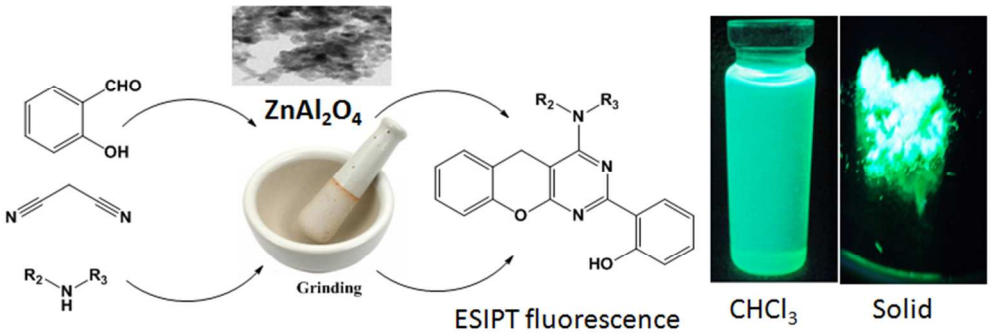
RSC Advances




ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances



Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

# A novel, facile, rapid, solvent free protocol for the one pot green synthesis of chromeno[2,3-d]pyrimidines using reusable nano $ZnAl_2O_4$ – NOSE approach and their photophysical studies

**Balijapalli Umamahesh, Triveni Rajashekhar Mandlimath and Kulathu I. Sathiyanarayanan***

***Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX***
**DOI: 10.1039/b000000x**

The current protocol manifested the preparation of an eco-friendly, highly stable, reusable nano $ZnAl_2O_4$ and for the first time this was used as an excellent catalyst for the pseudo four component synthesis of library of fluorescent chromeno[2,3-d]pyrimidines derivatives. This novel protocol involved grinding of salicylaldehydes, malononitrile and secondary amines in the presence of catalytic amount of nano $ZnAl_2O_4$ at room temperature which was extremely simple, facile, cost effective, solvent free protocol and also required just two minutes to achieve the products with excellent yields. The synthesized chromeno[2,3-d]pyrimidine derivatives showed significant absorption, emission properties and large Stoke's shift values due to their characteristic feature of excited state intramolecular proton transfer (ESIPT) mechanism. Nano $ZnAl_2O_4$ exhibited better catalytic activity than that of the bulk due to its larger surface area of 63 $m^2/g$, and was recycled for 5 times without loss of activity.

## Introduction

The development of a facile, efficient protocol for the multi-component reactions (MCRs) which meet the credentials of green chemistry aspects as well as cost effectiveness has gained a great importance in synthetic as well as medicinal chemistry. MCRs involving carbon-carbon[1], carbon-oxygen[2] and carbon-nitrogen[3] bond formation are very attractive as they allow synthesizing a wide range of complicated medicinal scaffolds[4]. It is extremely important to explicate a protocol which can construct such complex molecules in a single step using reusable heterogeneous, inexpensive catalyst in a simple solvent-free rapid procedure at room temperature, with excellent yields. In recent years, nano metal oxides have attracted much attention as excellent catalysts for MCRs because of their high thermal[5], chemical stability[6], large surface area[7], high efficiency[8] and ease of separation from the reaction mixture[9]. Being cheap[10] and environmentally benign[11], these nano metal oxides facilitate the reactions as they possess active sites on their surface[12] by bringing the reactants close to each other, and thus accelerate the reaction rate[13] and also provide reusability[14], high selectivity[15] and excellent yields in shorter duration[16]. Nanomaterials have been employed to mimic the homogeneous catalysts for MCRs to carry out at room temperature and thus these materials could be the alternative catalysts for homogeneous catalysts[17].

* *Chemistry Division – School of Advanced Sciences VIT University, Vellore – 632014, Tamil Nadu, India. Fax:+914162243092; Tel: +914162244520; E-mail:sathiya_kuna@hotmail.com*

† Electronic Supplementary Information (ESI) available: [NMR copies of synthesized compounds were included]. See DOI: 10.1039/b000000x/

Chromeno[2,3-d]pyrimidine derivatives are the important class of compounds constructed by the fusion of chromenes and pyrimidines. These are the potential candidates, which exhibit *in vivo* antitumor activity, cytotoxic activity against P388 lymphocytic leukemia by causing significant perturbation in cell cycle kinetics, and also by being selectively active against a number of human ovarian cell lines[18]. Chromeno[2,3-d] pyrimidines possess in vitro activity against both gram positive and negative bacteria[19]. The derivatives with this moiety are also active against fungi and their antimicrobial activities are higher than that of 4H- chromenes[19]. In addition, these molecules exhibit excellent photophysical properties but detailed study has not been carried out so far[20].

