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# Catalytic synthesis of 1-benzyl-4-fluoro-2- phenyl-1 *H*- benzo [d] imidazole: Dual applications in sensor and antimicrobial properties

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**KEYWORDS**
*ZnO nano flowers*; *Antimicrobial properties*; *Sensor*; *Benzimidazole*.

**ABSTRACT**:
Binding interaction of 1-benzyl-4-fluoro-2-phenyl-1H-benzo[d]imidazole (BFPB) functionalized ZnO nano flowers have been studied by absorption and fluorescence spectral studies. Functionalization of BFPB with ZnO nano flowers results agglomeration of nanoparticles shown by SEM images. BFPB was synthesized using ZnO catalyst. The remarkable features of this nanocatalyst are high productivity, short reaction time, green reaction and diverse substrate applications. Synthesized BFPB was characterized by proton NMR, carbon NMR, mass spectral studies and elemental analysis. Binding of BFPB enhance the fluorescence intensity of ZnO nano flowers. BFPB adsorbs on the surface of ZnO nano flowers which induce the electron transfer. BFPB is highly effective against *S.aureus* and *S.typhi*, for antibacterial studies and it was more active against *A.flavus* and *C.albicans* for antifungal studies compared to the standard drug.

## Introduction

In the ever expanding domain of fluorescence probes and related devices, the organic fluorescent molecules with distinct emissive nature have grabbed the attention of researchers. [1-5]. Benzimidazole, a heterocyclic multifunctional scaffold is considered as one such molecule used as a structural unit in fluorescent chemical sensors. Benzimidazole and its derivatives are exhibiting various potential and preferred spectral properties and are capable of accurate detection of a wide range of analytes. [6]. Particularly, their metal-ion binding properties, electron accepting, pi-bridging capability and biomolecule compatibility are pushing their applicability above the bar in the scientific fields of sensing, photovoltoics, bio-imaging and nonlinear optics. [7-10]. The benzimidazole derivatives are also found their applications in fabricating intramolecular charge transfer (ICT) fluorophores owing to their effective and simple accommodation of D-pi-A structural moiety. [11]. Hence, efforts have been taken to synthesise the benzimidazole and their derivatives using various synthetic routes. [12-15]. Anyhow the conventional synthetic routes may encounter practical difficulties such as longer reaction time, formation of by products or mixture of products, reduction in the expected yield, maintaining the vigorous reaction parameters, usage of toxic catalysts and hazardous solvents. [16]. To overcome such drawbacks, using heterogeneous metal oxide catalysts are suggested as better alternatives.[17].

With the advancements in the nano chemistry, it is further substantiated that the nano metal oxide counterparts, owing to their higher surface area to volume ratio, showed higher catalytic activity than their bulk metal oxides.[18]. One such facile nano $SiO_2$ catalyst has been chosen in the present investigation in the synthesis of benzimidazole by considering its salient features of its easy availability, non-complicated recovery, non-toxicity, higher order surface area, economic value, stability in terms of thermal, chemical and mechanical properties, above all itseco-friendliness.[19]

Fine tuning of florescent molecules are carried out by incorporation of semiconductor nanoparticles [20]. On account of the desirable chemical and physical properties, small size, nano ZnO particles are capable of receding scattering of visible light and providing non-opaque products which will retain ultra violet absorption [21]. Impact of ZnO clusters binding with various macro molecules have been investigated experimentally and theoretically by DFT calculation [22]. Nano ZnO prefers to bind with a ring nitrogen

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atom (N-site) relative to other binding sites of the biological DNA bases; [23]. As an attempt to enhance the UV spectral response of zinc oxide nano particles, other metal particles have been anchored on the surface of ZnO nanostructures which showed satisfactory results with proven increase in the charge separation [24]. Along this direction, the current investigation has been focussed on the synthesis of benzimidazole, subjecting them to the binding interactions with ZnO nano metal oxides and probing their applications for photodynamic cancer therapy.

