$VOSO_4$ catalyzed highly efficient synthesis of benzimidazoles, benzothiazoles and quinoxalines

Chander Singh Digwal, Upasana Yadav, Akash P. Sakla, P.V. Sri Ramya, Shams Aaghaz, Ahmed Kamal

PII: S0040-4039(16)30743-2
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.06.074
Reference: TETL 47801

To appear in: *Tetrahedron Letters*

Received Date: 18 May 2016
Revised Date: 15 June 2016
Accepted Date: 16 June 2016

Please cite this article as: Digwal, C.S., Yadav, U., Sakla, A.P., Sri Ramya, P.V., Aaghaz, S., Kamal, A., $VOSO_4$ catalyzed highly efficient synthesis of benzimidazoles, benzothiazoles and quinoxalines, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.06.074

Tetrahedron Letters
journal homepage: www.elsevier.com

$VOSO_4$ catalyzed highly efficient synthesis of benzimidazoles, benzothiazoles and quinoxalines

Chander Singh Digwal, Upasana Yadav, Akash P. Sakla, P. V. Sri Ramya, Shams Aaghaz, Ahmed Kamal*

Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Balanagar, Hyderabad 500037, India

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Benzimidazoles
Benzothiazoles
Quinoxalines
$VOSO_4$

ABSTRACT

Herein, we describe a highly efficient and eco-friendly protocol for the synthesis of benzimidazoles, benzothiazoles and quinoxalines using $VOSO_4$ as a catalyst in ethanol. Use of nontoxic and recyclable catalyst, clean reaction profile, high yields, scalability and broad substrate scope are the important practical features of the present protocol.

1. Introduction

Benzimidazole and its derivatives occupy an important place in medicinal chemistry due to their synthetic utility and diversified biological activities.[1a-c] It is considered to be privileged component because many drugs such as albendazole (anthelmintic), astemizole (antihistaminic), telmisartan (antihypertensive), omeprazole (antiulcer), etc. contain benzimidazole as a core template (Figure 1).[1d-f] Owing to such a wide range of biological activities, constant efforts have been made by different research groups worldwide to develop efficient strategies for the synthesis of various substituted benzimidazoles and their derivatives.

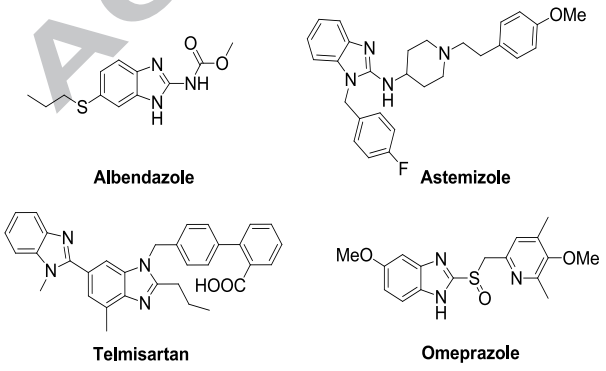


Figure 1. Biologically active benzimidazole derivatives.

Benzimidazole moiety can be accessed by direct C-N bond activation,[2] redox condensation of 2-nitro aniline with benzyl amine/benzyl alcohol[3] and condensation of *o*-phenylenediamines with carboxylic acids or its derivatives (nitriles, imidates or orthoesters) requiring high temperatures and strong acidic conditions.[4] Moreover, the most commonly used method for the synthesis of 2-substituted benzimidazoles is oxidative cyclodehydrogenation of Schiff base obtained by reacting *o*-phenylenediamines and aldehydes. In recent times, several catalysts and reagents such as $Na_2S_2O_4$,[5] $FeCl_3{\cdot}6H_2O$,[6] Zn-proline,[7] CAN,[8] $NaHSO_3$,[9] $ZrCl_4$,[10] $PhI(OAc)_2$,[11] $Pb(OAc)_4$,[12] sulfamic acid,[13] $HfCl_4$,[14] DMP,[15] nanoporous aluminosilicate,[16] $CoCl_2{\cdot}6H_2O$,[17] $Co(OH)_2/CoO(II)$,[18] $VO(acac)_2$-$CeCl_3$,[19] $MgCl_2{\cdot}6H_2O$,[20] Heuland natural zeolite,[21] animal bone meal,[22] sodium perborate,[23] $Sc(OTf)_3$,[24] $In(OTf)_3$,[25] $Cu(OTf)_2$,[26] $TiCl_3OTf$,[27] and $B(C_6F_5)_3$[28] have been reported for the synthesis of benzimidazoles. Weinreb amide reagent has also been successfully utilized as a substitute for aldehydes for the synthesis of benzimidazoles and benzothiazoles in presence of $BF_3{\cdot}OEt_2$.[29] However, some of the previously reported methods have several limitations like harsh reaction conditions, longer reaction times, high temperatures, low yields, generation of toxic side products, use of expensive and/or toxic catalysts.