Chromeno[2,3-d]pyrimidine moiety was reported by O'Callaghan by the condensation of 2-iminocoumarin-3-carboxamide with aldehyde, which involves multistep reaction procedure[21]. $LiClO_4$ has been used as catalyst for the synthesis of chromeno[2,3-d]pyrimidine derivatives but it requires 15 h of stirring[22]. There are only few reports in the literature for the synthesis of chromeno[2,3-d]pyrimidines by the one pot tandem condensation of salicylaldehydes, malononitrile and secondary amines: high temperature solvent-free microwave assisted synthesis[23], expensive $[Bmim]BF_4$ ionic liquid[24], less active heterogeneous catalyst[25] and magnetic nanomaterial[26] synthesis. Homogeneous Lewis acid catalysts such as CuCl, $ZnCl_2$ and $ZrOCl_2.8H_2O$ have been used for this synthesis. Even though this protocol involves room temperature synthesis, it takes long time to achieve the good yields and the catalysts are not reusable[20].

Keeping the drawbacks of existing methods in our mind for the synthesis of chromeno[2,3-d]pyrimidines, we prepared $ZnAl_2O_4$

nanoparticles and employed them as catalyst for MCRs. We developed a new protocol for the pseudo four component synthesis of chromeno [2,3-d]pyrimidines using salicylaldehydes, malononitrile and secondary amines. The protocol demonstrated was a room temperature synthesis, rapid, solvent free, environmentally benign and cost effective method. The catalysts were chemically stable and also reused successfully for 5 cycles. To the best of our knowledge, we report nano $ZnAl_2O_4$ for the first time for the pseudo four component synthesis of library of fluorescent chromeno[2,3-d]pyrimidines synthesis.

## Results and discussion

### Characterization of nano $ZnAl_2O_4$

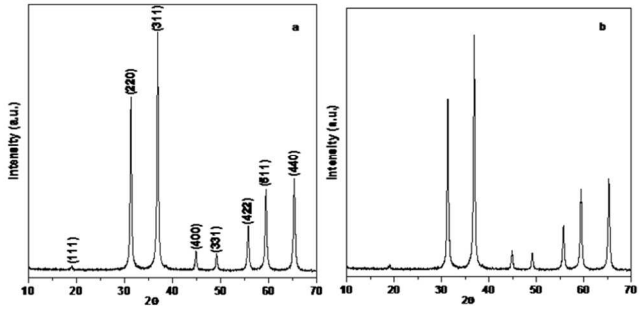



**Fig.1** Powder X-ray diffraction pattern of fresh nano $ZnAl_2O_4$ (a) and after 5 cycles (b).

Fig 1a. shows that the synthesized fresh nano $ZnAl_2O_4$ was phase pure, and was crystallized in face centered cubic phase with the diffraction peaks at 2θ = 19.0, 31.3, 36.8, 44.8, 49.1, 55.6, 59.3, 65.3, 74.2 and 77.3 which were indexed based on ICDD data (# 821043). The average crystallite size of nano $ZnAl_2O_4$ was calculated using full width half maximum values in Scherrer's formula and was found to be 20 nm which corroborates the TEM result. Fig 1b affirms that the nano $ZnAl_2O_4$ was stable even after 5 cycles. BET surface area of the catalyst was 63 $m^2/g$. FTIR spectrum of the nano $ZnAl_2O_4$ is shown in Fig. 2. It gives the bands at 662 $cm^{-1}$, 558 $cm^{-1}$ and 501 $cm^{-1}$ corresponding to stretching and bending modes of Al-O of octahedral $AlO_6$ units respectively. The absence of stretching vibration bands of inverse spinel units ($AlO_4$) in the range 700-850 $cm^{-1}$ confirms $ZnAl_2O_4$ was purely normal spinel structure[27]. EDX spectrum (Fig. 2), confirmed the presence of atoms Zn, Al and O in the catalyst. TEM images (Fig. 3) affirmed that the particles exhibited oval shape and found in the range 6-20 nm (the inset in Fig. 4). Selected area electron diffraction pattern (SAED) indicated the presence of pure and crystalline spinel $ZnAl_2O_4$.

