Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 61 (2005) 3539–3546

# Room temperature ionic liquid promoted improved and rapid synthesis of 2,4,5-triaryl imidazoles from aryl aldehydes and 1,2-diketones or α-hydroxyketone

Shapi A. Siddiqui, Umesh C. Narkhede, Sanjay S. Palimkar, Thomas Daniel, Rajgopal J. Lahoti and Kumar V. Srinivasan*

*Division of Organic Chemistry; Technology, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411 008, India*

Received 7 October 2004; revised 4 January 2005; accepted 28 January 2005

**Abstract**—An improved and rapid one-pot synthesis of 2,4,5-triaryl imidazoles in a room temperature ionic liquid is described, which does not need any added catalyst. Different ionic liquids based on 1-*n*-butyl and 1,3-di-*n*-butyl imidazolium salts were screened and their efficacy in terms of acidity and polarity have been correlated with yields and reaction period. The one-pot methodology resulting in excellent isolated yields in short reaction times is characterized by simple work up procedures and efficient recovery and recycling of the ionic liquid, which acts as a promoter.


## 1. Introduction

The development of a simple, efficient and general synthetic method for widely used organic compounds from readily available reagents is one of the major challenges in organic synthesis. In 1858 Debus[1] reported the reaction between glyoxal and ammonia, a reaction that pioneered a novel synthetic route to imidazole. Over the century, the importance of imidazoles in biological system has attracted much interest due to their chemical and biochemical properties. Even today, 147 years later, research in imidazole chemistry continues unabated. Compounds with imidazole ring system have many pharmacological properties and play important roles in biochemical process.[2] Many of the substituted imidazoles are known as inhibitors of P38 MAP kinase,[3] fungicides and herbicides,[4] plant growth regulators[5] and therapeutic agents.[6] Recent advances in green chemistry and organometallic chemistry have extended the boundary of imidazoles to the synthesis and application of a large class of imidazoles as ionic liquids and imidazole related N-heterocyclic carbenes (NHC).[7,8]

There are several methods reported in literature for the synthesis of imidazoles such as hetero-Cope rearrangement,[9] four-component condensation of arylglyoxals, primary amines, carboxylic acids and isocyanides on Wang resin,[10] reaction of N-(2-oxo)-amides with ammonium trifluroacetate,[11] 1,2-aminoalcohols in the presence of $PCl_5$,[12] diketones, aldehyde, amine and ammonium acetate in phosphoric acid,[13] in acetic acid,[14] organo catalyst in acetic acid[15] as well as $H_2SO_4$,[16] DMSO.[17] Several micro-wave (MW) assisted syntheses of imidazoles from 1,2-diketones and aldehydes in the presence of a variety of catalysts have been recently reported. These include MW/silica-gel,[18] MW/silica-gel/H-Y,[19] MW/$Al_2O_3$,[20] MW/acetic acid,[21] in DMF.[22] The condensation of α-hydroxy ketones with aldehydes and ammonium acetate on solid supported silica gel or alumina in the presence of MW has been reported recently.[23]

Many of the synthetic protocols for imidazoles reported so far suffer from one or more disadvantages such as harsh reaction conditions, poor yields, prolonged time period, use of hazardous and often expensive acid catalysts. Moreover, the synthesis of these heterocycles have been usually carried out in polar solvents such as ethanol, methanol, acetic acid, DMF and DMSO leading to complex isolation and recovery procedures. These processes also generate waste containing catalyst and solvent, which have to be recovered, treated and disposed off.

One of the biggest problems posed to the chemical industry is to continuously deal with the fact that all chemical plants

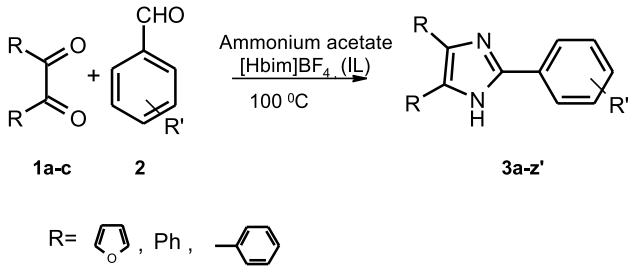
*Keywords*: 2,4,5-Triaryl imidazoles; Ionic liquid (IL); Ammonium acetate; Benzaldehydes; 1,2-Diketones; α-Hydroxyketone.
* Corresponding author. Tel.: +91 20 25889089; fax: +91 20 25893614; e-mail: kvsri@dalton.ncl.res.in

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.01.116

rely heavily on toxic, hazardous and flammable organic solvents. Organic solvents used in most of the synthetic processes in chemical industries evaporate into the atmosphere with detrimental effects on the environment as well as human health. Most of the time, these volatile organic solvents are expensive to purchase, difficult to recycle or reuse, and impractical to dispose of without incurring substantial costs and/or adversely affecting the environment and/or personnel.

Recently, room temperature ionic liquids (RTILs) have attracted much attention as promising alternative 'green' solvents to hazardous traditional organic solvents, due to their properties such as non-flammability, negligible vapour pressure, high thermal stability, solvating ability and easy recyclability.[7] They have the potential to be highly polar yet non-coordinating. In addition to the above-mentioned salient features of ionic liquids (ILs) as reaction media, we have also recently shown that they can promote and catalyze important organic transformations under ambient conditions without the need for any added catalyst or ligand. The reactions investigated by us are Heck and Suzuki reactions,[24] bromination of aromatics,[25] Friedlander heteroannulation,[26] synthesis of benzodiazepines, benzimidazoles and benzthiazole,[27] which proceed with significantly enhanced reaction rates, high regioselectivity and excellent isolated yields.

As part of an ongoing development of efficient protocols for the preparation of biologically active heterocycles from common intermediates using RTILs, we herein report for the first time, a one-pot condensation of 1,2-diketones or α-hydroxy ketone, aromatic aldehydes and ammonium acetate in the IL, 1-butyl imidazolium tetrafluoroborate ([Hbim]$BF_4$) which afforded a diverse array of 2,4,5-triaryl imidazoles in excellent isolated yields in the absence of any added catalyst.