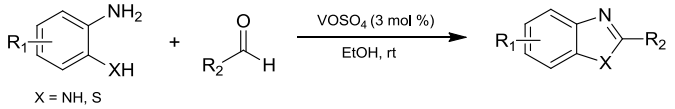
Vanadium is nontoxic, inexpensive and readily available.[30a] Not only is it known to be present in various bacterial enzymes such as bromoperoxidase,[30b] nitrogenase[30c] but also plays an important role in redox chemistry in complex biological systems.[30d,e] The role of vanadium based catalysts in organometallic chemistry as well as in a number of organic reactions has been well documented.[31] However, vanadium sulfate oxide ($VOSO_4$), a commercially available nontoxic and recyclable catalyst has not much been explored. Recently, catalytic activity of $VOSO_4$ was found prominent in the synthesis

* Corresponding author. Tel.: +91 40 27193157; fax: +91 40 27193189.
E-mail: ahmedkamal@iict.res.in

of pyrazoles *via* C-N dehydrogenative cross coupling.[32] Based on this knowledge and in view of the efforts towards development of simple, mild, eco-friendly reaction protocol, we explored the potential of $VOSO_4$ as a catalyst for the synthesis of benzimidazoles, benzothiazoles and quinoxalines (Scheme 1 & 2). To our delight, $VOSO_4$ catalyzed reactions not only required shorter reaction times but also provided the desired products in good to excellent yields with low catalyst loading.

2. Results and discussion

To standardize the reaction conditions, a model reaction of *o*-phenylenediamine and benzaldehyde was carried out in the presence of $VOSO_4$ in ethanol at room temperature and the results are summarized in Table 1. As evident from the results, the reaction proceeds smoothly on addition of 0.5 mol % of $VOSO_4$ unlike in case of the reaction without the catalyst (entry 1, 2, Table 1). Further, to demonstrate the effect of catalyst



1 2 3a-3u

Scheme 1. Synthesis of 2-substituted benzimidazole derivatives.

loading, we carried out a series of reactions with increasing amount of $VOSO_4$. It was observed that increasing the catalyst loading beyond 3 mol % showed no significant improvement in terms of yield and reaction time (entry 5, 6, Table 1). Finally, we could obtain the desired product in 92% yield at room temperature with 3 mol % of $VOSO_4$. With these optimized reaction conditions, effect of different solvents such as methanol, dichloromethane, acetonitrile, *N*,*N*-dimethylformamide and water

Table 1

Optimization of the reaction conditions for the synthesis of 2-phenyl-1*H*-benzo[*d*]imidazole (**3a**)[a]

Entry	Catalyst (mol %)	Solvent	Time	Yield[b] (%)
1	Nil	EtOH	24 h	23
2	0.5	EtOH	6 h	75
3	1	EtOH	5 h	83
4	2	EtOH	2.5 h	89
5	3	EtOH	60 min	92
6	5	EtOH	60 min	93
7	3	MeOH	60 min	82
8	3	CH_2Cl_2	60 min	56
9	3	CH_3CN	60 min	63
10	3	DMF	60 min	70
11	3	H_2O	60 min	52

[a] Reaction conditions: *o*-phenylenediamine (1 mmol) and benzaldehyde (1 mmol) are used at room temperature.
[b] Isolated yield.

was investigated (entries 7-11, Table 1). However, ethanol showed excellent yield (92%) in 60 min and was established to be the best solvent for this transformation.