## 2. Experimental

### *2.1. Synthesis of 1-benzyl-4-fluoro-2-phenyl-1H-benzo[d]imidazole*

1-benzyl-4-fluoro-2-phenyl-1*H*-benzo[d]imidazole *was* synthesized by three component assembling of 3-fluorobenzene-1,2-diamine, benzaldehyde and ammonium acetate in the ratio of 1:2:1 in presence of in the presence of ZnO nano catalyst at 353 K. Yield: 99%. mp. 214 °C, Anal. calcd. for $C_{20}H_{15}FN_2$: C: 79.5, H: 5.00, N: 9.27, F: 6.28. Found: C: 79.3, H: 5.10, N: 9.35, F: 6.30. $^1$H NMR (500 MHz, $CDCl_3$): δ 5.79 (s, 2H) methylene protons, 6.97 - 7.51 (m, 12 H), 8.28 (q, 2 H). $^{13}$C (100 MHz, $CDCl_3$): δ 52.2 (methylene carbon), 105.6, 109.9, 124.6, 124.9, 125.7, 127.5, 127.6, 131.1, 128.6, 129.2, 130.6, 135.8, 137.3, 149.0, 153.3.

### *2.2. Synthesis of nano ZnO Flowers*

To zinc acetate solution under continuous stirring, aqueous ammonia has been added to reach a pH of 7. The stirring has been continued for another 30 minutes. The formed glassy like white gel has been allowed to age overnight. It has been filtered, washed with water and ethanol, dried at 100 ºC for 10 h calcinated at 450 ºC for 2 h (heating rate 20 ºC per min) to white solid [25].

### *2.3. Surface functionalization of nano ZnO Flowers*

1 g nano ZnO nano flowers and 0.5 g of 1-benzyl-4-fluoro-2-phenyl-1H-benzo[d]imidazole in 50ml ethanol have been kept at 80 °C for 2 hours under continuous stirring. After that, the imidazole functionalized ZnO nano flowers have been collected and dried under vacuum.

### *2.4. Antibacterial studies*

The study involved gram-positive and gram-negative strains such as Staphylococcus aureus (gram-positive), Bacillus subtilis (gram-negative), Escherichia coli (gram-negative), Salmonella typhi (gram-negative), Klebsiella pneumonia (gram-negative), Pseudomonas aeruginosa (Gram-negative) were used. Nutrient agar plates prepared in a sterile environment were incubated overnight to detect bacteria. Use an infected vessel after transferring approximately 0.2 mL of the working culture to a food agar plate. Whatmann no-1 discs (6 mm diameter) were immersed in the test solution in DMSO (200 µg/mL) for almost half an hour. Commercially available disk solution (streptomycin 10 µg/disk) was used as standard. Negative controls were prepared by soaking disks of the same size in DMSO solution. Place the disk on the inoculated agar plate and allow incubation for approximately 18-24 hours. To evaluate antimicrobial activity, the zone of inhibition against the tested bacteria was measured.

### *2.5. Antifungal studies*

The fungal strains such as Cryptococcus neoformans, Candida albicans, Rhizopus sp, Aspergillus niger, Aspergillus flavus, and Mucor were used for the study. The medium tested for fungal infections was Sabouraud Dextrose Agar (SDA) and was tested on Sabouraud Dextrose Broth (SDB) medium. Use the same method for subculturing and counting viable organisms, except that the temperature is maintained at 28 ± 1 °C for approximately 72 h. In the past, almost the same quality solvent (DMSO) and amphotericin B (standard) were used for research purposes to prepare the drug combination.

## 3. Result and Discussion

### *3.1. Impact of catalytic activity of ZnO*

The reaction is first run with ethanol for 48 hours and stirred to ensure there is no catalyst. Just find the treasure. In order to increase the yield and shorten the reaction time, the reaction was carried out using nano-ZnO as a catalyst. Nano-ZnO was found to be more effective in ethanol media. This catalyst is very special and best in nature. The main features of this process are high productivity, short time, easy post-processing and low catalyst dosage, making the process simple, efficient and friendly. This method has proven useful in the field of benzimidazole synthesis.

### *3.2. Switch-on fluorescence and Energetics*

Uv-Vis spectra of newly prepared ZnO nano flowers and BFPB functionalized ZnO nano flowers are presented in **Figure 1**. Transfer of electron takes place from BFBP to semiconductor which result the increase in absorbance. It is also noted there is no change in wavelength. The increase in absorbance is due to the physical adsorption of BFPB on the surface of semiconductor material.