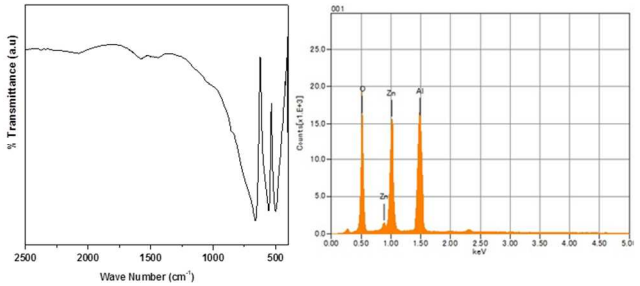



**Fig.2** FTIR spectrum of nano $ZnAl_2O_4$ (left) and EDX spectrum of nano $ZnAl_2O_4$(right).

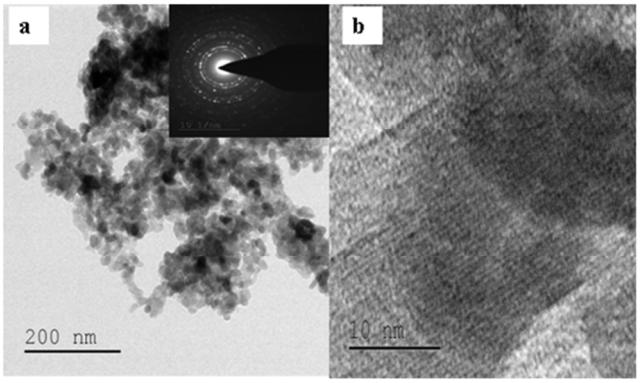
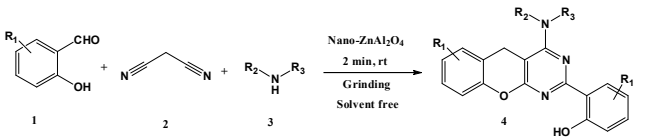



**Fig.3** TEM images and SAED pattern of nano $ZnAl_2O_4$.

### Catalytic role and optimization of nano $ZnAl_2O_4$ on the synthesis of chromeno[2,3-d]pyrimidines

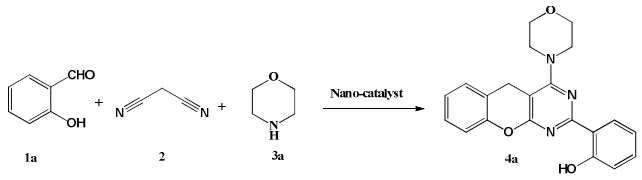
In the initial phase, we planned to study the catalytic role of nano $ZnAl_2O_4$ on one-pot pseudo four component reactions of salicylaldehyde, malononitrile and secondary amine as shown in Scheme 1. We focused our attention on designing and generalizing the optimal conditions of the reaction. At first, in order to carry out the synthesis of chromeno[2,3-d]pyrimidine derivatives in a more efficient way, the reaction among salicylaldehyde (2 mmol), malononitrile (1 mmol) and morpholine (1 mmol) was selected as a model reaction at room temperature (Scheme 2). Without catalyst, the reaction did not proceed by grinding or stirring conditions and even with ethanol as solvent. Very low yields were obtained by employing bulk $Al_2O_3$ as a catalyst in ethanol. Then we attempted preliminary screening tests of catalysts using bulk and nano-$Al_2O_3$, ZnO, $ZnAl_2O_4$, and these tests are summarized in Table 1. Significant improvements in the yields were observed when the reaction conditions were switched from bulk $Al_2O_3$ to nano-$Al_2O_3$ under same experimental conditions. But when we carried out the same reaction in ethanol by using bulk ZnO as a catalyst, interestingly yields were moderately increased with reduced reaction time. Almost similar results were obtained using nano ZnO as a catalyst. By keeping these interesting key properties in our mind, i.e., significant yield improvement using nano- $Al_2O_3$ and reduction in the time taken for the completion of reaction using ZnO, it was of interest to design spinel $ZnAl_2O_4$ for employing as a catalyst for these MCRs.