The generality and substrate scope for the described protocol were explored by using different substituted *o*-phenylenediamines and aryl/heteroaryl aldehydes. The reaction of *o*-phenylenediamine with a variety of arylaldehydes bearing electron withdrawing as well as electron donating groups provided the corresponding 2-arylbenzimidazoles in 84-92% yield in short reaction times (entries **3a-3k**, Table 2). Notably, the present method is compatible with a wide range of functional groups such as methoxy, halogens, cyano, hydroxyl, carboxyl and functional group nature does not significantly affect the yield of the reaction. Next, when the reaction was carried out using *N*-

Table 2

Reaction of *o*-phenylenediamine or 2-aminothiophenol with aldehydes in ethanol at room temperature[a]

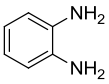
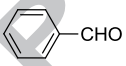
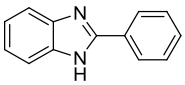
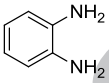
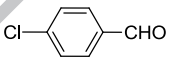
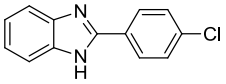
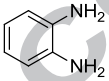
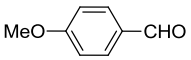
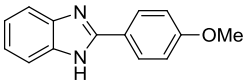
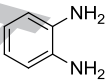
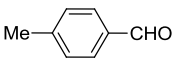
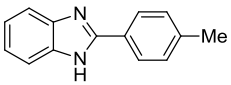
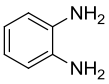
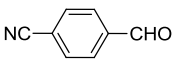
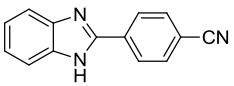
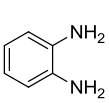
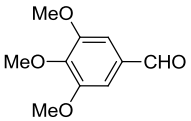
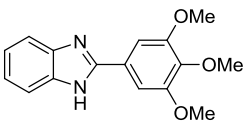
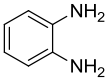
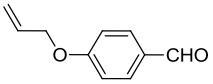
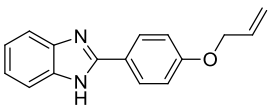
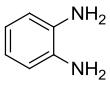
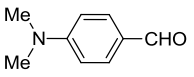
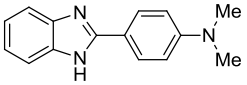
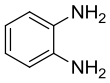
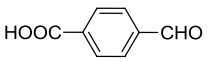
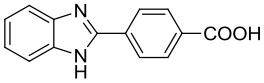
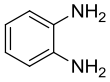
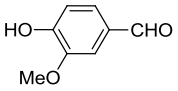
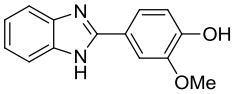
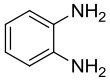
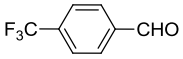
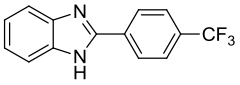
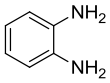
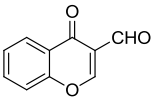
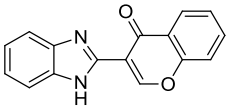
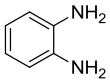
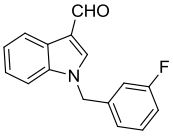
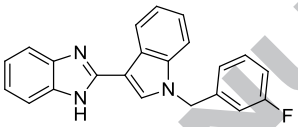
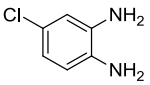
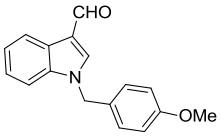
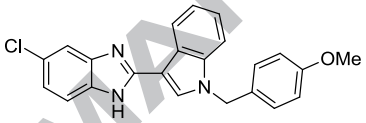
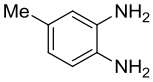
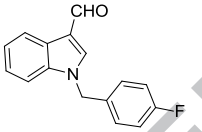
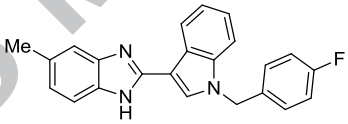
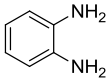
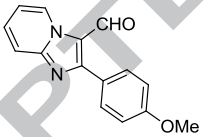
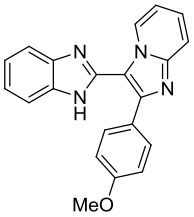
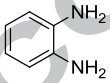
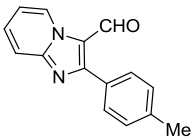
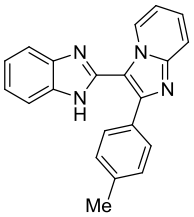
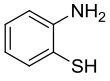
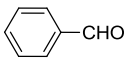
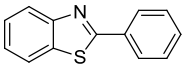
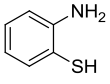
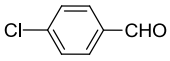
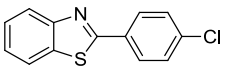
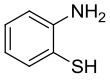
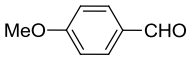
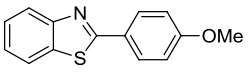
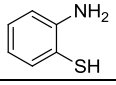
Entry	Amine	Aldehydes	Product	Time	Yield[b] (%)	Mp (°C)[Refs.]
3a				60 min	92	291-293[2b,29]
3b				45 min	89	289-291[2b]
3c				50 min	91	222-224[2b,27]
3d				50 min	92	263-265[27]
3e				40 min	90	248-250[27]
3f				70 min	88	258-260[13]
3g				60 min	86	205-208