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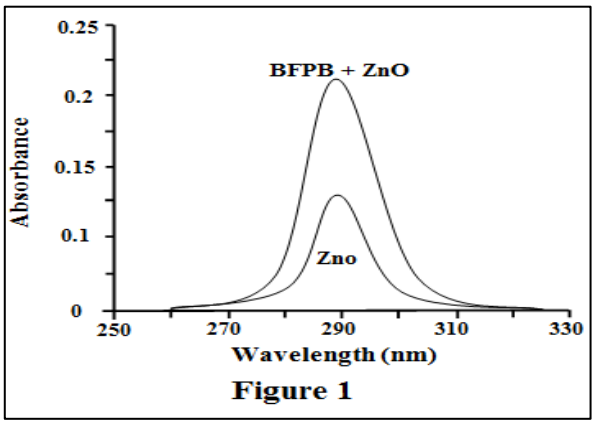


**Figure 1.** Uv-Vis spectra of newly prepared ZnO nano flowers and BFPB functionalized ZnO nano flowers

Fluorescence spectra of newly prepared ZnO nano flowers and BFPB functionalized ZnO nano flowers are presented in **Figure 2**.

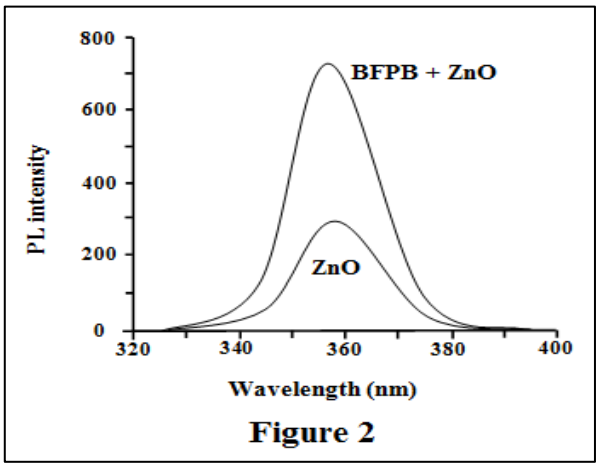


**Figure 2.** Fluorescence spectra of newly prepared ZnO nano flowers and BFPB functionalized ZnO nano flowers

Increase in fluorescence intensity was observed when BFPB is functionalized with ZnO nano flowers. Here also it is noted there is no change in wavelength of fluorescence. This is due to relocate from the higher energy state of BFPB to CB of ZnO nano flowers. The interfacial electron injection from the excited singlet of BFPB to CB of ZnO would be thermodynamically permitted based on the relative locations of BFPB and interfacial energy levels. Both the ZnO and the BFPB are stimulated by lights at the excitation wavelength. Due to the electron transfers from CB to VB and LUMO to HOMO, dual emission is anticipated. The likelihood is an electron jump from the excited BFPB to ZnO produced in a sol-gel. Compared to the CB of ZnO made by sol-gel, the electron in the LUMO of the excited BFPB has a higher energy. This should cause the fluorescence in the BFPB to quench. Contrary to expectations, fluorescence is seen to be enhanced in the presence of ZnO semiconductor material. This might be the result of adsorption on ZnO nano flowers, which lowers the HOMO and LUMO energy levels of BFPB. Due to adsorption, the polar ZnO nano flowers surface reduces the HOMO and LUMO energy levels and improves the delocalization of the electrons. The excited state energy of BFPB is higher than the sol-gel produced ZnO's CB energy levels. This enables the energy transfer from the excited state of the BFPB to the ZnO nano flowers produced in the sol-gel process. SEM images of bare ZnO nanomaterials and BFPB functionalized ZnO nano flowers are shown in **Figure 3**.