**Scheme 1** Nano ZnAl2O4 catalyzed synthesis of chromeno[2,3-d]pyrimidine derivatives under solvent free conditions.

In order to study the catalytic role of bulk $ZnAl_2O_4$, a controlled experiment was carried out by adopting the above model reaction conditions by stirring at room temperature using appropriate 20 mol % catalysts (Table 1, entry 1). Under these conditions, the reaction proceeded moderately with 66% yield and took less reaction time compared to ZnO. With the same standard conditions, when nano $ZnAl_2O_4$ was employed as a catalyst, surprisingly 86 % of desired chromeno[2,3-d]pyrimidine **4a** was obtained within 30 min. This was because of the higher

surface area of nano $ZnAl_2O_4$ (63 $m^2/g$) when compared to bulk $ZnAl_2O_4$ (10.4 $m^2/g$). In order to study the effect of quantity of nano $ZnAl_2O_4$ on the reaction, we monitored the same reaction using 5, 10, 15, 20 and 25 mol % of nano $ZnAl_2O_4$ catalyst and found that the quantity of catalyst had a significant effect on the formation of the desired product. The use of 5 mol % and 15 mol % of nano- $ZnAl_2O_4$ resulted in low yields (Table 1, entries 6 and 8). Whereas, 86 % of the desired product **4a** was obtained by employing 20 mol % of nano-$ZnAl_2O_4$ at room temperature (Table 1, entry 5).




**Scheme 2** Nano $ZnAl_2O_4$ catalyzed synthesis of chromeno[2,3-d]pyrimidines using salicylaldehyde, malononitrile and morpholine.

**Table 1** Screening of the catalyst for one-pot synthesis of chromeno[2,3-d]pyrimidines

| Entry | Nano catalyst [a] | Solvent [i] | | Without solvent | | | |
|---|---|---|---|---|---|---|---|
| | | | | Stirring | | Grinding | |
| | | Time (min) | Yield (%) | Time (min) | Yield (%) | Time (min) | Yield (%) |
| 1 | No catalyst | 720 | 10 | 720 | ND | 720 | ND |
| 2 | $Al_2O_3$(b, n) [c] | 720 | 25, 45 | 720 | 12, 29 | 30 | 10, 28 |
| 3 | $Al_2O_3$(b, n) [d] | 720 | 30, 47 | 720 | 10,32 | 30 | 10, 27 |
| 4 | ZnO(b, n) | 360 | 61, 63 | 360 | 68, 69 | 30 | 71, 78 |
| 5 | **$ZnAl_2O_4$(b, n)** | **60, 30** | **66, 86** | **30, 2** | **84, 93** | **30, 2** | **80, 96** |
| 6 | $ZnAl_2O_4$(b,n) [e] | 75, 30 | 10, 25 | 45, 30 | 25, 44 | 45, 30 | 5, 40 |
| 7 | $ZnAl_2O_4$(b,n) [f] | 60, 30 | 30, 50 | 30, 10 | 39, 70 | 30, 10 | 35, 60 |
| 8 | $ZnAl_2O_4$(b,n) [g] | 60, 30 | 55, 78 | 30, 5 | 77, 88 | 30, 5 | 79, 90 |
| 9 | $ZnAl_2O_4$(b,n) [h] | 60, 30 | 65, 84 | 30, 2 | 83, 89 | 30, 2 | 81, 95 |

Reaction Conditions: Salicylaldehyde (2 mmol), malononitrile (1 mmol), morpholine (1 mmol) and catalyst (20 mol %) in 10 ml solvent; a. 20 mol % catalyst loaded; b.bulk; c. acedic; d. basic; e. 5 mol % catalyst loaded; f. 10 mol % catalyst loaded; g. 15 mol % catalyst loaded; h. 25 mol % catalyst loaded; i. Ethanol used as solvent; n. nano.

