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Graphical Abstract

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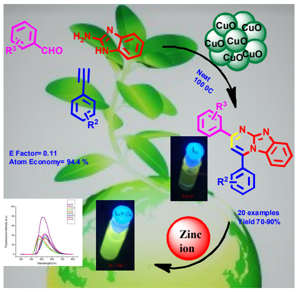
Manish Rawat and Diwan S. Rawat*



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Copper oxide nanoparticle catalysed synthesis of imidazo[1,2-*a*]pyrimidine derivatives, their optical properties and selective fluorescent sensor towards zinc ion

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ABSTRACT

Synthesis of biologically active fused imidazo[1,2-*a*] pyrimidines were achieved *via* A^3 coupling involving 2-aminobenzimidazole, aldehyde and terminal alkyne, followed by 6-endo-dig cyclization using copper oxide nanoparticles under solvent free condition. Further optical properties of imidazo[1,2-*a*]pyrimidines were studied which showed the effect of electron-donating and electron-withdrawing substitution on the fluorescence intensities of these compounds. Out of 20 compounds, 2,4-bis(4-methoxyphenyl)benzo[4,5]imidazo[1,2-*a*] pyrimidine can act as a fluorescent sensor for zinc ion with detection limit 4.74 µM, which is much lower than the maximum allowable zinc concentration in drinking water by WHO.

1. Introduction

Imidazo-fused heterocyclic scaffolds are one of the important core moieties which is found in many natural products and biologically active molecules which shows antibacterial,[1] anticancer,[2] antimicrobial[3] and antifungal[4] activities. These are one of the structural motifs of various marketed drugs[5-8] such as divaplon[9] and fasiplon[10] (figure 1). Apart from biological importance, these moieties possess interesting optical properties and behave as organic fluorophores.[11] Various methods have been reported for the synthesis of fused imidazo[1,2-*a*]pyrimidines but most of these methods suffers from a drawback of longer reaction time, multistep synthetic protocol, use of expensive/harmful chemicals, non-recyclable catalytic system and generation of unwanted side products.[12]

In order to make the synthetic protocol sustainable and environment friendly, green synthetic methods have gained importance in recent times. So, in order to meet the green chemistry requirements efforts are being made to develop a catalytic system that is robust and environment friendly for the synthesis of biologically active heterocycles such as imidazo[1,2-*a*]pyrimidines. Literature survey revealed that only two methods are reported for the synthesis of this class of compounds using homogeneous catalyst[13] and heterogeneous nano catalyst[14] and this gives a scope to develop an alternative methodology for the synthesis of imidazo[1,2-a] pyrimidines so as to overcome some of the problems associated with known methods. Detection of zinc ion in the biological system is essential to avoid various neurological disorders like Alzheimer's disease and Parkinson's disease associated with accumulation of zinc ions in the body.[15-18] In recent years various fluorescent chemosensors containing quinoline[19,20] and coumarin[21,22] have been designed but complicated and multistep synthesis, makes these chemosensors less enthralling. To avoid these complications, imidazo[1,2-a]pyrimidines can be used as fluorescent chemosensors specifically for the detection of zinc ion in biological system.

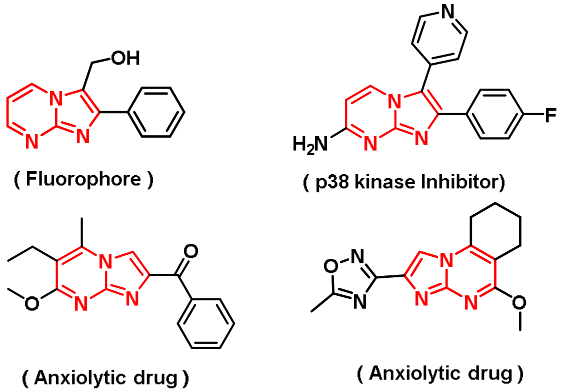

Figure 1: Biologically active molecules and organic fluorophores

With this background in mind and in continuation of our interest towards nanocatalysis,[23-29] we propose an alternative eco-friendly synthetic methodology for the synthesis of imidazo[1,2-a]pyrimidines using copper oxide (CuO) nanoparticles[29,30] under neat condition *via* A^3 coupling followed by 6-endo-dig cyclization. The structural and spectroscopic properties of imidazo[1,2-a]pyrimidines can be helpful in the optoelectronic application of these compounds and it can be used for the detection of zinc ion.