**Scheme 1.**

**Table 1**. Synthesis of imidazole **3k** in [bbim] X

| ILs | p$K_a$[a] | $E_T$ (30) (kcal mol$^{-1}$)[28] | Yield[b] (%) |
|---|---|---|---|
| [bbim]$ClO_4$ | −11 | 76.34 | 21 |
| [bbim]Br | −9 | 66.49 | 27 |
| [bbim]Cl | −7 | 68.89 | 29 |
| [bbim]$BF_4$ | 0.5 | 75.73 | 43 |

[a] The p$K_a$ values of the parent acid of the anions.[29]
[b] Isolated yield after column chromatography.

## 2. Results

### 2.1. Synthesis of 2,4,5-triaryl imidazoles from 1,2-diketones

Ionic liquids (ILs) based on 1,3-di-*n*-butyl imidazolium salts [bbim]X and *N*-butyl imidazolium salts [Hbim]X with varying basicity of anions were tested as solvents and promoters for the typical reaction of 1,2-diphenyl-ethane-1,2-dione (**1b**) with *p*-anisaldehyde in the absence of any added catalyst to afford 2-(4-methoxy-phenyl)-4,5-diphenyl-1*H*-imidazole (**3k**) (Scheme 1). The reactions in the various ILs were carried out at 100 °C for 24 h. The yield data are recorded in Tables 1 and 2.

The polarity of different ionic liquids based on 1,3-di-*n*-butyl imidazolium salts and 1-*n*-butyl imidazolium salts were evaluated using Reichardt's dye as per the procedure reported.[28] The p$K_a$ values are those of the parent acid of the anions and taken from literature.[29]

It was observed that for a typical reaction of **1b** with *p*-anisaldehyde at the reaction temperature of 90 °C, the conversion does not go beyond 45% even after 24 h and at 130 °C the IL decomposed to give a black charry material. Hence, a reaction temperature of 100 °C was found to be optimum.

It becomes evident from these results, that the IL [Hbim]$BF_4$ afforded the best results. Consequently, all further studies were conducted using this IL as the reaction medium and promoter to generate a variety of imidazoles (**3a**–**z′**) by the reaction of 1, 2-di-furan-2-yl-ethane-1,2-dione (**1a**), 1,2-diphenyl-ethane-1,2-dione (**1b**) and 1,2-di-*p*-toluyl-ethane-1,2-dione (**1c**) with benzaldehydes (**2**), and ammonium acetate, respectively at 100 °C (Scheme 1).

The results are recorded in Table 3. All the reactions proceed to completion at the time indicated in the Table 3 and the yield data are for the isolated products after column chromatography. All the compounds were well characterized by melting point, IR, $^1$H NMR and $^{13}$C NMR. Their elemental analyses were in conformity with their structures.

**Table 2**. Synthesis of imidazole **3k** in [Hbim]X

| ILs | p$K_a$[a] | Chemical shift –NH proton δ ppm | $E_T$ (30) (kcal mol$^{-1}$)[28] | Yield[b] (%) |
|---|---|---|---|---|
| [Hbim]$ClO_4$ | −11 | 11.83 | 63.82 | 61 |
| [Hbim]Br | −9 | 12.17 | 73.68 | 81 |
| [Hbim]Cl | −7 | 12.22 | 73.59 | 80 |
| [Hbim]$BF_4$ | 0.5 | 14.59 | 74.35 | 95 |

[a] The p$K_a$ values of the parent acid of the anions.[29]
[b] Isolated yield after column chromatography.

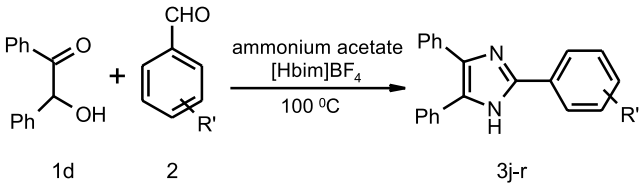
**Table 3**. Syntheses of imidazoles **3a–z′** from 1,2-diketones

| Sr. no. | Imidazole **3** | | | Time (min) | Yield[a] (%) |
|---|---|---|---|---|---|
| | R | R′ | **3a–z′** | | |
| 1 | *o*-Furyl | H | **3a** | 25 | 93 |
| 2 | *o*-Furyl | *p*-OMe | **3b** | 25 | 94 |
| 3 | *o*-Furyl | *o*-OH | **3c** | 35 | 92 |
| 4 | *o*-Furyl | *p*-OH | **3d** | 40 | 93 |
| 5 | *o*-Furyl | *o*-Cl | **3e** | 70 | 85 |
| 6 | *o*-Furyl | *p*-Br | **3f** | 65 | 92 |
| 7 | *o*-Furyl | *o*-OH, *m*-OMe | **3g** | 70 | 88 |
| 8 | *o*-Furyl | *m*-OMe, *p*-OH | **3h** | 75 | 85 |
| 9 | *o*-Furyl | *p*-$NO_2$ | **3i** | 70 | 87 |
| 10 | Phenyl | H | **3j** | 60 | 95 |
| 11 | Phenyl | *p*-OMe | **3k** | 60 | 95 |
| 12 | Phenyl | *o*-OH | **3l** | 70 | 93 |
| 13 | Phenyl | *p*-OH | **3m** | 90 | 94 |
| 14 | Phenyl | *o*-Cl | **3n** | 70 | 96 |
| 15 | Phenyl | *p*-Br | **3o** | 65 | 95 |
| 16 | Phenyl | *o*-OH, *m*-OMe | **3p** | 60 | 95 |
| 17 | Phenyl | *m*-OMe, *p*-OH | **3q** | 70 | 87 |
| 18 | Phenyl | *p*-$NO_2$ | **3r** | 60 | 94 |
| 19 | *p*-Tolyl | H | **3s** | 60 | 91 |
| 20 | *p*-Tolyl | *p*-OMe | **3t** | 60 | 88 |
| 21 | *p*-Tolyl | *o*-OH | **3u** | 70 | 90 |
| 22 | *p*-Tolyl | *p*-OH | **3v** | 100 | 93 |
| 23 | *p*-Tolyl | *o*-Cl | **3w** | 110 | 98 |
| 24 | *p*-Tolyl | *p*-Br | **3x** | 95 | 87 |
| 25 | *p*-Tolyl | *o*-OH, *m*-OMe | **3y** | 110 | 91 |
| 26 | *p*-Tolyl | *m*-OMe, *p*-OH | **3z** | 120 | 87 |
| 27 | *p*-Tolyl | *p*-$NO_2$ | **3z′** | 70 | 87 |

[a] Isolated yield after column chromatography.