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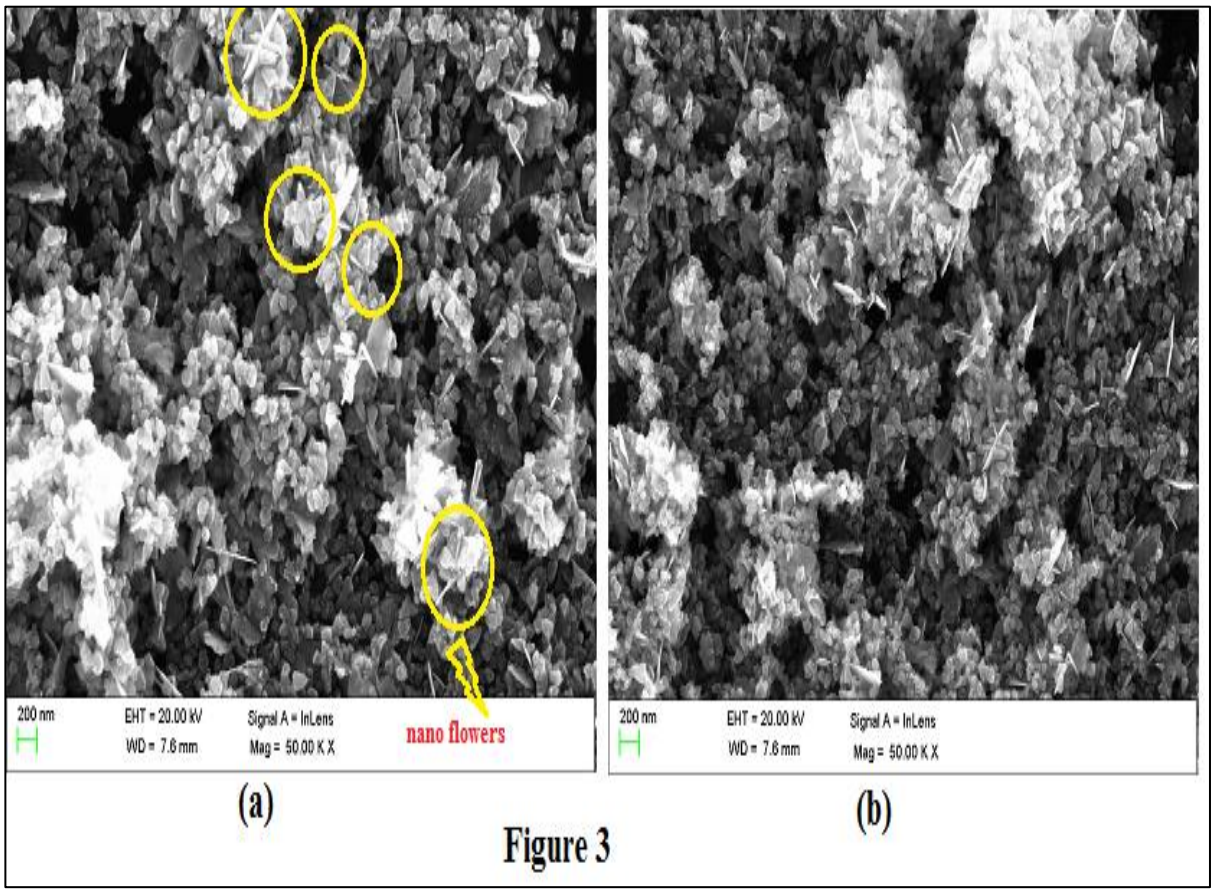


**Figure 3.** SEM images of (a) bare ZnO nanomaterials and (b) BFPB functionalized ZnO nano flowers

The shape of the ZnO nanomaterials is considerably changed by the adsorption of BFPB, as seen by the SEM photos. The BFPB adsorption on the semiconductor surface is confirmed by compares untreated ZnO nano flowers to vigin of EDS spectrum which is displayed in **Figure 4** [26-32].