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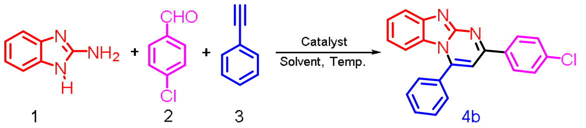
2. Results and discussion

Table 1: Optimization of CuO NPs catalysed synthesis of Fused Imidazo[1,2-a]pyrimidines[a]

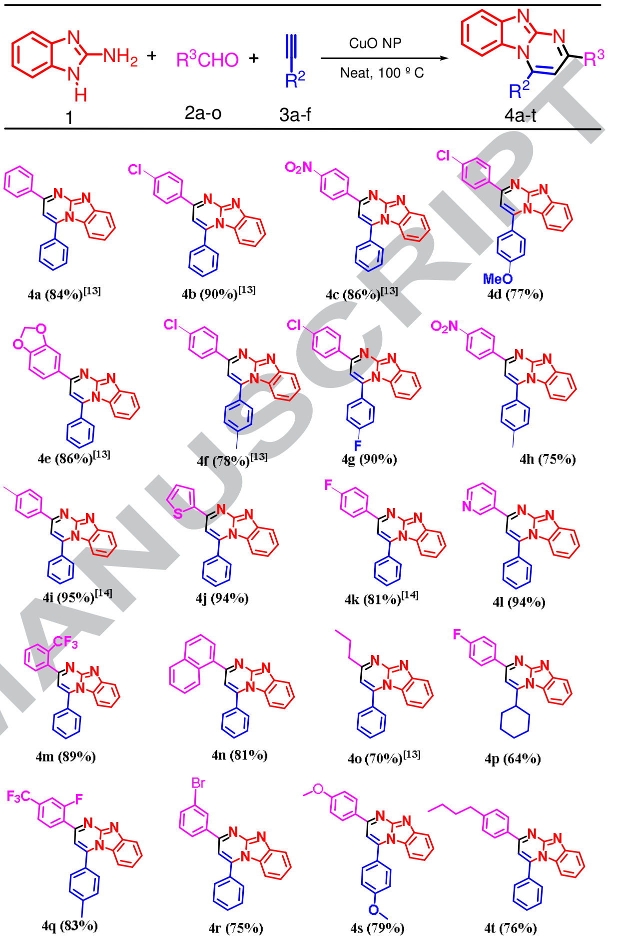


Entry	Catalyst (mg)	Solvent	Temp. (ºC)	Time (h)	Yield[b] (%)
1.	HS-CuO* (10mg)	Toluene	80	6	65
2.	HS-CuO (10mg)	ACN	80	6	63
3.	HS-CuO (10mg)	DMF	80	12	30
4.	HS-CuO (10mg)	EG	80	12	63
5.	HS-CuO (10mg)	PEG	80	12	35
6.	HS-CuO (10mg)	EtOH	80	12	52
7.	HS-CuO (10mg)	water	80	3	72
8.	HS-CuO (10mg)	Neat	80	4	74
9.	**HS-CuO (10mg)**	**Neat**	**100**	**1**	**90**
10.	HS-CuO (10mg)	Neat	120	24	52
11.	HS-CuO (10mg)	Neat	60	24	Trace amount
12.	No Catalyst	Neat	100	24	-
13.	HS-CuO (5 mg)	Neat	100	4	53
14.	HS-CuO (20 mg)	Neat	100	2	76

[a]Reaction conditions: 2-aminobenzimidazole **1** (0.5 mmol), *para*-chloro benzaldehyde **2** (0.5 mmol), phenylacetylene **3** (0.5 mmol) CuO NPs (5-20 mg) solvent (2ml) were stirred at mentioned temperatures. [b]Isolated Yield. *Hierarchically porous sphere like copper oxide (HS-CuO)