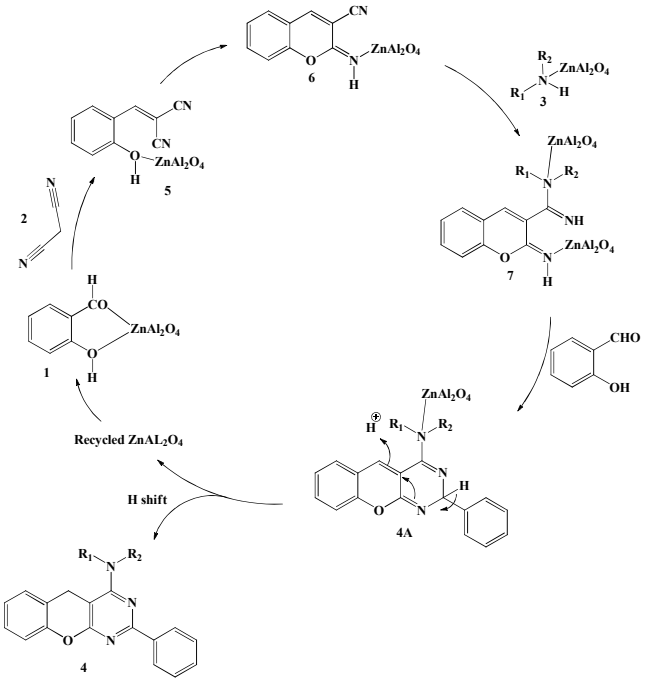
In order to achieve high yield in a shorter duration, we performed the reactions in various solvents at room temperature as well as under reflux conditions. A range of nonpolar to polar solvents such as toluene, chloroform, dioxane, tetrahydrofuron, ethanol, methanol and acetonitrile were used for these MCRs, but there was no significant effect on the yields of product even after few hours (Table 2). Unsatisfied with these results, we also tested the influence of solvent-free conditions on the reaction rate and yield by screening several conditions at room temperature in the presence of $ZnAl_2O_4$ nanoparticles and found that the product formation took place rapidly under solvent-free stirring conditions than in the presence of a solvent (Table 1). Satisfactory results were obtained with the use of liquid reactants but moderate yields were achieved with solid reactants due to the improper mixing of solid reactants, which in turn reduced the feasibility to react each other due to heterogenity. To overcome this drawback, a systematic procedure was followed. Mixture of salicylaldehydes (2 mmol), malononitrile (1 mmol), and nano $ZnAl_2O_4$ catalyst (20 mol %) in mortar was well ground with pestle at room temperature for 60 sec. Then the secondary amine (1 mmol) was added to the well ground reaction mixture which resulted in a vigorous exothermic reaction within few seconds. Realizing this catalytic enhancement of the MCRs reaction by nano-$ZnAl_2O_4$ with this 'NOSE' approach, the desired chromeno[2,3-d]pyrimidine derivatives were obtained up to 97 % yield in 2 min reaction time under solvent-free grinding conditions.

**Table 2** Effect of solvents on the synthesis of chromeno[2,3d]pyrimidines

| Sl. No. | Solvent | Yield (%) [a, b] |
|---|---|---|
| 1 | Toluene | 59, 61 |
| 2 | Chloroform | 60, 62 |
| 3 | Dioxane | 69, 68 |
| 4 | Tetrahyrofuron, | 66, 70 |
| 5 | Ethanol | 86, 86 |
| 6 | Methanol | 81, 85 |
| 7 | Acetonitrile | 79, 80 |

a. Under room temperature; b. under reflux conditions; Reaction Conditions: Salicylaldehyde (2 mmol), malononitrile (1 mmol), morpholine (1mmol) and nano $ZnAl_2O_4$ catalyst (20 mol %) in 10 ml solvent

To estimate the scope and generality of the NOSE protocol, 2-hydroxy aromatic aldehydes having both electron-withdrawing and electron-donating groups were allowed to react with an active methylene compound malononitrile and secondary amine based nucleophile like morpholine, piperidine, 1-phenylpiperazine, 1-benzylpiperazine, N-Benzhydrylpiperazine, pyrrolidine, diethyl amine, n-ethylaniline, and n-ethyltoluidine under optimized reaction conditions. The results are depicted in Table 4. The reaction proceded smoothly with the substituted salicylaldehydes i.e., **4a, 4b, 4c, 4d, 4e** yielding 96, 94, 89, 93, 89 % respectively except 4f which yielded only 72 %. Similarly, the reaction with the cyclic secondary amines such as **4a, 4g, 4k, 4l, 4m** gave better yields of 96, 97, 85, 89, 90 % respectively when compared to dialkyl substituted amines such as **4q, 4r** giving 81,




**Scheme 3** Plausible mechanism for nano $ZnAl_2O_4$ catalyzed synthesis of chromeno[2,3-d]pyrimidines.

80 % respectively. No products were obtained with the use of alkyl-aryl substituted amines. The reactions were consistently carried out at 1 mmol scale, and no change of product yield was observed when scaled up to 10 mmol scale under the same reaction conditions.

