Water mediated chemoselective synthesis of 1,2-disubstituted benzimidazoles using *o*-phenylenediamine and the extended synthesis of quinoxalines†

Jie-Ping Wan, Shi-Feng Gan, Jian-Mei Wu and Yuanjiang Pan*

Received 29th May 2009, Accepted 14th July 2009
First published as an Advance Article on the web 29th July 2009
DOI: 10.1039/b914286j

By applying water as the reaction medium, the one-pot synthesis of 1,2-disubstituted benzimidazoles has been achieved in excellent efficiency and selectivity at room temperature *via* trimethylsilyl chloride promoted reaction of *o*-phenylenediamine with aldehyde. This green catalyst system has also been successfully extended to the synthesis of quinoxalines *via* the reaction of *o*-phenylenediamine with α-bromoketone. Water displayed a specific functionality in mediating the selectivity, and remarkable advantages over organic solvents in terms of yields as well as in the work up procedure of the reactions.

Introduction

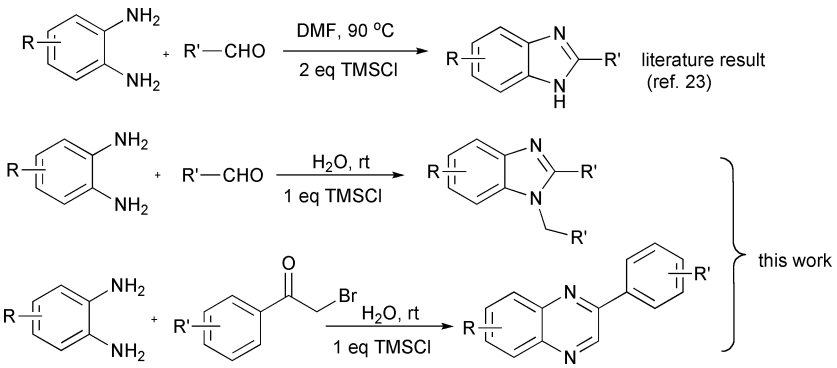
Benzimidazole and quinoxaline are ubiquitous heterocyclic units in pharmaceuticals and bioactive natural products. Benzimidazole derivatives bear versatile pharmacological properties[1] based on their presence in both clinical medicines[2] and compounds of broad biological functions.[3] In addition, the treatment potency of benzimidazoles in diseases such as ischemia-reperfusion injury[4a], hypertension,[4b] obesity[4c] *etc.* have been recently reported. Quinoxaline is also a heteroaromatic unit of extensive interests owing to its occurrence in many biocides[5a], pharmaceuticals[5b] and various biofunctional molecules.[5c] Moreover, quinoxalines displayed practical utilities in the fields of organic semiconductor materials[6] and organic synthons.[7]

There are currently a number of synthetic methodologies available for both the synthesis of benzimidazoles and quinoxalines. Generally, the condensation of *o*-phenylenediamines and carboxylic acids (or their derivatives such as nitriles, imidates, orthoesters) had been widely used for the benzimidazole synthesis, but harsh dehydrating conditions (170–180 °C) are usually required.[8] Alternative approaches such as palladium catalyzed tandem carbonylation–cyclization reaction of *o*-phenylenediamine[9], palladium catalyzed tandem dehydration-coupling reaction of 2-bromoaniline[10], rhodium catalyzed hydroformylation reaction of *N*-alkenyl phenylenediamines[11], reductive cyclization reaction of *o*-nitroaniline with aldehydes[12], solid-phase supported synthesis[13] *etc.* have been also developed to prepare functionalized benzimidazoles. However, directly employing the condensation–aromatisation reaction of *o*-phenylenediamines and aldehydes under oxidative condition turned out to be the most facile and effective method to synthesize 2-substituted benzimidazole **4**[14] and 1,2-disubstituted benzimidazole **3**.[15] On the other hand, the synthesis of quinoxalines was usually achieved by the reactions of *o*-phenylenediamine with dicarbonyl compounds[16], the oxidative cascade reactions of *o*-phenylenediamine with α-hydroxyketones[17], epoxides[18] and diols[19] in the presence of either noble metal or additional oxidants/microwave assistance. The synthesis using multicomponent reactions has also been recently reported.[20] Interestingly, as an equivalent chemical precursor of α-hydroxyketones, α-bromoketones has been claimed in much less cases as reaction partners of *o*-phenylenediamine to prepare quinoxalines.[21]