## 2.2. Synthesis of 2,4,5-triaryl imidazoles from α-hydroxy ketone, benzoin (1d)

Although there are several papers reporting the synthesis of tri-substituted imidazoles using 1,2-diketones, there are very few reports in the literature using α-hydroxyl-ketone as starting material. We found that our methodology works very well even for a α-hydroxyl-ketone such as benzoin (**1d**) under similar conditions to those used for the 1,2-diketones (Scheme 2). The results are summarized in Table 4.




**Scheme 2.**

## 3. Discussion

It is important to note that in all the cases, imidazoles were precipitated on dilution of the reaction mixtures with water and were isolated by a simple filtration. The dried product thus obtained showed a single spot on TLC and was pure enough for all practical purposes. The aqueous filtrate was then subjected to distillation at 80 °C under reduced pressure (10 mmHg) for 4 h to recover the IL almost

**Table 4**. Synthesis of imidazoles **3j–r** from benzoin

| Sr. no. | Imidazole **3** | | | Time (min) | Yield[a] (%) |
|---|---|---|---|---|---|
| | R | R′ | **3j–r** | | |
| 1 | Phenyl | H | **3j** | 60 | 95 |
| 2 | Phenyl | *p*-OMe | **3k** | 60 | 95 |
| 3 | Phenyl | *o*-OH | **3l** | 70 | 93 |
| 4 | Phenyl | *p*-OH | **3m** | 90 | 94 |
| 5 | Phenyl | *o*-Cl | **3n** | 70 | 96 |
| 6 | Phenyl | *p*-Br | **3o** | 65 | 95 |
| 7 | Phenyl | *o*-OH, *m*-OMe | **3p** | 60 | 95 |
| 8 | Phenyl | *m*-OMe, *p*-OH | **3q** | 70 | 87 |
| 9 | Phenyl | *p*-$NO_2$ | **3r** | 60 | 94 |

[a] Isolated yield after column chromatography.

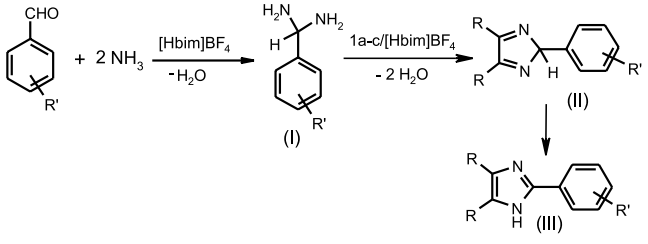
completely. The IL, thus recovered could be reused three times without loss of activity for the typical reaction of **1b** or **1d** with anisaldehyde.

The 2,4,5-triaryl imidazoles have been obtained in excellent isolated yields in relatively short reaction times. It can be observed that the process tolerates both electron donating and electron withdrawing substituents on the aldehyde. This methodology also gives the imidazoles using the 1,2-diketone or α-hydroxy ketone in more or less the same yield and same reaction period. It is worth noting here that 1,2-diketones such as benzil (**1b**) are usually prepared from benzoins catalysed by various toxic oxidants.[30] Consequently, the direct use of benzoin (**1d**) in our methodology constitutes a significant improvement in the synthesis of tri-substituted imidazoles towards green chemistry.

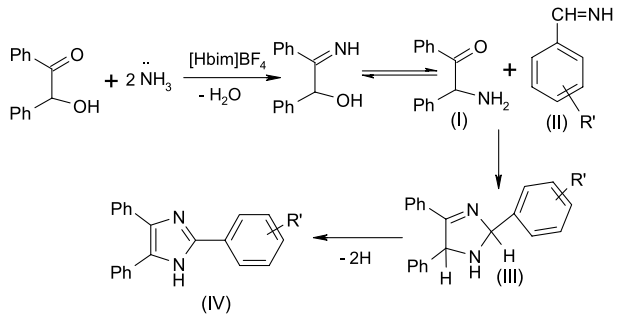
A typical reaction of **1b** with anisaldehyde under similar conditions in the absence of a catalyst using molecular solvents such as ethanol, toluene, DMF, DMSO showed no conversion beyond 30% even after 24 h and acetic acid gave 80% conversion only even after 6 h, thus highlighting the role of the IL in promoting the reaction.

The efficacy of the ILs to promote these heterocyclization reactions was correlated to the basicity of the anions of the ILs as well as the polarity of ionic liquids. The polarity of ionic liquids in terms of $E_T$ values was measured by using Reichardt's dye as reported earlier.[28] It was assumed that the nature of the anion would govern the electrophilicity of the imidazolium cation, which in turn has a bearing on the acidity of the ILs. It was observed that with increasing basicity of the anion (increasing p$K_a$ of the corresponding acid), there is a progressive increase in yield (Tables 1 and 2). This correlation was also evident when the yield of **3k** was compared with –NH proton chemical shifts of the ILs indicative of the Bronsted acidities of the [Hbim] ILs (Table 2). The yield of **3k** increases progressively not only with increasing Bronsted acidity of the ILs as indicated by the increasing downfield shift of the NH proton but also with increasing polarity of these ILs as indicated by their $E_T$ values.

The IL, [Hbim]$BF_4$ has promoted this heterocyclization reaction by virtue of its inherent Brønsted acidity conferred by the most acidic –N–H hydrogen [chemical shift $\delta$ ppm = 14.6]. This makes the IL capable of bonding with the carbonyl oxygen increasing the reactivities of the parent carbonyl compounds. Evidence in the form of significant $^{13}$C NMR and IR spectral shifts of the carbonyl group by its




**Scheme 3.**




**Scheme 4.**

interaction with [Hbim]$BF_4$ has already been given in a previous communication by us.[31] Based on this, the following probable mechanisms may be postulated for this methodology as shown in Schemes 3 and 4. In both the mechanisms, the IL promotes the splitting of ammonium acetate to generate the ammonia required for the initial condensation.

For the postulated mechanism starting from 1,2-diketone (Scheme 3). The IL may facilitate the formation of a diamine intermediate I, which under Brønsted acid catalysis of the IL condenses with the carbonyl carbons of the 1,2-diketone followed by dehydration to afford the imino intermediate II, which rearranges to the required tri-aryl imidazole III.