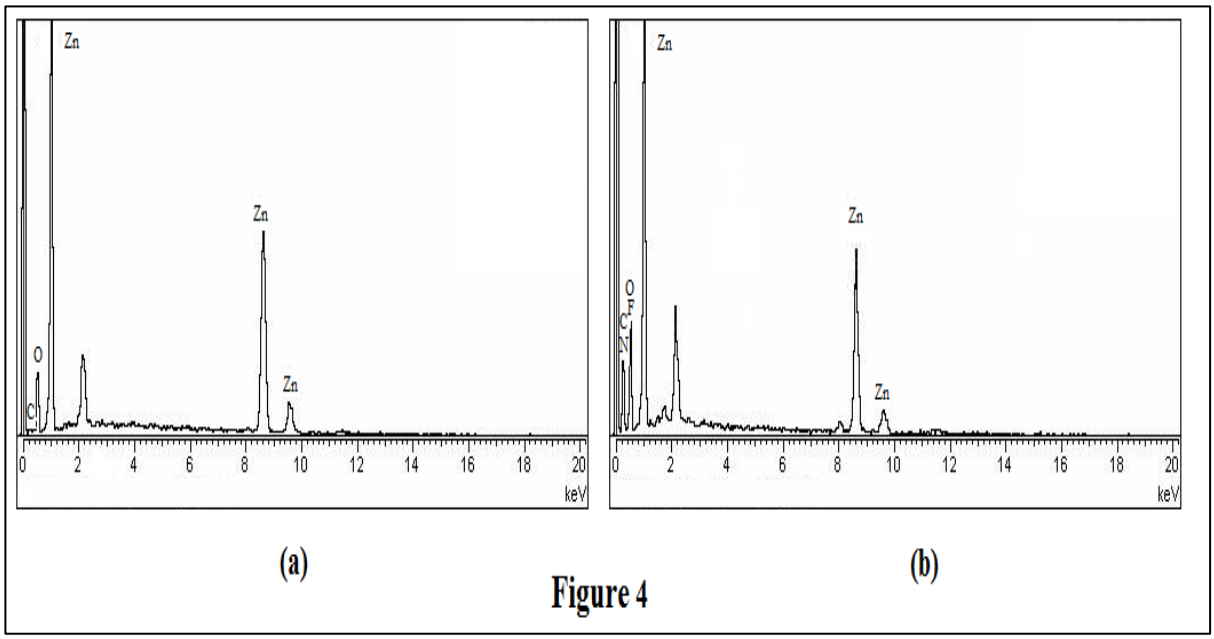


**Figure 4.** EDS spectrum of (a) bare ZnO nanomaterials and (b) BFPB functionalized ZnO nano flowers

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### *3.3. Antimicrobial studies*

The major antibacterial activity of BFPB was examined using the twofold serial dilution method [33-35]. Antibiotic studies have been conducted on bacteria such as *Salmonella typhi, Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumoniae* and *Escherichia coli*. The control used was DMSO. The standard for bacterial infections is streptomycin. **Table 1** lists the minimum inhibitory concentrations (MIC, in µM) of BFPB and samples against the organisms tested. The derivatives have been shown to be effective against all bacteria tested. BFPB is more resistant to *Salmonella typhi* and *Staphylococcus aureus*. The fungal strains such as *Aspergillus niger, Aspergillus flavus* and *Candida albicans* are used in our antifungal study. The control used was DMSO. *Amphotericin B* was used as the standard for fungal infections. **Table 2** lists the minimum inhibitory concentrations (MICs in µM) of BFPB and sample against fungal pathogens. BFPB was found to have good resistance to all fungal diseases tested. It is more resistant to *Aspergillus flavus* and *Candida albicans* than standard drugs.

**Table 1**: Antibacterial activities of BFPB (MIC, µM)

| Bacteria | BFPB | Streptomycin |
|---|---|---|
| ***S.aureus*** | 12.01 | 85.97 |
| ***B.subtilis*** | 103.12 | 21.49 |
| ***S.typhi*** | 66.31 | 85.97 |
| ***E.coli*** | 202.30 | 21.49 |
| ***K.pneumoniae*** | 50.03 | 42.98 |

**Table 2**: Antifungal activities of BFPB(MIC, µM)

| Fungal | BFPB | Amphotericin B |
|---|---|---|
| ***C.albicans*** | 11.78 | 27.05 |
| ***A.niger*** | 99.24 | 54.10 |
| ***A.flavus*** | 198.50 | 54.10 |

## 4. Conclusions

1-benzyl-4-fluoro-2-phenyl-1H-benzo[d]imidazole (BFPB) was designed and synthesized using ZnO catalyst. Product yield was excellent. This catalyst is unique and effective. ZnO nanoflowers were used for functionalization process which was done by BFPB. Functionalized ZnO nano flowers is studied by absorption, emission, scanning electron microscope images and energy dispersive spectrum. The loading of BFPB on ZnO nanoflower results the enhancement of fluorescence. The observed intensity enhancement is evidence that energy is transferred during the imidazole-ZnO nanoflower interaction. BFPB is highly effective against *S.aureus* and *S.typhi*, for antibacterial studies and it was more active against *A.flavus* and *C.albicans* for antifungal studies compared to the standard drug.