Optimization of synthesis of fused imidazo[1,2-a]pyrimidines was started from 2-aminobenzimidazole (**1**), *para*-chloro benzaldehyde (**2**) and phenylacetylene (**3**) with CuO NPs in the presence of various solvents as mentioned in Table 1. Initially reaction was performed in non-polar and polar solvents like toluene (Table 1, entry 1), acetonitrile (Table 1, entry 2), DMF (Table 1, entry 3) and product was isolated in poor to moderate yields (Table 1, entry 1-3). When reaction was carried out in green solvents such as ethylene glycol, PEG, ethanol and water the desired product was isolated in poor to moderate yields (Table 1, entry 4-7), with maximum yield in water. Under neat condition the desired product was isolated in 90% yield in 1h at 100 ℃ (Table 1, entry 9). Increasing temperature to 120 ℃ or lowering the reaction temperature to 60 ℃ has negative affect in the isolated yield of the product (Table 1, entry 10, 11). Similarly increase or decrease of catalyst amount led to lower the yield of the product (Table 1, entry 13, 14) and no product formation was observed in the absence of the catalyst (Table 1, entry 12). Therefore, 10 mg of CuO NPs at 100 ℃ under neat condition was the optimum condition for the synthesis of fused imidazo[1,2-a]pyrimidine (Table 1, entry 9). Next, heterocyclic aldehydes were screened and corresponding products were obtained in excellent yield (Table 2, entry **4j, 4l**) whereas the aliphatic aldehyde like butyraldehyde afford the moderate yield of the product (Table 2, entry **4o**). Unfortunately, cyclic aldehydes and aromatic nitrogen-containing aldehydes such as pyridine-2-carboxaldehyde, pyrrole-2-carboxaldehyde and cyclohexanecarboxaldehyde were failed to afford the corresponding desired products. Aromatic alkynes bearing electron donating and withdrawing groups provided the desired product in good and moderate yield (Table 2, entry **4d, 4f, 4s**). Aliphatic alkyne like pentyne failed to provide the desired product whereas the alkyne containing cyclic substituent like cyclohexylacetylene afforded the moderate yield of the product (Table 2, **4p**).

Table 2: CuO NPs catalyzed synthesis of imidazopyrimidine derivatives.[a]



[a]Reaction condition: 2-amino-benzimidazole (**1**, 0.5 mmol), aldehydes (**2,** 0.5 mmol), alkynes (**3,** 0.5 mmol) and CuO NPs (10 mg) were stirred at 100℃ for 1-2 hours

Next, we examined the recyclability of CuO NPs catalyst for the synthesis of product **4b** under optimized conditions. Reaction mixture was centrifuged, washed with ethanol and catalyst was dried in the oven after completion of reaction. The catalyst was further used to carry out five cycles of reaction, there was no significantly loss of catalytic activity of catalyst as shown in figure 2.

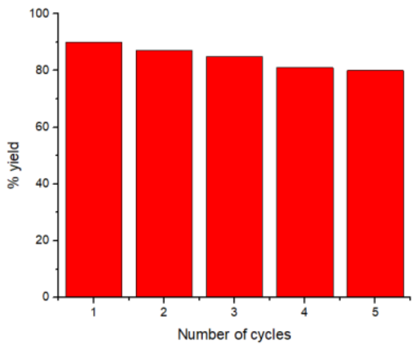


Figure 2: Recyclability of CuO NPs catalysed synthesis of **4a.**

The green chemistry metrics was calculated for compound **4b** under optimized condition as shown in table 3. It is evident from the table that the green chemistry metrices are close to ideal values (detailed calculations can be seen in supporting documents).

Table 3: Measurement of Green chemistry metrices for **4b**

S.No.	**GC metrices**	**Ideal value**	**Calulated 4b**
1.	E factor	0	0.11
2.	Process mass intensity (PMI)	1	1.11
3.	Reaction mass efficiency (RME)	100%	90%
4.	Atom economy (AE)	100%	94.4%
5	Carbon efficiency (CE)	100%	96%

The plausible mechanism for the synthesis of imidazo[1,2-a]pyrimidine is shown in figure 3. The first step is formation of CuO complex as shown in figure 3.

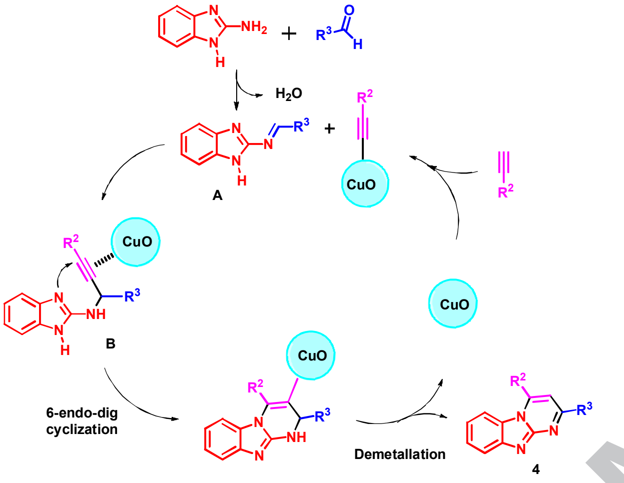
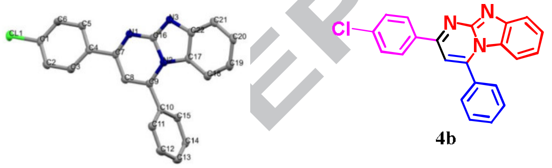


Figure 3: Plausible mechanism for CuO NPs catalyzed synthesis of Fused Imidazo[1,2-a] pyrimidines.

