. Org. Chem.*, 2012, **77**, 8787.

12 (*a*) K. Pericherla, A. Jha, B. Khungar and A. Kumar, *Org. Lett.*, 2013, **15**, 4304; (*b*) K. Pericherla, P. Khedar, B. Khungar and A. Kumar, *Chem. Commun.*, 2013, **49**, 2924.

13 T. M. Potewar, S. A. Ingale and K. V. Srinivasan, *Tetrahedron*, 2008, **64**, 5019.

14 Z.-G. Le, Z.-B. Xie and J.-P. Xu, *Molecules*, 2012, **17**, 13368.

15 A. R. Katritzky, G. Qiu, Q.-H. Long, H.-Y. He and P. J. Steel, *J. Org. Chem.*, 2000, **65**, 9201.