Table 2 *(Continued)*

Entry	Amine	Aldehydes	Product	Time	Yield[b] (%)	Mp (°C)[Refs.]
3h				50 min	90	276-278 (lit.[20] 295-298)
3i				30 min	84	>300
3j				40 min	87	221-223[20]
3k				40 min	88	265-267
3l				8 h	78	263-265 (lit.[4c] 270)
3m				4 h	85	197-199
3n				5 h	82	212-214
3o				4 h	86	239-241
3p[c]				24 h	74	220-222
3q[c]				24 h	78	238-240
3r				45 min	92	110-112[22]
3s				40 min	87	114-116[22]
3t				50 min	89	117-119[22]
3u				40 min	90	102-104[22]

[a] Reaction conditions: *o*-phenylenediamine/2-aminothiophenol (1 mmol), benzaldehyde (1 mmol), $VOSO_4$ (3 mol %).

[b] Isolated yield.

[c] Reaction was carried out at 80 °C.

substituted indole-3-carbaldehydes or 4-oxo-4*H*-chromene-3-carbaldehyde, it was observed to proceed at room temperature in good yields, although required longer reaction times (entries **3l-3o**, Table 2). Furthermore, the reaction of imidazo[1,2-*a*]pyridine carbaldehydes with *o*-phenylenediamine proceeded only in refluxing ethanol and afforded the desired product in moderate yields after 24 h (entries **3p**, **3q**, Table 2). In order to study the synthetic scope of this method, we carried out the reaction using *o*-aminothiophenol and arylaldehydes. Gratifyingly, the reaction furnished the corresponding benzothiazole derivatives in high yields at room temperature (87-92%, entries **3r-3u**, Table 2).

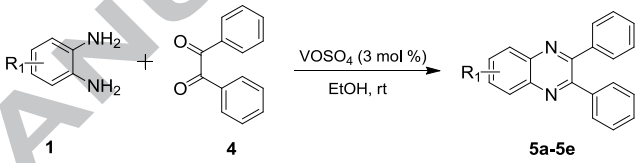
In addition, we studied the reusability of the $VOSO_4$ for the synthesis of **3a**. The catalyst was recovered as described in experimental procedure after completion of the reaction and re-used upto three times under the optimal reaction conditions. As shown in Table 3, the recovered catalyst showed good reusability with a slight decrease in yield over three runs. Also, the synthesis of **3a** was carried out on gram scale with 5 g of *o*-phenylenediamine and 4.91 g of benzaldehyde using 3 mol% $VOSO_4$ at room temperature in ethanol and the yield of product **3a** obtained was 90% (8.1 g), that was found comparable to the yield obtained in entry **3a**, Table 2.