Among the reactions of *o*-phenylenediamine with aldehyde, the selectivity in forming 1,2-disubstituted benzimidazole **3** and 2-substituted benzimidazole **4** is an issue of high interest. As a large body of protocols have been established for synthesizing benzimidazoles of type **4**[14], relatively rare methods have been reported to directly prepare 1,2-disubstituted benzimidazole **3** with ideal selectivity.[15] Recently, several elegant catalyst systems have been developed to prepare **3** in excellent chemoselectivity by employing water as the medium at the presence of organometallic catalysts.[15d–f] Given the desire for developing more economical and facile methods of less environmental impact in organic synthesis, we wish to report herein the trimethylsilyl chloride (TMSCl)[22] promoted benzimidazole synthesis in water. One highly interesting aspect of this protocol is that water as the medium displayed specific inducing effect for the selective formation of 1,2-disubstituted benzimidazole **3** since previous report on the TMSCl promoted, organic solvent (DMF) mediated condensation of *o*-phenylenediamine with aldehyde furnishes product **4** as the major product (Scheme 1).[23] In addition, the application scope of this highly green catalyst system has been successfully extended to the effective synthesis of quinoxaline by using *o*-phenylenediamine and α-bromoketones, which represents the first synthesis of quinoxalines in water through such transformations.

Department of Chemistry, Zhejiang University, Hangzhou, 310027, People's Republic of China. E-mail: panyuanjiang@zju.edu.cn; Fax: +86 57187951629; Tel: +86 571 87951264.

† Electronic supplementary information (ESI) available: General experimental procedure, analytical data as well as copies of ^{1}H and ^{13}C NMR spectra of all products. Copies of ^{1}H NMR and ESI-MS+ spectra of **3a-*d*$_2$**. See DOI: 10.1039/b914286j



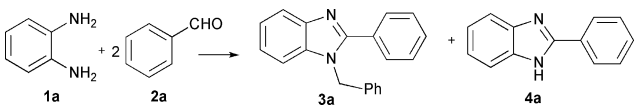
Scheme 1 Selective synthesis of 2- and 1,2-substituted benzimidazole as well as quinoxaline.

Results and discussion

We initially employed 1:1 mol *o*-phenylenediamine and benzaldehyde for reaction in water in the presence of TMSCl. To our surprise, the reaction did not proceed to give expected 2-substituted benzimidazole as expected, instead, the 1,2-disubstituted benzimidazole **3** was obtained as a single product after simple filtration. The excellent chemoselectivity mediated by water inspired us to further investigate this transformation. Various conditions have then been designed to determine the efficiency of this model reaction using *o*-phenylenediamine and 2 equiv mol of aldehydes (Table 1). Different acids, solvents as well as reaction temperature have been screened and TMSCl turned out to be the proper promoter to give ideal result. It is interesting that TMSCl in this reaction serves more than the acid source in water according to the remarkably better results in both the product yield and selectivity from these entries than those using acids (entries 2 and 3). In addition, the target product was isolated in 35% yield when 1 equiv mol of K_2CO_3 was added together with TMSCl, which further demonstrated that acid is not the sole promoting factor of the protocol reaction. The reaction conditions were finally optimized as follows: 1 equiv mole TMSCl in 2 mL water at room temperature (entry 13).