Then the attack of copper acetylide to *in situ* generated imine (A), resulting in the formation of CuO NPs complex intermediate (B). CuO NPs activates the triple bond which favors the intramolecular 6-endo-dig cyclization leading to the formation of desired product (**4**).



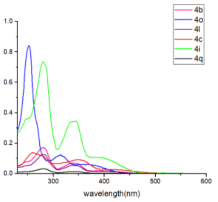
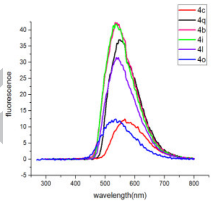
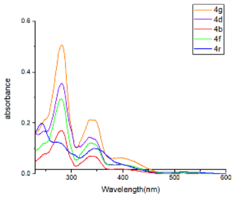
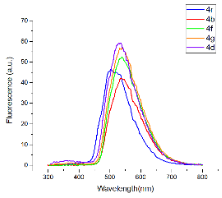
4b

Figure 4**:** X-ray Crystallography Structure of Compound **4b** (CCDC 1828497)

Next, we studied the photophysical properties of these compounds. The spectroscopic data of some of the derivatives are presented in figure 5. In Set A where R^3 group is varied and set B where R^2 group is varied, the electronic spectra of imidazo[1,2-a]pyrimidines exhibit two intense bands within 256 – 382 nm regions whereas in the fluorescence spectra one band was observed. In case of absorption spectra, there is bathochromic shift due to the electron-donating group like methyl group (**4i**), hypsochromic shift due to electron-withdrawing group like nitro, pyridine etc (**4c, 4l** and **4q**) whereas in case of aliphatic substitution Abs_{max} further decreases (**4o**).

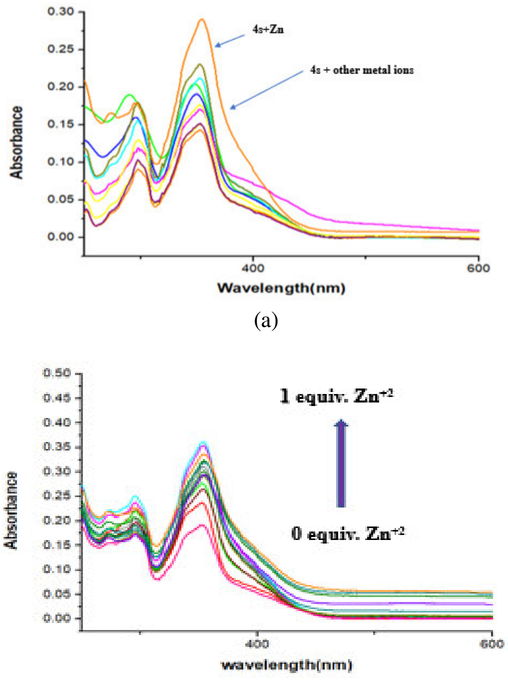
In set A, a hypsochromic shift is observed (**4b, 4i, 4o** and **4l**) in comparison to compounds **4c** and **4q** due to the electron withdrawing groups attached. In set B where R^2 group is varied, there is bathochromic shift of **4g, 4d, 4b** and **4f** in comparison to **4r** in absorption and emission maxima due to aliphatic chain attached to the moiety. Fluorescence studies revealed that electron-donating groups attached to imidazo[1,2-a]pyrimidines increases the fluorescence properties of the molecules as compared to electron-withdrawing groups and aliphatic groups attached to the moiety.

Figure 5: Absorption and fluorescence spectra of imidazo[1,2-a] pyrimidines measured in DCM.

	Absorption spectra of imidazo[1,2-a]pyrimidines measured in DCM.	**Fluorescence spectra of imidazo[1,2a]pyrimidines measured in DCM.**
Set A (R^3 is varied)		
Set B (R^2 is varied)		

Effect of metal ions on photophysical studies of 4s.