Table 3
Reusability of $VOSO_4$ (3 mol%) for the synthesis of **3a**

Entry	Reaction cycle	*o*-phenylene-diamine	Benzaldehyde	Time (min)	Yield[a] (%)
1	First (fresh run)	500 mg	491 mg	60	92
2	Second cycle	500 mg	491 mg	60	90
3	Third cycle	500 mg	491 mg	60	87
4	Fourth cycle	500 mg	491 mg	60	82

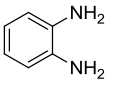
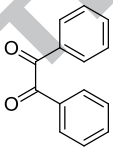
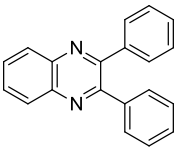
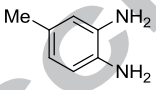
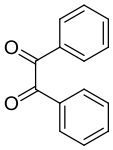
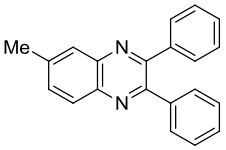
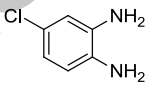
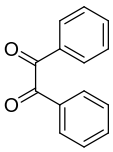
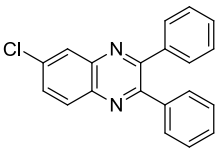
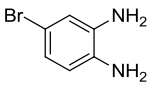
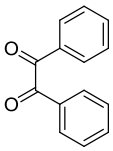
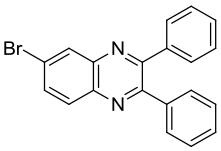
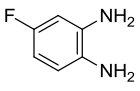
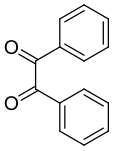
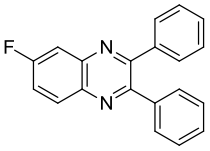
[a] Isolated yield.

Encouraged by these results, the applicability of this protocol was further extended for the synthesis of quinoxalines. The most common strategy for the synthesis of 2,3-disubstituted quinoxalines involves the condensation of an aryl 1,2-diamine with a 1,2-dicarbonyl compound in ethanol or acetic acid which often requires high reaction temperature and long reaction time.[33] In recent years, synthesis of quinoxalines *via* condensation of *o*-phenylenediamines with 1,2-dicarbonyl and/or α-hydroxy ketone compounds in presence of several catalysts such as I_2,[34] $Ga(OTf)_3$,[35] $CuSO_4{\cdot}5H_2O$,[36] sulfamic acid,[37] KF/alumina,[38] Amberlite IR-120H,[39] etc. have been well reported. To further evaluate the catalytic ability of $VOSO_4$, the present optimized conditions were applied to the reaction of substituted *o*-phenylenediamines and benzil, which underwent smooth conversion to provide the corresponding 2,3-diphenyl quinoxaline derivatives in excellent yields (91-96% yield after 20-40 min) (entries **5a-5e**, Table 4).



Scheme 2. Synthesis of 2,3-diphenylquinoxaline derivatives.

Table 4
Reaction of substituted *o*-phenylenediamines with benzil[a]

Entry	Amine	1,2-diketones	Product	Time (min)	Yield[b] (%)	Mp (°C)[Refs.]
5a				20	96	127-129[35,39]
5b				20	95	122-124[39]
5c				35	94	125-127[35]
5d				30	94	120-122[35]
5e				40	91	102-103[39]

[a] Reaction conditions: *o*-phenylenediamines (1 mmol), benzil (1 mmol), $VOSO_4$ (3 mol %).

[b] Isolated yield.