Following the determination of the optimal reaction conditions, the application scope of this reaction has been examined by subjecting different diamines and aldehydes. By using water as solvent at room temperature, 1,2-disubstituted benzimidazoles with various functional groups were obtained in excellent selectivity and yields (Table 2). Among the reactions of different aromatic aldehydes, no significant distinction on the yield

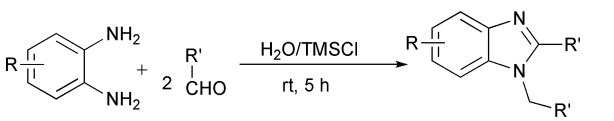
Table 1 Synthesis of 1-benzyl-2-phenyl-1*H*-benzo[*d*]imidazole under different conditions[a]



Entry	Catalyst (eq)	Solvent	T (°C)	Yield (%)[b]
1	no	H_2O	rt	25 (42)[c]
2	PTSA (0.6)	H_2O	rt	49 (18)
3	HCl (0.6)	H_2O	rt	30
4	TMSCl (0.6)	H_2O	rt	83
5	TMSCl (0.3)	H_2O	rt	51
6	TMSCl (0.6)	Hexane	rt	43
7	TMSCl (0.6)	Cyclohexane	rt	41 (26)
8	TMSCl (0.6)	Toluene	rt	25 (12)
9	TMSCl (0.6)	DMF	rt	40
10	TMSCl (0.6)	EtOH	rt	46
11	TMSCl (0.6)	H_2O	70	70
12	TMSCl (0.6)	H_2O	50	62
13	TMSCl (1.0)	H_2O	rt	87
14[d]	TMSCl (1.0)	H_2O	rt	35 (39)

[a] Unless specified, all reactions were carried out at 0.5 mmol diamine, 1.0 mmol aldehyde and open atmosphere. [b] All the yields in this section were obtained from the silica gel chromatography isolated products for accurate evaluation on the effect of reaction conditions. [c] The data in the parentheses refer to the yield of **4a**. [d] 1 equiv mol of K_2CO_3 was added.

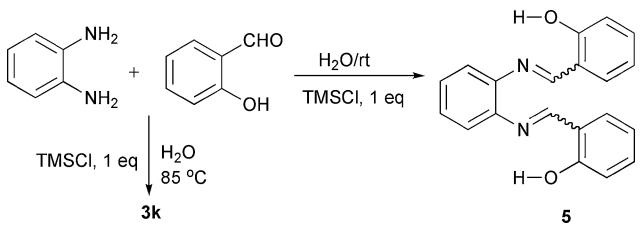
Table 2 Water mediated synthesis of 1,2-disubstituted benzimidazoles[a]



Entry	R′	R	Product	Yield (%)[b]
1	Ph	H	**3a**	87
2	4-$CH_3C_6H_4$	H	**3b**	85
3	4-$CH_3OC_6H_4$	H	**3c**	78
4	4-OHC_6H_4	H	**3d**	72
5	4-FC_6H4	H	**3e**	75
6	4-ClC_6H4	H	**3f**	80
7	4-BrC_6H_4	H	**3g**	85
8[d]	4-$NO_2C_6H_4$	H	**3h**	91
9	3-$NO_2C_6H_4$	H	**3i**	88
10	3-OHC_6H_4	H	**3j**	83
11[c]	2-OHC_6H_4	H	**3k**	85
12	2-$CH_3OC_6H_4$	H	**3l**	79
13	2-BrC_6H_4	H	**3m**	92
14	2-ClC_6H_4	H	**3n**	75
15	furan-2-yl	H	**3o**	75
16	thiophene-2-yl	H	**3p**	65
17[d]	$PhCH=CH_2$	H	**3q**	51
18	4-$CH_3C_6H_4$	3-CH_3O	**3r**	80
19	H	3-benzoyl	**3s**	43
20	4-$CH_3OC_6H_4$	3-benzoyl	**3t**	78
21	4-ClC_6H_4	3-benzoyl	**3u**	70
22	furan-2-yl	3-benzoyl	**3v**	66
23	C_2H_5CHO	H	**3w**	trace

[a] Unless specified, the reaction conditions are: 0.5 mmol diamine **1** and 1.0 mmol aldehyde **2** in 2 mL water stirred at rt for 5 h in the presence of 0.5 mmol TMSCl. [b] Yield of purified product by simple filtration or EtOH recrystallization. [c] The reaction mixture was heated at 85 °C for 8 h. [d] The product was purified by silical gel chromatography.