A probable mechanism for the synthesis involving benzoin may be postulated as shown above (Scheme 4). It is highly probable that the Brønsted acidity of the IL may have promoted the formation of α-amino ketone I, aryl aldimine II, their subsequent condensation and intramolecular cyclization to the imidazoline III which dehydrogenates to the triaryl imidazoles IV. It was thought that the dissolved oxygen in the IL may have brought about the formal oxidation of the imidazoline III. However, this possibility was discounted by subjecting the IL to a degassing protocol using an ultrasonic cleaning bath (Transsonic Model T710DH) at 40 KHz in the degassing mode at a reduced pressure of 15 mmHg for 2 h. The degassed IL was well flushed with argon and the typical reaction of benzoin with benzaldehyde was performed in it using an inert atmosphere of argon. Even under such conditions, no trace of the formation of the imidazoline III was observed (TLC and $^1$H NMR) and the triarylimidazole **3j** was obtained in excellent isolated yield (95%). It seems probable that apparently the fully conjugated nature of the product results in rapid oxidation in this case aided by the large chemical window and polarity of the IL.

Alternatively, the probability of benzoin itself undergoing oxidation under these conditions to benzil was explored. Thus, a solution of benzoin in the degassed IL was heated at 100 °C for 1 h in an atmosphere of argon. To our surprise, benzoin was converted to benzil in 85% isolated yield. The benzil so formed then can follow the pathway shown in Scheme 3 to afford the triaryl imidazoles. Further work is in progress to establish the role of the IL in such oxidations.

## 4. Conclusion

In conclusion, we have developed a mild, convenient and efficient protocol for the synthesis of biologically active 2,4,5-triaryl imidazoles via the condensation of 1,2-diketones and α-hydroxy ketones such as benzoin with aromatic aldehydes and ammonium acetate using a room temperature ionic liquid as a recyclable medium as well as promoter. The process gives rise to excellent isolated yields of 2,4,5-triaryl imidazoles in short reaction times (25–120 min). The reaction times achieved are shorter than those hitherto reported under thermal conditions excluding those wherein microwave assisted synthesis are carried out. Consequently, this methodology becomes an efficient strategy for the rapid synthesis of highly substituted imidazole libraries in a recyclable homogeneous medium in the absence of a catalyst. The corresponding reaction in molecular solvents under similar conditions in the absence of a catalyst are sluggish and poor yielding, highlighting the role of the IL in promoting this novel one-pot methodology. The experimental procedure, combining the features of simple isolation procedure, efficient recovery, and recycling of IL and the absence of a catalyst makes this an environmentally benign methodology amenable for scale up.

## 5. Experimental

### 5.1. General

NMR spectra were recorded on a Bruker AC-200 spectrometer in $CDCl_3$/DMSO-$d_6$ with TMS as an internal standard. Infra red spectra were recorded with ATI MATT-SON RS-1 FTIR spectrometer. Polarity of ILs was recorded on Lambda EZ 201, using Reichardt's dye. Melting points were recorded in open capillary and were uncorrected. All solvents and chemicals were of research grade and were used as obtained from Merck and Lancaster.

### 5.2. Typical procedure for synthesis of 2,4,5-triaryl imidazoles from 1,2-diketones or α-hydroxyketone

The ILs were prepared as per the procedure reported by us earlier.[26]

A mixture of 1,2-diketones (**1a**, **1b** or **1c**) or the α-hydroxyketone (benzoin) (**1d**) (4 mmol), substituted aldehydes (**2**, 4 mmol), ammonium acetate (10 equiv) and $[Hbim]BF_4$ (4 mmol) was heated at 100 °C with good stirring for the appropriate time mentioned in Tables 3 and 4. The completion of reaction was monitored by TLC using 25% ethyl acetate in petroleum ether. After completion of reaction, the reaction mixture was diluted with water (25 ml). The solid imidazole products, which separated out, were filtered, washed with water and dried. The crude products, thus isolated, were pure (single spot on TLC). They were subjected to further purification by chromatography through a column of silica-gel using 25% EtOAc in petroleum ether as eluent to yield the desired substituted imidazoles in excellent yields of 84–95% and were fully characterized.

The aqueous layer consisting of the IL was subjected to distillation (80 °C at 10 mmHg) for 4 h to remove water, leaving behind the IL $[Hbim]BF_4$ (recovery 98%), which was recycled.

### 5.3. Spectral data for compounds 3a–z′

**5.3.1. 4,5-Difuran-2-yl-2-phenyl-1*H*-imidazole (3a).** Mp 218 °C; IR ($cm^{-1}$) 718, 890, 1448, 1602, 3058; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.13–6.18 (dd, $J=7.5$ Hz, 2H), 6.85–6.89 (d, $J=8$ Hz, 2H), 7.18 (s, 2H), 7.22–7.48 (m, 5H), 12.42 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 106.9, 110.7, 123.9, 125.6, 127.7, 127.9, 128.9, 140.2, 146.1, 146.3; $C_{17}H_{12}N_2O_2$ (276): calcd C, 73.91, H, 4.34, N, 10.14; found C, 73.82, H, 4.24, N, 10.10.

**5.3.2. 4,5-Difuran-2-yl-2(4-methoxy-phenyl-1*H*-imidazole (3b).** Mp 198 °C; IR ($cm^{-1}$) 708, 880, 1508, 1610, 3105; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 3.75 (s, 3H), 6.14–6.19 (dd, $J=8$ Hz, 2H), 6.83–6.86 (dd, $J=8.5$ Hz, 2H), 7.16 (s, 2H), 7.41 (dd, $J=8$ Hz, 2H), 7.79–7.82 (dd, $J=8$ Hz, 2H), 12.53 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 54.5, 105.2, 111.6, 114.6, 128.0, 128.8, 142.2, 154.1, 162.0; $C_{18}H_{14}N_2O_3$ (306): calcd C, 70.58, H, 4.61, N, 9.15; found C, 70.42, H, 4.52, N, 9.10.