## Reference

1. V.S. Padalkar, D. Sakamaki, N. Tohnai, T. Akutagawa, K. Sakai, S. Seki, Highly emissive excited-state intramolecular proton transfer (ESIPT) inspired 2-(2'- hydroxy)benzothiazole-fluorene motifs: Spectroscopic and photophysical properties investigation, RSC Adv. 5 (2015) 80283–80296.
2. M.M. Islam, Z. Hu, Q.S. Wang, C. Redshaw, X. Feng, Pyrene-based aggregationinduced emission luminogens and their applications, Mater. Chem. Front. 3 (2019) 762–781.
3. M. Rahimi, A. Amini, H. Behmadi, Novel symmetric schiff-base benzobisthiazole-salicylidene derivative with fluorescence turn-on behavior for detecting Pb2+ ion, J. Photoch. Photobio.A 388 (2020) 112190.
4. K.K. Pei, H.T. Zhou, Y. Yin, G.Z. Zhang, W.Y. Pan, Q.L. Zhang, H.F. Guo, Highly fluorescence emissive 5, 5'-distyryl-3, 3'-bithiophenes: Synthesis, crystal structure, optoelectronic and thermal properties, Dyes Pigments 179 (2020) 108396.
5. Y.H. Zhao, H. Pan, G.L. Fu, J.M. Lin, C.H. Zhao, A highly emissive cruciform triarylborane as a ratiometric and solid state fluorescence sensor for fluoride ions, Tetrahedron Lett. 52 (2011) 3832–3835.
6. Ema Horak, Petar Kassal &Ivana Murković Steinberg (2017): Benzimidazole as a structural unit in fluorescent chemical sensors: the hidden properties of a multifunctional heterocyclic scaffold, Supramo lecular Chemistry, DOI: 10.1080/10610278.2017. 1403607]
7. Lai, M.Y.; Chen, C.H.; Huang, W.S.; Lin, J.T.; Ke, T.H.; Chen, L.Y.; Tsai, M.H.; Wu, C.C. Angew. Chem.-Int. Edit. 2008, 47, 581–585
8. Manoharan, S.; Anandan, S. Dyes Pigm. 2014, 105, 223–231.
9. Saltan, G.M.; Dincalp, H.; Kiran, M.; Zafer, C.; Erbas, S.C. Mater. Chem. Phys. 2015, 163, 387–393.
10. Perin, N.; Hranjec, M.; Pavlovic, G.; Karminski-Zamola, G. Dyes Pigm. 2011, 91, 79–88.
11. Kulhanek, J.; Bures, F. Beilstein J. Org. Chem. 2012, 8, 25–49
12. Mohammadpoor-Baltork, A.R. Khosropour, S.F. Hojati, Cata. Commun.8 (2007) 1865e1870.
13. Y. Kim, M.R. Kumar, N. Park, Y. Heo, S. Lee, J. Org. Chem. 76 (2011) 9577e9583.
14. K. Bahrami, M.M. Khodaei, I. Kavianinia, J. Chem. Res. 2006 (2006) 783e784.
15. L.H. Du, Y.G. Wang, Synthesis (2007) 675e678
16. Leila Dinparast, Hassan Valizadeh, Mir BabakBahadori, Somaieh Soltani, Behvar Asghari, Mohammad-RezaRashidi, Design, synthesis, a-glucosidase inhibitory activity, molecular docking

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4s), 486-491 | ISSN:2251-6727

and QSAR studies of benzimidazole derivatives, Journal of Molecular Structure 1114 (2016) 84-94