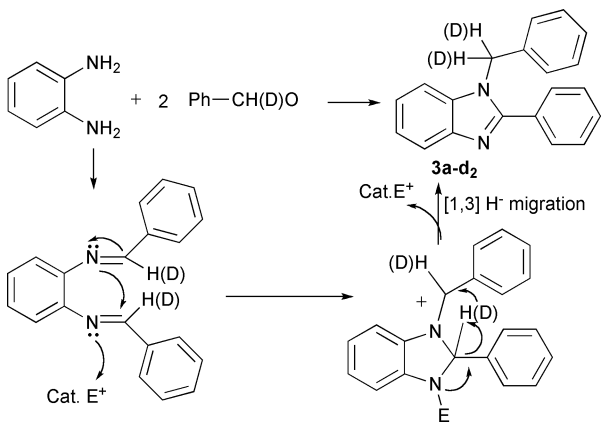
of target products has been observed regardless of the high diversity of the functional groups. An exception is the reaction of salicylaldehyde (entry 11), which led to the formation of the Schiff base product **5** (Scheme 2)[24] under the standard condition, instead, heating the reaction at 85 °C provided the corresponding benzimidazole **3k**. This unexpected phenomenon was probably due to the existence of intramolecular hydrogen bonds which prevented **5** from further cyclization to give **3k**, while heating the reaction could effectively break the energy barrier of these hydrogen bonds to ensure the further process of the reaction.



Scheme 2 Unexpected formation of Schiff base from salicylaldehyde.

Following the reactions of aromatic aldehydes, similar reactions using aliphatic aldehydes have been investigated. As shown in Table 2 (entries 17 and 23), cinnamaldehyde furnished corresponding product **3q** in modest yield whereas propanaldehyde gave only trace amounts of target product.

In order to probe the possible mechanism of the reaction forming **3**, we designed the isotope labeling reaction using benzaldehyde-d_1 to incorporate with *o*-phenylenediamine. Under the standard catalyst condition used in above experiment, the product was isolated as full deuterium labeled product in the form of **3a-d_2** (Scheme 3 and see ESI† for the characterization). Combining the formation of Shiff base product **5** observed in previous experiments, we could therefore deduce the general homogeneous reaction mechanism as outlined in Scheme 3. The aldehyde firstly reacted with diamine to form Shiff base of type **5** as the intermediate, in the presence of electrophilic catalyst, the intramolecular 1,3-hydride migration was induced to directly give the 1,2-disubstituted benzimidazole. It is noteworthy that although this kind of mechanism has been previously proposed in literature[15a,d], the results obtained from the isotope labeling



Scheme 3 Plausible mechanism of the reaction furnishing 1,2-disubstituted benzimidazoles.

experiment in our study provided the first direct evidence to support this mechanism.

Enlightened by the successful reaction of *o*-phenylenediamines with aldehydes in this system, we envisioned that functional ketones might also incorporate into *o*-phenylenediamine to give functional heterocyclic compounds. Despite many reports demonstrated that α-hydroxyketones are the excellent reaction partners to incorporate *o*-phenylenediamines to give quinoxalines,[17] we wish to construct the same scaffold using α-bromoketones due to the easier access of this kind of reactants.[21] However, the expected transformation was not detected when we employed the aforementioned room temperature catalysis condition for the reaction of *o*-phenylenediamine with benzoyl bromomethane, instead, heating the reaction at 70 °C furnished anticipated quinoxaline **7a** in good yield. This modified method has been subsequently applied to the reaction of *o*-phenylenediamine and α-bromoketones of various substitutions (Table 3). According to the obtained data, this water-mediated catalyst system bears general tolerance to functional groups in the substrates, the 2-substituted quinoxalines were isolated generally in satisfactory yields, which suggested that the functional groups in the arene unit of α-bromoketones have no evident influence on the reaction.

Conclusions

In summary, a practical and green synthetic method has been developed for the facile synthesis of both 1,2-disubstituted benzimidazoles and quinoxalines. In the presence of TMSCl, a broad range of functional heterocyclic compounds have been easily synthesized in water without using any additional surfactant or oxidant. In addition, the isotope labeling experiment has been firstly employed in the reaction of benzaldehyde with *o*-phenylenediamine, which demonstrated the 1,3-hydride migration process during the formation of 1,2-disubstituted benzimidazoles.