Absorption Spectra



(a)

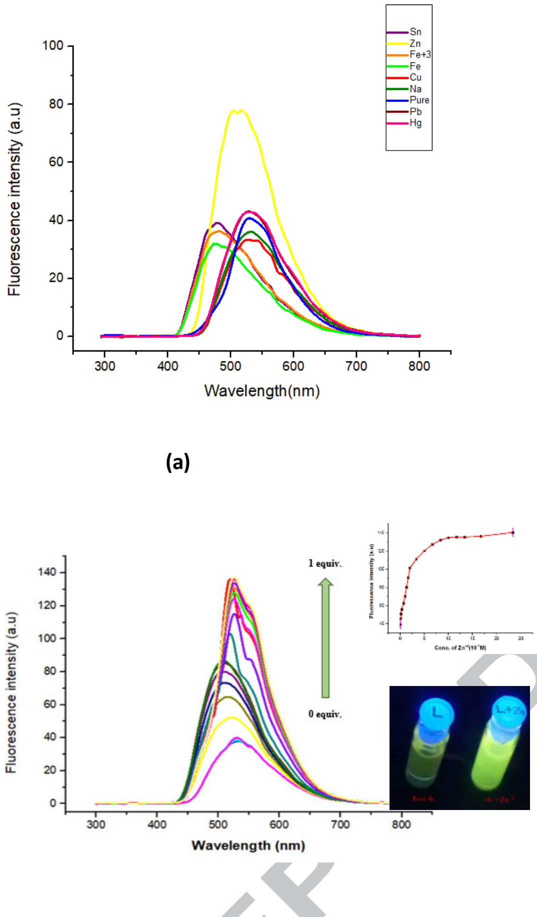
(b)

Figure 6: UV-vis spectra of **4s** (a) upon addition of different metal ions Na^{+1}, Cu^{+2}, Fe^{+2}, Fe^{+3}, Hg^{+2}, Ni^{+2}, Pb^{+2}, $Sn^{+2}$and Zn^{+2} (b) upon varying amount of zinc ions from 0 to 1 equivalent.

The photophysical properties (UV-vis and fluorescence) of compound **4s** (4.9 ×10^{-4} M, MeOH: H_2O (4:1, v/v) was explored by the addition of different metal ions such as sodium, iron, lead, mercury, copper, nickel, tin and zinc in water (10^{-1} M buffered with HEPES solution at pH = 7.2).

The UV-vis absorption spectra of compound **4s** showed two peaks at 297.32 and 352.33 nm. After addition of one equivalent of Na^{+1}, Cu^{+2}, Fe^{+2}, Fe^{+3}, Hg^{+2}, Ni^{+2}, Pb^{+2}, Sn^{+2} slight change in absorbance value was observed in all cases but addition of Zn^{+2} exhibited significant change in absorbance value of compound **4s** (Fig 6(a)). The absorption spectrum of **4s** was further analyzed by changing the concentration of zinc ions. The absorbance value at 352.33 nm increases as the concentration of zinc ion increases (Fig 6(b)).

Fluorescence spectra



(a)

(b)

Figure 7: Fluorescence spectrum of 4s (4.9×10^{-4} M, MeOH: H_2O (4:1, v/v) containing HEPES, pH=7.2) a) upon addition of different metal ions Na^{+1}, Cu^{+2}, Fe^{+2}, Fe^{+3}, Hg^{+2}, Ni^{+2}, Pb^{+2}, $Sn^{+2}$and Zn^{+2} (b) upon varying amount of zinc ions from zero to one equivalent.

The fluorescence spectrum of **4s** was investigated in the presence of metal ions like Na^{+1}, Cu^{+2}, Fe^{+2}, Fe^{+3}, Hg^{+2}, Ni^{+2}, Pb^{+2}, Sn^{+2} and Zn^{+2}. The investigation revealed that there is prominent change in fluorescence intensity of **4s** compound in the presence of zinc ion whereas no significant change in fluorescence intensity was observed in case of other metal ions. From this observation, it can be concluded that there is strong binding between **4s** and zinc metal ion in comparison to other compounds. Generally, transition and post transition cations having open shell *d*-orbitals quenches the fluorescence due to the rapid electron transfer between cation and ligands which led to non-radiative decay of the excited states whereas these electron-transfer processes are not possible in case of transitions cations having close shell *d*-orbitals (like zinc).[31] The fluorescence spectrum of **4s** was investigated by varying the concentration of zinc ions. The fluorescence intensity of **4s** was increased initially with increasing the concentration of zinc ion and after a point it remained constant.