17. K. Sivakumar, V. Senthil Kumar, J.J. Shim, Y. Haldorai, Synth. React. Inorg.Met. Org. Nano-Met. Chem. 45 (2015) 660-666.
18. L. Guczi, D. Horvath, Z. Paszti, L. T oth, Z. Horvath, A. Karacs, G. Peto, J. Phys. Chem. B 104 (2000) 3183-3193.491
19. Mohammadpoor-Baltork, M. Moghadam, S. Tangestaninejad, V. Mirkhani, Z. Eskandari, H. Salavati, Chemoselective synthesis of 2-aryloxazines and 2aryltetrahydropyrimidines using nano-SiO as a reusable solid acid catalyst under thermal conditions and microwave irradiation, J. Iran. Chem. Soc. 8 (2011) S17–S27
20. Jayabharathi, J., Sundharesan, M., Prabhakaran, A., Karunakaran, C. (2015). Understanding the binding interaction of imidazole with ZnO nanomaterials and clusters. RSC Advances, 5(13), 9518–9531.
21. K. Schilling, B. Bradford, D. Castelli, E. Dufour, J. F. Nash, W. Pape, S. Schulte, I. Tooley, J. Bosch and F. Schellauf, Photochem. Photobiol.Sci., 2010, 9, 495.
22. F.D. Angelis and L. Armelao, Phys. Chem. Chem. Phys., 2011, 13, 467
23. V. Shewale, P. Joshi, S. Mukhopadhyay, M. Deshpande, R. Pandey, S. Hussain and S. P. Karna, J. Phys. Chem. C, 2011, 115, 10426.
24. Alharthi, F.A., Alghamdi, A.A., Al-Zaqri, N. et al. Facile one-pot green synthesis of Ag–ZnONanocomposites using potato peeland their Ag concentration dependent photocatalytic properties . Sci Rep 10, 20229 (2020).https://doi.org/10. 1038/s41598-020-77426-y
25. C. Karunakaran, J. Jayabharathi, K. Jayamoorthy, P. Vinayagamoorthy, J. Photochem. Photobiol. A. 247 (2012) 16–23.
26. K.I.Dhanalekshmi, K.Jayamoorthy, B. Subash, P. Magesan, Oguejiofo T. Ujam, Xiang Zhang & K. Kadambary (2022) Bi nding interaction of 5-amino-2-mercaptob enzimidazole with Au-TiO2: inhibition of switch-on fluorescence, Inorganic and Nano-Metal Chemistry , 52:6, 842-847.
27. S Suresh, K Jayamoorthy, S Karthikeyan, Switch-on fluorescence of 5-amino-2-mercapto benzimidazole by Mn3O4 nanoparticles: Experimental and theoretical approach, Journal of Luminescence 198, 2018, 28-33.
28. P. Saravanan, K. Jayamoorthy, S.A. Kumar, Fluorescence quenching of APTES by $Fe_2O_3$ nanoparticles–Sensor and antibacterial applications, Journal of Luminescence 178, 2016, 241-248.
29. S. Suresh, K. Jayamoorthy, P. Saravanan, S. Karthikeyan, Switch-Off fluorescence of 5-amino-2-mercapto benzimidazole with Ag3O4 nanoparticles: Experimental and theoretical investigations, Sensors and Actuators B: Chemical 225, 2016, 463-468.
30. P. Saravanan, K. Jayamoorthy, S.A. Kumar, Switch-On fluorescence and photo-induced electron transfer of 3-aminopropyl triethoxysilane to ZnO: Dual applications in sensors and antibacterial activity, Sensors and Actuators B: Chemical 221 (2015) 784-791.
31. C. Karunakaran, J. Jayabharathi, K. Jayamoorthy, P. Vinayagamoorthy, Benzimidazole based Ir(III) picolinate complexes as emitting materials and the fluorescent behavior of benzimidazole bound to Mn–TiO @ZnO core/shell nanospheres, Materials Express, 4 (2014) 279-292(14).
32. C. Karunakaran, J. Jayabharathi, R. Sathishkumar, K. Jayamoorthy, Interaction of fluorescent sensor with superparamagnetic iron oxide nanoparticles, Spectrochim.Acta Part A: 110 (2013) 151-156.
33. S. Suresh, P. Saravanan, K. Jayamoorthy, S. Ananda Kumar, S. Karthikeyan, Materials Science and Engineering C 64 (2016) 286–292.
34. Othmane Roby, Fatima Zahra Kadiri, Zineb Loukhmi, Mohamed Moutaouakil, Said Tighadouini , Rafik Saddik, Aziz Aboulmouhajir, Synthesis of new set of imidazo[1,2-a]pyridine-schiff bases derivatives as potential antimicrobial agents: Experimental and theoretical approaches, Journal of Molecular Structure, 1292 (2023) 136186.
35. Yıldız Uygun Cebeci, Özge Özşen Batur, Houssem Boulebd, New piperazine-hydrazone derivatives as potential antimicrobial agents: Synthesis, characterization, biological evaluation, and in silico investigations, Journal of Molecular Structure, 1289 (2023) 135791.