3. Conclusion

In conclusion, we have developed an efficient and eco-friendly method for the synthesis of 2-substituted benzimidazoles using $VOSO_4$ as a catalyst in ethanol. Wide applicability to various substrates makes this method useful for the synthesis of medicinally important benzimidazole, benzothiazole and quinoxaline derivatives. The other key features of this protocol include use of nontoxic and recyclable catalyst, scalability, high functional group tolerance, high yields and easy work up procedure.

Acknowledgement

We are thankful to the Department of Pharmaceuticals (DoP), Ministry of Chemical & Fertilizers, Govt. of India, for the award of NIPER fellowship.

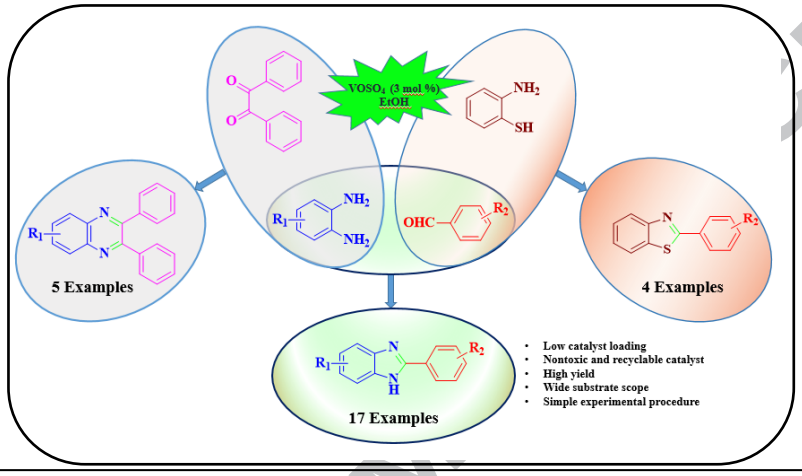
References and notes

1. (a) Narasimhan, B.; Sharma, D.; Kumar, P. *Med. Chem. Res*. **2012**, 21, 269; (b) Shah, K.; Chhabra, S.; Shrivastava, S. K.; Mishra, P. *Med. Chem. Res.* **2013**, 22, 5077; (c) Gaba, M.; Singh, S.; Mohan, C. *Eur. J. Med. Chem.* **2014**, 76, 494; (d) Yadav, G.; Ganguly, S. *Eur. J. Med. Chem*. **2015**, 97, 419; (e) Kaur, G.; Kaur, M.; Silakari, O. *Mini. Rev. Med. Chem*. **2014**, 14, 747; (f) Reddy, T. S.; Kulhari, H.; Reddy, V. G.; Bansal, V.; Kamal, A.; Shukla, R. *Eur. J. Med. Chem.* **2015**, 101, 790.
2. (a) Deng, X.; McAllister, H.; Mani, N. S. *J. Org. Chem*. **2009**, 74, 5742; (b) Kim, Y.; Kumar, M. R.; Park, N.; Heo, Y.; Lee, S. *J. Org. Chem*. **2011**, 76, 9577.
3. (a) Nguyen, T. B.; Bescont, J. L.; Ermolenko, L.; Mourabit, A. *Org. Lett*. **2013**, 15, 6218; (b) Li, G.; Wang, J.; Yuan, B.; Zhang, D.; Lin, Z.; Li, P.; Huang, H. *Tetrahedron Lett*. **2013**, 54, 6934.
4. (a) Wright, J. B. *Chem. Rev*. **1951**, 48, 396; (b) Middleton, R. W.; Wibberley, D. G. *J. Heterocycl. Chem.* **1980**, 17, 1757; (c) Risitano, F.; Grassi, G.; Foti, F. J. *J. Heterocycl. Chem.*, **2001**, 38, 1083. (d) Kin, J.; Kim, J.; Lee, H.; Lee, B. M.; Kim, B. H. *Tetrahedron* **2011**, 67, 3027.
5. Kamal, A.; Rao, A. V. S.; Nayak, V. L.; Reddy, N. V. S.; Swapna, K.; Ramakrishna, G.; Alvala, M. *Org. Biomol. Chem*. **2014**, 12, 9864.
6. Singh, M. P.; Sasmal, S.; Lu, W.; Chatterjee, M. N. *Synthesis* **2000**, 10, 1380.
7. Ravi, V.; Ramu, E.; Vijay, K.; Srinivas Rao, A. *Chem. Pharm. Bull*. **2007**, 55, 1254.
8. Bahrami, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem*. **2008**, 73, 6835.
9. Yoon, Y. K.; Ali, M. A.; Wei, A. C.; Choon, T. S.; Ismail, R. *Eur. J. Med. Chem.* **2015**, 93, 614.
10. Zhang, Z. H.; Yin, L.; Wang, Y. M. *Catal. Commun*. **2007**, 8, 1126.
11. Du, L. H.; Wang, Y. G. *Synthesis* **2007**, 5, 675.