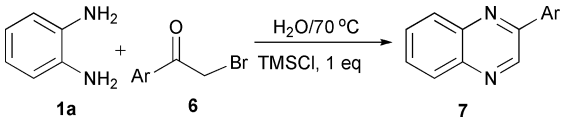
Experimental

Typical procedure for the synthesis of 1,2-disubstituted benzimidazoles in water

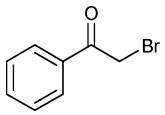
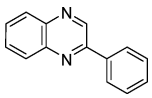
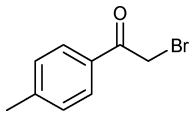
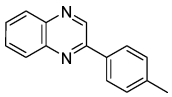
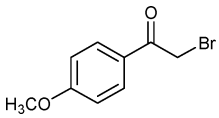
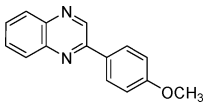
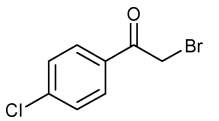
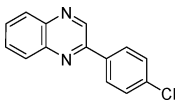
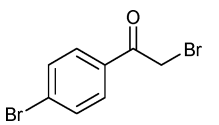
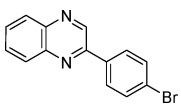
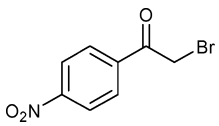
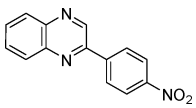
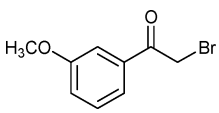
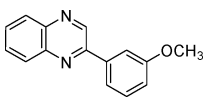
1.0 mmol aldehyde **2** and 2 mL water were located in a round bottom flask, and 0.5 mmol diamine was then added. Finally, 0.5 mmol TMSCl was injected to the mixture. The reaction was stirred at room temperature for 5 h to form homogeneous suspension. The suspension was then filtered and the residue was washed with 10 mL water to give analytically pure product. When necessary, the crude product was recrystallized with ethanol.

1-(2-chlorobenzyl)-2-(2-chlorophenyl)-1*H*-benzo[*d*]imidazo le (3n). Pale yellow crystal; mp: 158–159 °C;[15a] ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.76 (d, 1 H, J = 8.5 Hz), 7.62 (d, 1 H, J = 7.5 Hz), 7.55 (t, 1 H, J = 8.0 Hz),7.50 (d, 2 H, J = 8.0 Hz), 7.42 (t, 1 H, J = 7.5 Hz), 7.38 (d, 1 H, J = 8.0 Hz), 7.29 (t, 2 H, J = 4.5 Hz), 7.25 (d, 1 H, J = 7.5 Hz), 7.16 (t, 1 H, J = 7.5 Hz), 6.65 (d, 1 H, J = 8.0 Hz), 5.43 (s, 2 H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 151.93, 143.67, 136.09, 134.58, 134.30, 133.36, 133.02, 132.77, 130.85, 130.63, 130.58, 130.54, 129.37,

Table 3 Water mediated one-pot synthesis of quinoxalines[a]



1a 6 7

Entry	Substrate **6**	Product	Yield (%)[b]
1		**7a** 	62
2		**7b** 	57
3		**7c** 	82
4		**7d** 	73
5		**7e** 	60
6		**7f** 	90
7		**7g** 	91

[a] Reaction conditions: 0.6 mmol **1a**, 0.5 mmol **6** and 0.5 mmol TMSCl mixed in 2 mL H_2O, stirred at 70 °C for 8 h. [b] Yield of purified products based on **6**.

128.59, 128.50, 124.24, 123.44, 120.78, 112.14, 46.25; ESI-MS [M+H$^+$]: $m/z = 353$.

Typical procedure for the synthesis of quinoxalines in water

0.6 mmol diamine **1a** and 0.5 mmol α-bromoketone **6** were located in a round bottom flask with 2 mL water, and 0.5 mmol TMSCl was added. The reaction was stirred at 70 °C for 8 h. After cooled down to room temperature, the mixture was extracted with 3 × 8 mL AcOEt. The combined organic phase was dried with anhydrous sodium sulfate. After removing the organic solvent, the residue was subjected to silical gel chromatography to give pure products.