Determination of binding constant and detection limit

The stoichiometry of complex formed was determined by the Job's plot which clearly indicated that there is 1:1 binding mode between zinc ion and compound **4s**. The binding constant between **4s** and Zn^{+2} can be determined from Benesi Hildebrand plot[32](Fig 9).

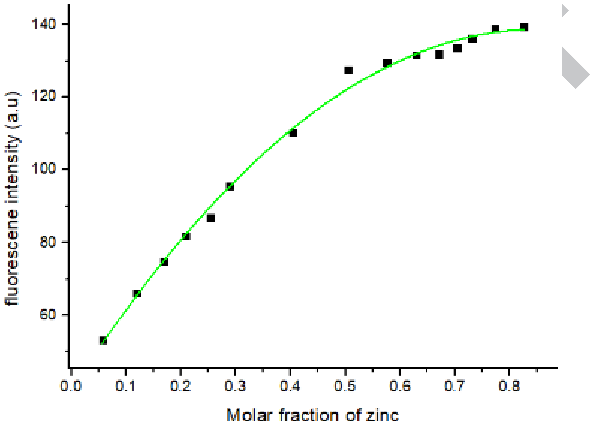


Figure 8: Job's plot for determination of stoichiometry of complex formed between **4s** and zinc ion

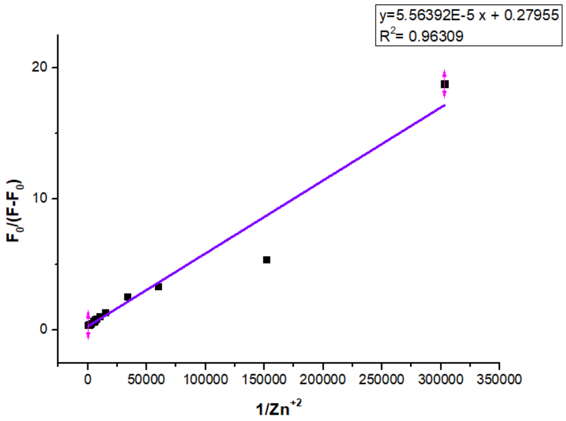


Figure 9: Benesi Hildebrand plot for the determination of binding constant between **4s** and Zn^{+2}.

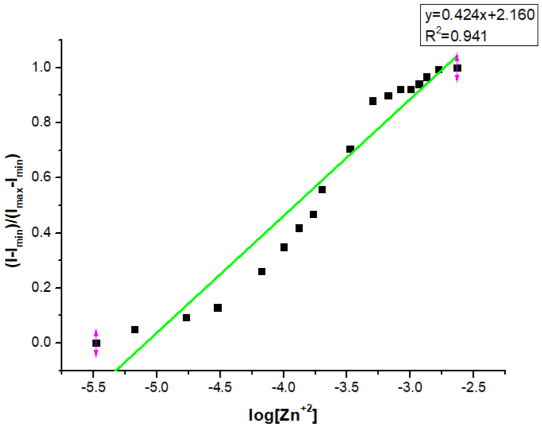


Figure 10: Plot between (I - Imin)/(Imax -Imin) and log $[Zn^{+2}]$ for determination of the detection limit for **4s**.

The binding constant of the 1:1 complex of compound **4s** and zinc ion can be obtained from the ratio of intercept/slope which comes out to be log $K_a = 3.698$ ($Ka = 0.05 \times 10^5$) which is in good agreement with the value of binding constant of some reported zinc-binding chemosensors (0.3-7.09).[33-35] The detection limit can be obtained from the reported methods[36-37] by plotting a normalized graph between (I - Imin)/ (Imax -Imin) and log $[Zn^{+2}]$ at 490 nm (Fig. 10). The detection limit of compound **4s** was found to be 4.79μM which is lower than the WHO guidelines for the tolerance limit of zinc in drinking water (76 μM).[38]

Conclusions

In conclusion, we have developed a green method for one-pot synthesis of imidazo[1,2-a]pyrimidines from easily available starting materials *via* 6-endo-dig cyclization using recyclable CuO nanoparticles without using bases and additives under solvent free condition. From sustainability point of view, green chemistry metrices like atom economy (94.4%) and E factor (0.11) are in the good agreement with the ideal values. Photophysical studies showed that these compounds possess good fluorescence quantum yield and one of the compound showed good affinity for zinc ion with stoichiometry ratio of 1:1, good binding constant and lower detection limit for detecting micromolar concentration of zinc ion.