12. Stephens, F. F.; Bower, J. D. *J. Chem. Soc*. **1949**, 2971.
13. Chakrabarty, M.; Karmakar, S.; Mukherji, A.; Arima, S.; Harigaya, Y. *Heterocycles* **2006**, 16, 4169.
14. Zhang, Z. H.; Yin, L.; Wang, Y. M. *Catal. Commun*. **2007**, 8, 1126.
15. Dabhade, S. K.; Bora, R. O.; Farooqui, M.; Gill, C. H. *Chin. Chem. Lett*. **2009**, 20, 893.
16. Chari, M. A.; Shobha, D.; Zaidi, S. M. J.; Reddy, B. V. S.; Vinu, A. *Tetrahedron Lett*. **2010**, 51, 5195.
17. Khan, A. T.; Parvin, T.; Choudhury, L. H. *Synth. Commun*. **2009**, 39, 2339.
18. Chari, M. A.; Shobha, D.; Sasaki, T. *Tetrahedron Lett*. **2011**, 52, 5575.
19. Maiti, D. K.; Haldar, S.; Pandit, P.; Chaterjee, N.; De Jordar, D.; Pramanik, N.; Saima, Y.; Patra, A.; Maiti, P. K. *J. Org. Chem.* **2009**, *74*, 8086.
20. Ghosh, P.; Subba, R. *Tetrahedron Lett*. **2015**, 56, 2691.
21. Heravi, M. M.; Tajbakhsh, M.; Ahmadi, A. N.; Mohajerani, B. *Monatsh. Chem*. **2006**, 137, 175.
22. Riadi, Y.; Mamouni, R.; Azzalou, R.; Haddad, M. El; Routier, S.; Guillaumet, G.; Lazar, S. *Tetrahedron Lett*. **2011**, 52, 3492.
23. Yuan, J.; Zhao, Z.; Zhu, W.; Li, H.; Qian, X.; Xu, Y. *Tetrahedron* **2013**, 69, 7026.
24. Itoh, T.; Nagata, K.; Ishikawa, H.; Ohsawa, A. *Heterocycles* **2004**, 63, 2769.
25. Trivedi, R.; De, S. K.; Gibbs, R. A. *J. Mol. Catal. A: Chem*. **2005**, 245, 8.
26. Chari, M. A.; Sadanandam, P.; Shobha, D.; Mukkanti, K. *J. Heterocycl. Chem*. **2010**, 47, 153.
27. Torabi, P.; Azizian, J.; Noei, J. *Tetrahedron Lett*. **2016**, 57, 185.
28. Prajapati, S. K.; Nagarsenkar, A.; Guggilapu, S. D.; Bathini, N. B. *Tetrahedron Lett*. **2015**, 56, 6795.
29. Bommegowda, Y. K.; Lingaraju, G. S.; Thamas, S.; Kumar, K. S. V.; Kumara, C. S. P.; Rangappa, K. S.; Sadashiva, M. P. *Tetrahedron Lett.* **2013**, 54, 2693.
30. (a) Cadene, A.; Gross, R.; Poucheret, P.; Mongold, J. J.; Masiello, P.; Roye, M.; Ribes, G.; Serrano, J. J.; Cros, G. *Eur. J. Pharmacol*. **1996**, 318, 145; (b) Hales, B. J.; Case, E. E.; Moringstar, J. E.; Dzeda, M. F.; Mautner, A. *Biochemistry* **1986**, 25, 7251; (c) Robson, R. L.; Eady, R. R.; Richardson, T. H.; Miller, R. W.; Hawkins, M.; Postgate, J. R. *Nature* **1986**, 322, 388; (d) Kustin, K.; Macara, I. G. *Comments Inorg. Chem*. **1982**, 2, 1; (e) Nechay, B. R. *Annu. Rev. Pharmacol. Toxicol*. **1984**, 24, 501.
31. Hirao, T. *Chem. Rev*. **1997**, 97, 2707.
32. Sar, D.; Bag, R.; Yashmeen, A.; Bag, S. S.; Punniyamurthy, T. *Org. Lett.* **2015**, 17, 5308.
33. Brown, D. J.; Taylor, E. C.; Ellman, J. A. *Quinoxalines: Supplement II. In The Chemistry of Heterocyclic Compounds*, John Wiley&Sons, New Jersey, **2004**.