2-phenylquinoxaline (7a). Pale orange solid; mp: 75–76 °C;[17c] ^{1}H NMR (DMSO-d_6, 500 MHz) δ 9.59 (s, 1 H), 8.35 (d, 2 H, J = 8.0 Hz), 8.13 (t, 2 H, J = 8.5 Hz), 7.89–7.84 (m, 2 H), 7.61–7.57 (m, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 152.17, 144.96, 142.60, 142.28, 137.23, 131.83, 131.63, 131.11, 130.41, 130.32, 130.05, 128.66; ESI-MS [M+H$^+$]: $m/z = 207$.

Acknowledgements

The authors thank the NSFC of China (20775069), NSFC of Zhejiang province (Z206510) and NCET-06–0520 of the National Ministry of Education of China for financial support on this work. We also thank professor Henry Rudler (Université Pierre et Marie Curie) for his valuable discussion on this work.

References

1 (*a*) For recent reviews, seeS. Bhattacharya and P. Chaudhuri, *Curr. Med. Chem.*, 2008, **15**, 1762; (*b*) D. A. Horton, G. T. Bourne and M. L. Smythe, *Chem. Rev.*, 2003, **103**, 893; (*c*) M. Boiani and M. González, *Mini-Rev. Med. Chem.*, 2005, **5**, 409.
2 (*a*) P. N. Preston, *Chem. Rev.*, 1974, **74**, 279; (*b*) H. Al Muhaimeed, *J. Int. Med. Res.*, 1997, **25**, 175; (*c*) L. J. Scott, C. J. Dunn, G. Mallarkey and M. Sharp, *Drugs*, 2002, **62**, 1503; (*d*) P. Venkatesan, *J. Antimicrob. Chemother.*, 1998, **41**, 145.
3 (*a*) W. A. Denny, G. W. Rewcastle and B. C. Baguley, *J. Med. Chem.*, 1990, **33**, 814; (*b*) L. K. Labanauskas, A. B. Brukstus, P. G. Gaidelis, V. A. Buchinskaite, E. B. Udrenaite and V. K. Dauksas, *Pharm. Chem. J.*, 2000, **34**, 353; (*c*) B. Can-Eke, M. O. Puskullu, E. Buyukbingol and M. Iscan, *Chem.-Biol. Interact.*, 1998, **113**, 65; (*d*) A. Benazzouz, T. Boraud, P. Dubédat, A. Boireau, J.-M. Stutzmann and C. Gross, *Eur. J. Pharmacol.*, 1995, **284**, 299; (*e*) R. Sevak, A. Paul, S. Goswami and D. Santini, *Pharmacol. Res.*, 2002, **46**, 351.
4 (*a*) G.-D. Zhu, V. B. Gandhi, J. Gong, S. Thomas, Y. Luo, X. Liu, Y. Shi, V. Klinghofer, E. F. Johnson, D. Frost, C. Donawho, K. Jarvis, J. Bouska, K. C. Marsh, S. H. Rosenberg, V. L. Giranda and T. D Penning, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 3955; (*b*) Y. Ogino, N. Ohtake, Y. Nagae, K. Matsuda, M. Moriya, T. Suga, M. Ishikawa, M. Kanesaka, Y. Mitobe, J. Ito, T. Kanno, A. Ishiara, H. Iwaasa, T. Ohe, A. Kanatani and T. Fukami, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 5010; (*c*) D. I. Shah, M. Sharma, Y. Bansal, G. Bansal and M. Singh, *Eur. J. Med. Chem.*, 2008, **43**, 1808.
5 (*a*) R. Sarges, H. R. Howard, R. G. Browne, L. A. Lebel and P. A. Seymour, *J. Med. Chem.*, 1990, **33**, 2240; (*b*) L. E. Seitz, W. J. Suling and R. C. Reynolds, *J. Med. Chem.*, 2002, **45**, 5605; (*c*) A. Gazit, H. App, G. McMahon, J. Chen, A. Levitzki and F. D. Bohmer, *J. Med. Chem.*, 1996, **39**, 2170and references cited therein.
6 S. Dailey, J. W. Feast, R. J. Peace, I. C. Sage, S. Till and E. L. Wood, *J. Mater. Chem.*, 2001, **11**, 2238.
7 (*a*) L. S. Jonathan, M. Hiromitsu, M. Toshihisa, M. L. Vincent and F. Hiroyuki, *Chem. Commun.*, 2002, 862; (*b*) L. S. Jonathan, M. Hiromitsu, M. Toshihisa, M. L. Vincent and F. Hiroyuki, *J. Am. Chem. Soc.*, 2002, **124**, 13474; (*c*) O. Sascha and F. Rudiger, *Synlett*, 2004, 1509.
8 (*a*) M. R. Grimmet, *Comprehensive Heterocyclic Chemistry*, (Ed.: A. R. KatritzkyC. W. Rees, K. T. Potts,), Pergamon Press, New York, 1984, Vol. 5; (*b*) P. N. Preston, *Chemistry, of Heterocyclic Compounds* (Ed.: A. Weissberger, E. C. Taylor, John Wiley and Sons, 1981, Vol. 40; (*c*) L. M. Dudd, E. Venardou, E. Garcia-Verdugo, P. Licence, A. J. Blake, C. Wilson and M. Poliakoff, *Green Chem.*, 2003, **5**, 187.
9 R. J. Perry and B. D. Wilson, *J. Org. Chem.*, 1993, **58**, 7016.
10 C. T. Brain and S. A. Brunton, *Tetrahedron Lett.*, 2002, **43**, 1893.
11 D. Anastasiou, E. M. Campi, H. Chaouk and W. R. Jackson, *Tetrahedron*, 1992, **48**, 7467.
12 D. L. Yang, D. Fokas, J. Z. Li, L. B. Yu and C. M. Baldino, *Synthesis*, 2005, 47.
13 Z. Wu, P. Rea and G. Wickam, *Tetrahedron Lett.*, 2000, **41**, 9871.
14 (*a*) For selected examples in selective synthesis of 2-substituted benzimidazole using *o*-phenylenediamine and aldehyde, seeR. Trivedi, S. K. De and R. A. Gibbs, *J. Mol. Catal. A: Chem.*, 2006, **245**, 8; (*b*) P. L. Beaulieu, B. Hache and E. Von Moos, *Synthesis*, 2003, 1683; (*c*) K. Bahrami, M. M. Khodaei and I. Kavianinia, *Synthesis*, 2007,