**5.3.3. 2-(4,5-Difuran-2-yl-1*H*-imidazole-2yl)-phenol (3c).** Mp 235 °C; IR ($cm^{-1}$) 718, 870, 1416, 1615, 3108, 3528; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.13–6.16 (dd, $J=7$ Hz, 2H), 6.18–6.23 (dd, $J=8.3$ Hz, 2H) 6.85–7.15 (m, 4H) 7.16 (s, 2H), 12.38 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 115.3, 121.6, 122.8, 124.5, 126.8, 127.3, 130.1, 135.1, 146.5; $C_{17}H_{12}N_2O_3$ (292): calcd C, 69.86, H, 4.10, N, 9.58; found C, 69.58, H, 3.92, N, 9.75.

**5.3.4. 4-(4,5-Difuran-2-yl-1*H*-imidazole-2yl)-phenol (3d).** Mp 223 °C; IR ($cm^{-1}$) 715, 860, 1416, 1615, 3108, 3550; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.14–6.18 (dd, $J=8$ Hz, 2H), 6.49–6.61 (dd, $J=7.5$ Hz, 2H) 6.85–6.89 (dd, $J=7$ Hz, 2H), 7.16 (s, 2H), 7.23–7.28 (dd, $J=8$ Hz, 2H), 12.41 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 116.3, 121.6, 123.4, 130.1, 134.9, 146.4; $C_{17}H_{12}N_2O_3$ (292): calcd C, 69.86, H, 4.1, N, 9.58; found C, 69.68, H, 3.91, N, 9.73.

**5.3.5. 2-(2-Chloro-phenyl) 4,5-difuran-1*H*-imidazole (3e).** Mp 240 °C; IR ($cm^{-1}$) 716, 865, 1420, 1618, 3110; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.31–6.39 (dd, $J=7$ Hz, 4H), 7.31–7.40 (d, $J=7$ Hz, 2H) 7.16–7.42 (m, 4H) 12.58 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 105, 111.6, 122.1, 127.1, 128.4, 129.9, 132.1, 135.9, 136.9, 142.2, 154.1; $C_{17}H_{11}N_2O_2Cl$ (311): calcd C, 65.59, H, 3.53, N, 9.0; found C, 65.48, H, 3.49, N, 8.93.

**5.3.6. 2-(4-Bromo-phenyl) 4,5-difuran-1*H*-imidazole (3f).** Mp 228 °C; IR ($cm^{-1}$) 708, 1416, 1608, 3108; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.28–6.33 (dd, $J=7$ Hz, 4H), 7.3–7.4 (d, $J=7$ Hz, 2H), 7.54–7.58 (d, $J=8.22$ Hz, 2H), 8.02–8.06 (d, $J=8.60$ Hz, 2H), 12.78 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 105.8, 111.6, 122.1, 127.1, 128.4, 129.4, 129.9, 132.1, 135.5, 136.4, 142.2, 154.2; $C_{17}H_{11}N_2O_2Br$ (355): calcd C, 57.46, H, 3.09, N, 7.88; found, C, 57.32, H, 2.98, N, 7.81.

**5.3.7. 2-(4,5-Difuran-1*H*-imidazol-2-yl)-6-methoxy phenol (3g).** Mp 238 °C; IR ($cm^{-1}$) 715, 864, 1416, 1610, 3130, 3600; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 3.65 (s, 3H), 6.30–6.33 (dd, $J=7$ Hz, 4H), 7.31–7.40 (d, $J=7$ Hz, 2H), 7.55–7.58 (m, 3H), 12.71 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 105.2, 111.6, 115.5, 120.2, 122.6, 124.2, 127.1, 140.1, 152.3, 156.2; $C_{18}H_{14}N_2O_4$ (322): calcd C, 67.08, H, 4.34, N, 8.69; found C, 66.98, H, 4.29, N, 8. 62.

**5.3.8. 2-(4,5-Difuran-1*H*-imidazol-2-yl)-2-methoxy phenol (3h).** Mp 225 °C; IR ($cm^{-1}$) 715, 864, 1416, 1610, 3130, 3600; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 3.87 (s, 3H), 6.47–6.49 (dd, $J=5$ Hz, 2H), 7.30–7.40 (d, $J=7$ Hz, 2H), 7.55–7.58 (m, 3H), 12.72 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 105.0, 111.6, 115.5, 120.0, 122.6, 124.0, 127.1, 140.1, 152.0, 156.0; $C_{18}H_{14}N_2O_4$ (322): calcd C, 67.08, H, 4.34, N, 8.69; found C, 66.98, H, 4.29, N, 8.62.

**5.3.9. 2-(4-Nitro-phenyl) 4,5-difuran-1*H*-imidazole (3i).** Mp 208 °C (decomposes); IR ($cm^{-1}$) 718, 865, 1408, 1605, 3120; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.29–6.33 (dd, $J=7.5$ Hz, 4H), 7.31–7.40 (d, $J=7$ Hz, 2H), 7.78–7.79 (d, $J=9$ Hz, 2H), 8.51–853 (d, $J=9$ Hz, 2H), 12.69 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 105.3, 111.6, 122.3, 124.1, 127.9, 136.3, 142.3, 142.6, 148.4, 154.4; $C_{17}H_{11}N_3O_4$ (321): calcd C, 63.55, H, 3.42, N, 13.08; found C, 63.45, H, 3.38, N, 12.98.

**5.3.10. 2,4,5-Triphenyl-1*H*-imidazole (3j).** Mp 269 (275[32]) °C; IR ($cm^{-1}$) 1216, 1638, 2470, 2993, 3434; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz): $\delta$ 7.42–8.12 (m, 15H), 12.61 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz): $\delta=122.1$, 127.2, 128.5, 129.1, 136.5; $C_{21}H_{16}N_2$ (296): calcd C, 85.11, H, 5.44, N, 9.45; found C, 85, H, 5.28, N, 9.35.

**5.3.11. 2-(4-Methoxy-phenyl)-4,5-diphenyl-1*H*-imidazole (3k).** Mp 222 °C; IR ($cm^{-1}$) 1216, 1636, 2465, 2893, 3428; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 3.85 (s, 3H), 6.93–6.96 (d, $J=8.8$ Hz, 2H), 7.25–7.59 (m, 10H), 8.02–8.05 (d, $J=8.8$ Hz, 2H), 12.52 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 54.6, 113.2, 122.7, 126.3, 126.5, 127.4, 127.6, 132.8, 145.7, 159.1; $C_{22}H_{18}N_2O$ (326): calcd C, 80.96, H, 5.56, N, 8.58; found C, 80.85, H, 5.48, N, 8.38.