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References and notes

1 Rival, Y.; Grassy, G.; Michel, G. *Chem. Pharm. Bull.* **1992**, 40, 1170-1176.

2 Catena, R. J. L.; Farrerons, G. L.; Fernandez, S. A.;Serra, C. C.; Balsa, L. D.; Lagunas, A. C.; Salcedo, R. C.; Fernandez, G. A. WO05014598A1, 2004 (*Chem. Abstr.* **2005,** 142, 240458z).

3 Revankar, G. R.; Matthews, T. R.; Robins, R. K. *J. Med. Chem.* **1975,** 18, 1253–1255.

4 Rival, Y.; Grassy, G.; Taudou, A.; Ecalle, R. *Eur. J. Med. Chem.* **1991**, 26, 13-18.

5 (a) George, P. G.; Rossey, G.; Sevrin, M.; Arbilla, S.; Depoortere, H.; Wick, A. E. L. E. R. S. *Monogr. Ser.* **1993,** 8, 49-59. (b) Berson, A.; Descatoire, V.; Sutton, A.; Fau, D.; Maulny, B.; Vadrot, N.; Feldmann, G.; Berthon, B.; Tordjmann, T.; Pessayre, D. J. *Pharmacol. Exp. Ther.* **2001,** 299, 793-800. (c) Saletu, J.; Grunberger, B.; Linzmayer, L. *Int. Clin. Psychopharmacol.* **1986,** 1, 145-164.

6 (a) Harrison, T. S.; Keating, G. M. *CNS Drugs* **2005,** 19, 65-89. (b) Hanson, S. M.; Morlock, E. V.; Satyshur, K. A.; Czajkowski, C. J. *Med. Chem.* **2008,** 51, 7243-7252. (c) Monti, J. M.; Warren, S.D.; Pandi Perumal, S. R.; Langer, S. Z.; Hardeland, R. *Clin. Med. Ther.* **2009,** 1, 123-140.

7 (a) Boerner, R.J.; Miller, H. J. *Psychopharmakother.* **1997**, 4, 145-148. (b) Sanger, D.J. *Behav. Pharmacol.* **1995**, 6, 116-126.

8 Enguehard-Gueiffier, C.; Gueiffier, A. *Mini-Rev. Med. Chem.* **2007**, 7, 888-899.

9 Feely, M.; Boyland, P.; Picardo, A.; Cox, A.; Gent, J. P. *Eur. J. Pharmacol*. **1989,** 164, 377−380.

10 Tully, W. R.; Gardner, C. R.; Gillespie, R. J.; Westwood, R. *J. Med. Chem.* **1991,** 34, 2060-2067.

11 Velazquez-Olvera, S.; Salgado-Zamora, H.; Velazquez-Ponce, M.; Campos-Aldrete, E.; Reyes-Arellano, A.; Perez-Gonzalez, C. *Chem. Cent. J.* **2012,** 6, 1-9.

12 (a) Gudmundsson, K. S.; Johns, B. A. *Org. Lett.* **2003,** 5, 1369-1372. (b) Denora, N.; Laquintana, V.; Pisu, M. G.; Dore, R.; Murru, L.; Latrofa, A.; Trapani, G.; Sanna, E. *J. Med. Chem.* **2008,** 51, 6876-6888. (c) Trapani, G.; Laquintana, V.; Denora, N.; Trapani, A.; Lopedota, A.; Latrofa, A.; Franco, M.; Serra, M.; Pisu, M.G.; Floris, I.; Sanna, E.; Biggio, G.; Liso, G.; *J. Med. Chem.* **2005,** 48, 292-305. (d) Jensen, M. S.; Hoerrner, R. S.; Li, W.; Nelson, D. P.; Javadi, G. J.; Dormer, P. G.; Cai, D.; Larsen, R. D. *J. Org. Chem.* **2005,** 70, 6034-6039. (e) Al-Tel, T. H.; Al Qawasmeh, R. A.; Voelter, W. *Eur. J. Org. Chem.* **2010,** 29, 5586-5593.