547; (*d*) K. Baharami, M. M. Khodaei and F. Naali, *J. Org. Chem.*, 2008, **73**, 6835; (*e*) H. Sharghi, M. Aberi and M. M. Doroodmand, *Adv. Synth. Catal.*, 2008, **350**, 2380; (*f*) Y. X. Chen, L. F. Qian, W. Zhang and B. Han, *Angew. Chem., Int. Ed.*, 2008, **47**, 9330; (*g*) D. Saha, A. Saha and B. C. Ranu, *Green Chem.*, 2009, **11**, 733.

15 (*a*) For typical example in selective synthesis of 1,2-disubstituted benzimidazoles using *o*-phenylenediamine and aldehyde, seeN. D. Kokare, J. N. Sangshetti and D. B. Shinde, *Synthesis*, 2007, 2829; (*b*) P. Salehi, M. Dabiri, M. A. Zolfigol, S. Otokesh and M. Baghbanzadeh, *Tetrahedron Lett.*, 2006, **47**, 2557; (*c*) M. Chakrabarty, R. Mukherjee, S. Karmakar and Y. Harigaya, *Monatsh. Chem.*, 2007, **138**, 1279; (*d*) V. Ravi, E. Ramu, K. Vljay and A. S. Rao, *Chem. Pharm. Bull.*, 2007, **55**, 1254; (*e*) J. S. Yadav, B. V. S. Reddy, K. Premalatha and K. S. Shankar, *Can. J. Chem.*, 2008, **86**, 124; (*f*) P. Salehi, M. Dabiri, M. A. Zolfigol, S. Otokesh and M. Baghbanzadeh, *Tetrahedron Lett.*, 2006, **47**, 2557.