34. Bhosale, R. S.; Sarda, S. R.; Ardhapure, S. S.; Jadhav, W. N.; Bhusare, S. R.; Pawar, R. P. *Tetrahedron Lett.* **2005**, 46, 7183.
35. Cai, J. J.; Zou, J. P.; Pan, X. Q.; Zhang, W. *Tetrahedron Lett*. **2008**, 49, 7386.
36. Heravi, M. M.; Bhaktiari, K.; Taheri, S.; Oskooie, H. A. *Catal. Commun*. **2007**, 8, 211.
37. Darabi, H. R.; Mohandessi, S.; Aghapoor, K.; Mohsenzadeh, F. *Catal. Commun*. **2007**, 8, 389.
38. Paul, S.; Basu, B. *Tetrahedron Lett.* **2011**, 55, 6597.
39. Kamal, A.; Babu, K.S.; Hussaini, S. M. A.; Mahesh, R.; Alarifi, A. *Tetrahedron Lett.* **2015**, 56, 2803.
40. *General procedure for synthesis of benzimidazole and benzothiazole derivatives*: To a magnetically stirred solution of *o*-phenylenediamine or *o*-aminothiophenol (1 mmol) and aldehyde (1 mmol) in ethanol (5 ml) was added 3 mol % of $VOSO_4$ at room temperature. After completion of the reaction, as indicated by TLC analysis, the catalyst was recovered by filtration and washed with ethanol. The filtrate was concentrated under reduced pressure and treated with cold water (10 ml) to precipitate the product. The precipitate was collected by filtration, washed with water, dried and recrystallized from ethanol or purified by column chromatography using neutral alumina. The recovered catalyst was dried under reduced pressure and then reused for next cycle. The products were characterized by HRMS, ^{1}H and ^{13}C NMR or by comparison with available literature data.
41. *General procedure for synthesis of quinoxaline derivatives*: To a magnetically stirred solution of *o*-phenylenediamine (1 mmol) and benzil (1 mmol) in ethanol (5 ml) was added $VOSO_4$ (3 mol %) at room temperature. After completion of the reaction, as indicated by TLC analysis, the reaction mixture was cooled to 0 ℃. The solid obtained was filtered, washed with water and dried. The crude product obtained was recrystallized using methanol. The products were characterized by HRMS, ^{1}H and ^{13}C NMR or by comparison with available literature data.

Graphical Abstract

$VOSO_4$ catalyzed highly efficient synthesis of benzimidazoles, benzothiazoles and quinoxalines

Chander Singh Digwal, Upasana Yadav, Akash P. Sakla, P. V. Sri Ramya, Shams Aaghaz, Ahmed Kamal*



Tetrahedron Letters

Highlights

- Synthesis of benzimidazoles, benzothiazoles and quinoxalines using $VOSO_4$ as catalyst.
- Environmentally benign protocol with mild reaction conditions and high yields.
- Wide substrate scope shown by synthesis of structurally diverse benzimidazole derivatives.
- Reusability of $VOSO_4$ for at least three times.
- The protocol is also useful in gram scale synthesis.