13 Kumar, A.; Kumara, M.; Mauryaa, S.; Khannab, R. S. *J. Org. Chem.* **2014,** 79, 6905−6912.

14 Shinde, V. V.; Jeong, Y.T. *New J. Chem.* **2015,** 39, 4977-4986.

15 Bush, A. I. *Curr. Opin. Chem. Biol.* **2000,** 4, 184-191.

16 Bush, A. I. *Trends Neurosci.* **2003,** 26, 207-214.

17 Cuajungco, M. P.; Lees, G. J. *Brain Res.* **1997,** 23, 219-236.

18 Takeda, A. *Biometals*, **2001,** 14, 343-351.

19 Park, H. M.; Oh, B. N.; Kim, J. H.; Qiong, W.; Hwang, I. H.; Jung, K.D.; Kim, C.; Kim, J. *Tetrahedron Lett.* **2011,** 52, 5581-5584.

20 Lee, H. G.; Lee, J. H.; Jang, S. P.; Hwang, I. H.; Kim, S. J.; Kim, Y.; Kim, C.; Harrison, R. G. *Inorg. Chim. Acta.* **2013,** 394, 542-551.

21 Lee, J.; Kim, H.; Kim, S.; Noh, J. Y.; Song, E. J.; Kim, C.; Kim, J. *Dyes Pigm.* **2013,** 96, 590-594.

22 Kang, J.; Kang, H. K.; Kim, H.; Lee, J.; Song, E. J.; Jeong, K.D.; Kim, C.; Kim, J. *Supramol. Chem.* **2013,** 25, 65-68.

23 Rajesh, U. C.; Pavan, S. V.; Rawat, D. S. *RSC Adv.* **2016***,* 6, 2935-2943.

24 Rajesh, U. C.; Manohar, S.; Rawat, D. S. *Adv. Synth. Catal.* **2013,** 355, 3170-3178.

25 Arya, K.; Rawat, D. S.; Sasai, H. *Green Chem.* **2012,** 14, 1956-1963.

26 Arya, K.; Rajesh, U. C.; Rawat, D. S. *Green Chem.* **2012,** 14, 3344-3351.

27 Arya, K.; Rawat, D.S.; Dandia, A.; Sasai, H. *J. Flourine Chem.* **2012,** 137, 117-122.

28 Gulati, U.; Rajesh, U. C.; Bunekar, N.; Rawat, D. S. *ACS Sustainable Chem. Eng.* **2017**, 5, 4672-4682.

29 Purohit, G.; Rajesh, U.C.; Rawat, D.S. *ACS Sustainable Chem. Eng***. 2017**, 5, 6466-6477**.**

30 Xu, J.; Xue, D. *J. Phys. Chem. B.* **2005,** 109, 17157-17161.

31 Gunnlaugsson, T.; Lee, T. C.; Parkesh, R. *Tetrahedron* **2004,** 60, 11239-11249.

32 Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949,** 71, 2703-2707.

33 Gupta, V. K.; Singh, A. K.; Ganjali, M. R.; Norouzi, P.; Faridbod, F.; Mergu, N. *Sens. Actuators, B.* **2013,** 182, 642-651.

34 Wang, L.; Qin, W.; Liu, W. *Inorg. Chem. Commun.* **2010,** 13, 1122-1125.

35 Kim, J. H.; Hwang, I. H.; Jang, S. P.;Kang, J.; Kim, S.;Noh, I.; Kim, Y.; Kim, C.; Harrison, R. G. *Dalton Trans.* **2013**, 42, 5500-5507.

36 Shortreed, M.; Kopelman, R.; Kuhn, M.; Hoyland, B. *Anal. Chem.* **1996**, 68, 1414-1418.

37 Lin, W.; Yuan, L.; Long, L.; Guo, C.; Feng, J. *Adv. Funct. Mater.* **2008,** 18, 2366-2372.

38 Kumar, Y. P.; King, P.; Prasad, V. S. K. R. *Chem. Eng. J.* **2006,** 124, 63-70.

Supplementary Material

Supplementary data (procedure for catalyst preparation, FESEM of recycled catalyst, green chemistry metrics calculations, experimental data and ^{1}H NMR and ^{13}C NMR spectra of all compounds) associated with this article can be found, in the online version

Highlights:

- Solvent free synthesis of fused imidazo[1,2-*a*]pyrimidines *via* A^3 coupling.
- Use of copper oxide nanoparticles as a recyclable catalyst.
- Short reaction time and good yield.
- Imidazo[1,2-*a*]pyrimidines act as a sensor for zinc ion.