16 (*a*) Z. Zhao, D. D. Wisnoski, S. E. Wolkenberg, W. H. Leister, Y. Wang and C. W. Lindsley, *Tetrahedron Lett.*, 2004, **45**, 4873; (*b*) S. V. More, M. N. Sastry and C.-F. Yao, *Green Chem.*, 2006, **8**, 91.

17 (*a*) S. Sithambaram, Y. Ding, W. Li, X. Shen, F. Gaenzler and S. L. Suib, *Green Chem.*, 2008, **10**, 1029; (*b*) S. Y. Kim, K. H. Park and Y. K. Chung, *Chem. Commun.*, 2005, 1321; (*c*) C. S. Cho and S. G. Oh, *J. Mol. Catal. A: Chem.*, 2007, **276**, 205; (*d*) S. A. Raw, C. D. Wilfred and R. J. K. Taylor, *Org. Biomol. Chem.*, 2004, **2**, 788; (*e*) R. S. Robinson and R. J. K. Taylor, *Synlett*, 2005, 1003; (*f*) S. A. Raw, C. D. Wilfred and R. J. K. Taylor, *Chem. Commun.*, 2003, 2286.

18 S. Antoniotti and E. Duñach, *Tetrahedron Lett.*, 2002, **43**, 3971.

19 C. S. Cho and S. G. Oh, *Tetrahedron Lett.*, 2006, **47**, 5633.

20 C. Neochoritis, J. Stephanidou-Stephanatou and C. A. Tsoleridis, *Synlett*, 2009, 302.

21 (*a*) B. Das, K. Venkateswarlu, K. Suneel and A. Majhi, *Tetrahedron Lett.*, 2007, **48**, 5371; (*b*) J. Ishida, H. Yamamoto, Y. Kido, K. Kamijo, K. Murano, H. Miyake, M. Ohkubo, T. Kinoshita, M. Warizaya, A. Iwashita, K. Mihara, N. Matsuoka and K. Hattori, *Bioorg. Med. Chem. Lett.*, 2006, **14**, 1378.

22 (*a*) For the reviews on silica Lewis acid mediated reaction and selected examples of TMSCl promoted organic conversions, seeA. D. Dilman and S. L. Ioffe, *Chem. Rev.*, 2003, **103**, 733; (*b*) Q. Xia and B. Ganem, *Org. Lett.*, 2002, **4**, 1631; (*c*) M. Krasavin, S. Tsirulnikov, M. Nikulnikov, V. Kysil and A. Ivachtchenko, *Tetrahedron Lett.*, 2008, **49**, 5241; (*d*) B. Sreedhar, M. A. Reddy and P. S. Reddy, *Synlett*, 2008, 1949; (*e*) S. V. Ryabukhin, A. S. Plashkon, D. M. Volochnyuk and A. A. Tolmachev, *Synthesis*, 2007, 3155; (*f*) L.-W. Xu and C.-G. Xia, *Tetrahedron Lett.*, 2004, **45**, 4507; (*g*) Y. Zhu, S. Huang, J. Wan, L. Yan, Y. Pan and A. Wu, *Org. Lett.*, 2006, **8**, 2599; (*h*) J.-P. Wan, S.-F. Gan, G.-L. Sun and Y.-J. Pan, *J. Org. Chem.*, 2009, **74**, 2862; (*i*) J.-P. Wan and Y.-J. Pan, *Chem. Commun.*, 2009, 2768; (*j*) J.-P. Wan, J. Zhou, H. Mao and Y.-J. Pan, *Tetrahedron*, 2008, **64**, 11115.

23 S. V. Ryabukhin, A. S. Plashkon, D. M. Volochnyuk and A. A. Tolmachev, *Synthesis*, 2006, 3715.

24 For the synthesis and characterizaition of Shiff base **5**, seeD. M. Boghaei and S. Mohebi, *Tetrahedron*, 2002, **58**, 5357.