**5.3.12. 2-(4,5-Diphenyl-1*H*-imidazol-2-yl)-phenol (3l).** Mp 205 °C; IR ($cm^{-1}$) 1216, 1638, 2465, 2998, 3432, 3596; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.87–6.95 (d, $J=7.5$ Hz, 2H), 6.97–7.01 (d, $J=8.06$ Hz, 2H), 7.17–7.23 (m, 10H), 12.74 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 112.7, 116.4, 118.1, 124.8, 126.8, 127.4, 127.8, 129.1, 145.7, 156.6; $C_{21}H_{16}N_2O$ (312): calcd C, 80.75, H, 5.16, N, 8.97; found C, 80.62, H, 5.08, N, 8.85.

**5.3.13. 4-(4,5-Diphenyl-1*H*-imidazol-2-yl)-phenol (3m).** Mp 233 °C; IR ($cm^{-1}$) 1216, 1638, 2465, 2998, 3432, 3596; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 6.93–6.97 (d, $J=8$ Hz, 2H), 7.52–7.87 (m, 10H), 7.88–7.92 (d, $J=8.5$ Hz, 2H), 12.58 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 113.7, 119.9, 125.1, 125.3, 126.1, 126.5, 144.7, 159.2; $C_{21}H_{16}N_2O$ (312): calcd C, 80.75, H, 5.16, N, 8.97; found C, 80.68, H, 5.05, N, 8.90.

**5.3.14. 2-(2-Chloro-phenyl)-4,5-diphenyl-1*H*-imidazole (3n).** Mp 188 °C; IR ($cm^{-1}$) 1216, 1638, 2470, 2993, 3434; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 7.27–7.37 (m, 10H), 7.45–7.49 (dd, $J=9$ Hz, 1H), 7.57–7.59 (d, $J=8$ Hz, 2H), 8.02–8.05 (dd, $J=8.79$ Hz, 1H), 12.5 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 125.4, 125.6, 126.5, 126.9, 127.2, 128.4, 128.6, 128.8, 129.6, 130.1, 130.5, 142.2; $C_{21}H_{15}ClN_2$ (330): calcd C, 76.24, H, 4.57, N, 8.47; found C, 76.12, H, 4.49, N, 8. 38.

**5.3.15. 2-(4-Bromo-phenyl)-4,5-diphenyl-1*H*-imidazole (3o).** Mp 248 °C; IR ($cm^{-1}$) 1261, 1645, 2255, 2473, 3417; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 7.25–7.48 (m, 10H), 7.50–7.52 (d, $J=8$ Hz, 2H), 7.80–7.92 (d, $J=8.6$ Hz, 2H), 12.49 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 120.1, 125.5, 126.3, 126.7, 127.1, 128.1, 129.5, 129.9, 130.5, 143.3; $C_{21}H_{15}BrN_2$ (374): calcd C, 67.21, H, 4.03, N, 7.47; found C, 67.10, H, 3.95, N, 7. 32.

**5.3.16. 2-(4,5-Diphenyl-1*H*-imidazol-2-yl)-6-methoxy phenol (3p).** Mp 170 °C; IR ($cm^{-1}$) 1253, 1654, 2925, 3412, 3610; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 3.86 (s, 3H), 6.82–6.85 (m, 3H), 7.29–7.32 (m, 5H), 7.53–7.55 (m, 5H), 12.5 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 54.7, 110.9, 112.1, 155.6, 117.1, 126.3, 126.7, 127.3, 127.4, 129.8, 145.1, 146.1, 147.3; $C_{22}H_{18}N_2O_2$ (342): calcd C, 77.17, H, 5.30, N, 8.18; found C, 77.08, H, 5.18, N, 8.02.

**5.3.17. 2-(4,5-Diphenyl-1*H*-imidazol-2-yl)-2-methoxy phenol (3q).** Mp 197 °C; IR ($cm^{-1}$) 1230, 1450, 1605, 2924, 3512, 3614; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 3.80 (s, 3H), 6.75–6.69 (d, $J=8.22$ Hz, 1H), 7.11–7.19 (m, 5H), 7.22–7.23 (d, $J=8.1$ Hz, 1H), 7.40–7.45 (m, 5H), 7.55–7.56 (d, $J=8$ Hz, 1H), 12.52 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 55.1, 108.5, 114.6, 118.1, 121.1, 126.2, 127.3, 127.5, 132.3, 146.3, 146.8; $C_{22}H_{18}N_2O_2$ (342): calcd C, 77.17, H, 5.30, N, 8.18; found C, 77.05, H, 5.18, N, 8.02.

**5.3.18. 2-(4-Nitro-phenyl)-4,5-diphenyl-1*H*-imidazole (3r).** Mp 196 °C (decomposes); IR ($cm^{-1}$) 845, 1443, 1522, 1540, 1602, 3056; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 7.25–7.57 (m, 10H), 7.78 (d, $J=9$ Hz, 2H), 8.50 (d, $J=9$ Hz, 2H), 12.59 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 122.7, 124.2 127.3, 127.6, 132.8, 146.7, 160.8; $C_{21}H_{15}N_3O_2$ (341): calcd C 73.88, H 4.43, N 12.31; found C 73.85, H 4.38, N 12.25.

**5.3.19. 2-Phenyl-4,5-di-*p*-tolyl-1*H*-imidazole (3s).** Mp 254 °C; IR ($cm^{-1}$) 1216, 1638, 2465, 2998, 3432; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.36 (s, 6H), 7.14–7.34 (m, 8H), 7.35–7.38 (m, 5H), 12.56 (brs, 1H); $^{13}C$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.7, 124.1, 126.4, 126.6, 127.1, 127.5, 127.7, 128.3, 129.1, 129.2, 135.1; $C_{23}H_{20}N_2$ (324): calcd C, 85.15, H, 6.21, N, 8.63; found C, 85, H, 6.11, N, 8. 50.

**5.3.20. 2-(4-Methoxy-phenyl)-4,5-di-*p*-tolyl-1*H*-imidazole (3t).** Mp 243 °C; IR ($cm^{-1}$) 1216, 1638, 2475, 2988, 3430; $^1H$ NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.37 (s, 6H), 3.86 (s, 3H), 6.94–6.96 (d, $J=8.25$ Hz, 2H), 7.13–7.15 (m, 4H), 7.46–7.48 (m, 4H), 8.03–8.05 (d, $J=8.25$ Hz, 2H),

12.59 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 20.2, 54.3, 112.9, 122.6, 126.1, 126.9, 128.1, 135.4, 145.1, 158.6; $C_{24}H_{22}N_2O$ (354): calcd C, 81.33, H, 6.26, N, 7.90; found C, 81.20, H, 6.11, N, 7.58.

**5.3.21. 2-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl) phenol (3u).** Mp 223 °C; IR (cm$^{-1}$) 1216, 1638, 2465, 2998, 3432, 3596; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.36 (s, 6H), 6.85–6.90 (t, $J$=8.3 Hz, 1H), 6.95–6.98 (d, $J$=8.06 Hz, 1H), 7.14–7.17 (m, 4H), 7.21–7.23 (d, $J$=7.33 Hz, 1H), 7.43–7.46 (m, 4H), 7.96–7.99 (d, $J$=8.06 Hz, 1H), 12.84 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.7, 114.2, 118.5, 126.1, 126.5, 126.8, 127.6, 127.7, 127.9, 129.7, 135.5, 144.4, 157.2; $C_{23}H_{20}N_2O$ (340): calcd C, 81.15, H, 5.92, N, 8.23; found C, 81.05, H, 5.81, N, 8.18.

**5.3.22. 4-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl) phenol (3v).** Mp 218 °C; IR (cm$^{-1}$) 1216, 1638, 2465, 2975, 3422, 3610; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.38 (s, 6H), 6.88–6.92 (d, $J$=8.61 Hz, 2H), 7.15–7.19 (m, 4H), 7.41–7.45 (m, 4H), 7.91–7.96 (d, $J$=8.61 Hz, 2H), 12.77 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.7, 114.2, 118.5, 126.1, 126.5, 126.8, 127.6, 127.7, 127.9, 129.7, 135.5, 144.4, 157.2; $C_{23}H_{20}N_2O$ (340): calcd C, 81.15, H, 5.92, N, 8.23; found C, 81.10, H, 5.85, N, 8.18.

**5.3.23. 2-(2-Chlor-phenyl)-4,5-di-*p*-tolyl-1*H*-imidazole (3w).** Mp 195 °C; IR (cm$^{-1}$) 1216, 1638, 2465, 2998, 3432; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.39 (s, 6H), 7.27–7.37 (m, 8H), 7.45–7.49 (dd, $J$=9 Hz, 1H), 7.57–7.59 (d, 2H), 8.02–8.05 (dd, $J$=8.79 Hz, 1H), 12.54 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.6, 125.4, 125.6, 126.5, 126.9, 127.2, 128.4, 128.7, 128.8, 129.7, 130.1, 130.6, 142.2; $C_{23}H_{19}ClN_2$ (358): calcd C, 76.98, H, 5.34, N, 7.81; found C, 76.88, H, 5.28, N, 7.72.

**5.3.24. 2-(4-Bromo-phenyl)-4,5-di-*p*-tolyl-1*H*-imidazole (3x).** Mp 215 °C; IR (cm$^{-1}$) 1216, 1638, 2465, 2978, 3432; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.35 (s, 6H), 7.11–7.15 (m, 4H), 7.42–7.46 (m, 4H), 7.54–7.58 (d, $J$=8.22 Hz, 2H), 8.02–8.06 (d, $J$=8.60 Hz, 2H), 12.78 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.4, 119.8, 125.4, 126.1, 127.3, 129.8, 134.7, 142.8; $C_{23}H_{19}BrN_2$ (402): calcd C, 68.49, H, 4.75, N, 6.95; found C, 68.38, H, 4.68, N, 6.82.

**5.3.25. 2-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl)-6-methoxy-phenol (3y).** Mp 230 °C; IR (cm$^{-1}$) 1216, 1638, 2475, 2978, 3442, 3616; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.36 (s, 6H), 3.79 (s, 3H), 6.82–6.85 (m, 3H), 7.31–7.34 (m, 4H), 7.55–7.58 (m, 4H), 12.71 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.4, 54.7, 110.9, 112.1, 155.6, 117.1, 126.3, 126.7, 127.3, 127.4, 129.8, 145.1, 146.1, 147.3; $C_{24}H_{22}N_2O_2$ (370): calcd C, 77.81, H, 5.99, N, 7.56; found C, 77.68; H, 5.89, N, 7.47.

**5.3.26. 4-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl)-2-methoxy-phenol (3z).** Mp 245 °C; IR (cm$^{-1}$) 1216, 1638, 2475, 2988, 3422, 3616; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.37 (s, 6H), 3.80 (s, 3H), 6.75–6.69 (d, $J$=8.22 Hz, 1H), 7.14–7.19 (m, 4H), 7.23–7.25 (d, $J$=8.7 Hz, 1H), 7.43–7.47 (m, 4H), 7.56–7.57 (d, $J$=8.3 Hz, 1H), 12.72 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 19.4, 55.1, 108.7, 114.7, 118.1, 121.2, 126.3, 127.3, 127.5, 132.3, 146.4, 146.9; $C_{24}H_{22}N_2O_2$ (370): calcd C, 77.81, H, 5.99, N, 7.56; found C, 77.72; H, 5.89, N, 7.47.

**5.3.27. 2-(4-Nitro-phenyl)-4,5-di-*p*-tolyl-1*H*-imidazole (3z′).** Mp 198 °C (decomposes); IR (cm$^{-1}$) 845, 1443, 1522, 1540, 1602, 3056; $^1$H NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 2.37 (s, 6H) 7.25–7.57 (m, 8H), 7.78 (d, $J$=9 Hz, 2H), 8.5 (d, $J$=9 Hz, 2H), 12.59 (brs, 1H); $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$, 200 MHz) $\delta$ 122.8, 124.3, 127.3, 127.6, 132.8, 146.7, 160.8; $C_{23}H_{20}N_3O_2$ (370): calcd C, 74.58, H, 5.44, N, 11.34; found C, 74.49, H, 5.40, N, 11.28.

## Acknowledgements

SAS and SSP thank CSIR, New Delhi, for the award of Research Fellowships. The authors also acknowledge financial assistance from Department of Science and Technology (DST), New Delhi, vide Project No. SR/S5/OC-23/2002).

## References and notes

1. Debus, H. *Liebigs Ann. Chem.* **1858**, *107*, 199–208.
2. (a) Lambardino, J. G.; Wiseman, E. H. *J. Med. Chem.* **1974**, *17*, 1182–1188. (b) Philips, A. P.; White, H. L.; Rosen, S. *Eur. Pat. Appl.* EP 58890, 1982.
3. Lee, J. C.; Laydon, J. T.; McDonnell, P. C.; Gallagher, T. F.; Kumar, S.; Green, D.; McNulty, D.; Blumenthal, M.; Heys, J. R.; Landvatter, S. W.; Strickler, J. E.; McLaughlin, M. M.; Siemens, I. R.; Fisher, S. M.; Livi, J. P.; White, J. R.; Adams, J. L.; Young, P. R. *Nature* **1994**, *372*, 739–746.
4. Maier, T.; Schmierer, R.; Bauer, K.; Bieringer, H.; Buerstell, H.; Sachse, B. US Patent 4820335, **1989**; *Chem. Abstr.* **1989**, *111*, 19494.
5. Schmierer, R.; Mildenberger, H.; Buerstell, H. German Patent 361464, **1987**; *Chem. Abstr.* **1988**, *108*, 37838.
6. Heeres, J.; Backx, L. J. J.; Mostmans, J. H.; Van Custem, J. *J. Med. Chem.* **1979**, *22*, 1003–1005.
7. (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2084. (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3772–3789.
8. (a) Hermann, W. A.; Kocher, C. *Angew. Chem., Int. Ed. Eng.* **1997**, *36*, 2162. (b) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804–3805. (c) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39–92.
9. Lantos, I.; Zhang, W. Y.; Shiu, X.; Eggleston, D. S. *J. Org. Chem.* **1993**, *58*, 7092–7095.
10. Zhang, C.; Moran, E. J.; Woiwade, T. F.; Short, K. M.; Mjalli, A. M. M. *Tetrahedron Lett.* **1996**, *37*, 751–754.
11. Claiborne, C. F.; Liverton, N. J.; Nguyen, K. T. *Tetrahedron Lett.* **1998**, *39*, 8939–8942.
12. Bleicher, K. H.; Gerber, F.; Wuthrich, Y.; Alanine, A.; Capretta, A. *Tetrahedron Lett.* **2002**, *43*, 7687–7690.
13. Liu, J.; Chem, J.; Zhao, J.; Zhao, Y.; Li, L.; Zhang, H. *Synthesis* **2003**, 2661–2666.
14. Sarshar, S.; Siev, D.; Mjalli, A. M. M. *Tetrahedron Lett.* **1996**, *37*, 835–838.

15. Frantz, D. E.; Morency, L.; Soheili, A.; Murry, J. A.; Grabowski, E. J. J.; Tillyer, R. D. *Org. Lett.* **2004**, *6*, 843–846.
16. Weinmann, H.; Harre, M.; Koeing, K.; Merten, E.; Tilstam, U. *Tetrahedron Lett.* **2002**, *43*, 593–595.
17. Clark, N. G.; Cawkill, E. *Tetrahedron Lett.* **1975**, 2717–2720.
18. Balalaie, S.; Hashemi, M. M.; Akhbari, M. *Tetrahedron Lett.* **2003**, *44*, 1709–1712.
19. Balalaie, S.; Arabanian, A. *Green Chem.* **2000**, *2*, 274–276.
20. Usyatinsky, A. Y.; Khemelnitsky, Y. L. *Tetrahedron Lett.* **2000**, *41*, 5031–5034.
21. Wolkenberg, S. E.; Wisnoski, D. D.; Leister, W. H.; Wang, Y.; Zhao, Z.; Lindsley, C. W. *Org. Lett.* **2004**, *6*, 1453–1456.
22. Cobb, J. M.; Grimster, N.; Khan, N.; Lai, J. Y. Q.; Payne, H. J.; Payne, L. J.; Raynham, T.; Taylor, J. *Tetrahedron Lett.* **2002**, *43*, 7557–7560.
23. Xu, L.; Wan, Li.-F.; Salehi, H.; Deng, W.; Guo, Q.-X. *Hetrocycles* **2004**, *63*, 1613–1658.
24. (a) Deshmukh, R. R.; Rajagopal, R.; Srinivasan, K. V. *Chem. Commun.* **2001**, 1544–1545. (b) Rajagopal, R.; Jarikote, D. V.; Srinivasan, K. V. *Chem. Commun.* **2002**, 616–617.
25. Rajagopal, R.; Jarikote, D. V.; Thomas, D.; Lahoti, R. J.; Srinivasan, K. V. *Tetrahedron Lett.* **2003**, *44*, 1815.
26. Palimkar, S. S.; Siddiqui, S. A.; Thomas, D.; Lahoti, R. J.; Srinivasan, K. V. *J. Org. Chem.* **2003**, *68*, 9371–9378.
27. (a) Jarikote, D. V.; Siddiqui, S. A.; Rajagopal, R.; Thomas, D.; Lahoti, R. J.; Srinivasan, K. V. *Tetrahedron Lett.* **2003**, *44*, 1835–1838. (b) Nadaf, R. N.; Siddiqui, S. A.; Thomas, D.; Lahoti, R. J.; Srinivasan, K. V. *J. Mol. Catal. A: Chem.* **2004**, *240*, 155–160.
28. Fletcher, K. A.; Storey, I. A.; Hendricks, A. E.; Pandey, S.; Pandey, S. *Green Chem.* **2001**, *3*, 210–215.
29. Perrin, D. D. *Ionization Constant of Inorganic Acids and Bases in Aqueous Solution*, 2nd ed.; Pergaman Elmsford: New York, 1982.
30. McKillop, A.; Swann, B. P.; Taylor, E. C. *Tetrahedron Lett.* **1970**, 5281–5284.
31. Gholap, A. R.; Venkatesan, K.; Thomas, D.; Lahoti, R. J.; Srinivasan, K. V. *Green Chem.* **2004**, *6*, 147–150.
32. Davidson, D.; Weiss, M.; Jelling, M. *J. Org. Chem.* **1937**, *2*, 319–327.