The plausible mechanism for the formation of chromeno[2,3-d]pyrimidine was proposed according to the literature. Initially the condensation of salicylaldehyde **1** and malononitrile **2** yielded Knoevenagel product **5**, which upon subsequent Pinner reaction formed cyclized product **6**. The reaction was initiated by catalytic nucleophilic attack of amines **3** on the cyano group of cyclized product **6** to produce intermediate **7**. Finally, intermediate **7** reacted with another molecule of salicylaldehyde 1 followed by proton transfer of **4A** to result in the product **4** with recyclable nano catalyst (Scheme 3). We assumed that the nano $ZnAl_2O_4$ initiated both Knoevenagel condensation of salicylaldehyde with malononitrile and nucleophilic attack of secondary amine as it possess Lewis acidic $Zn^{2+}$ and $Al^{3+}$ sites[7]. It is known from the previous report that the Lewis acid catalysts facilitate chromeno[2,3-d]pyrimidines synthesis and the zinc based catalyst is more reactive[20].

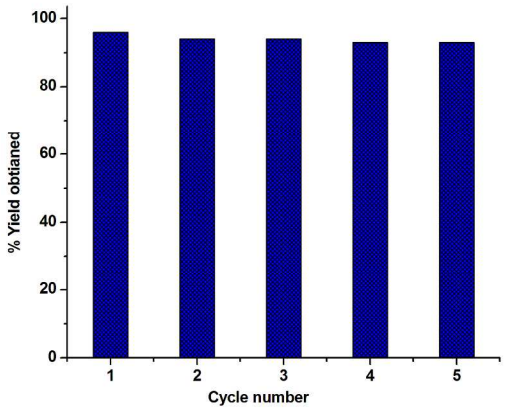



**Fig. 4** Reusability of nano ZnAl2O4 for the synthesis of chromeno[2,3-d]pyrimidines using salicylaldehyde, malononitrile and morpholine.

To examine the reusability of nano $ZnAl_2O_4$, the catalyst was collected by filtration after every cycle and it was washed with chloroform, tetrahydrofuran and acetone (each 5 mL) to remove the organic compound and dried overnight in the oven at 60 °C before it was used for the next cycle. To check the reusability of $ZnAl_2O_4$ nano, we have chosen Nano $ZnAl_2O_4$ and was found to be consistently active for 5 cycles (Fig. 4). AAS was used to find out the leaching of ions after each cycle, and it was found to be nil. We made a comparison of our protocol with the reported protocols (Table 3). It is understood that although there are few solvent free, short duration protocols for the synthesis of chromeno[2,3-d]pyrimidine available in literature, they suffer from drawbacks such as, high temperature reactions, use of expensive and non-reusable catalysts. Nano $ZnAl_2O_4$ took the shortest duration to synthesize these derivatives with reusability.

**Table 3** Comparison of the activity of the catalysts for the synthesis of chromeno[2,3-d]pyrimidine derivatives.

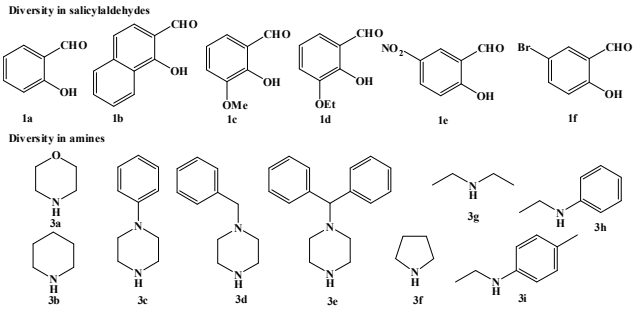
| Sl. No. | Catalyst | Solvent | Temperature/reaction condition | Reaction time | Yield (%) | Reference |
|---|---|---|---|---|---|---|
| 1 | $LiClO_4$ | $C_2H_5OH$ | RT/stirring | 15 h | 74 - 80 | 22 |
| 2 | - | - | 100 °C/ Microwave oven | 3- 6 min | 86 - 96 | 20 |
| 3 | $[Bmim]BF_4$* | - | RT/stirring | 20 min | 65 - 90 | 21 |
| 4 | CuCl, $ZnCl_2$ | $CH_2Cl_2$, $CH_3OH$ | 80 °C/reflux 80 °C/reflux | 7 h 4 h | 72 80 | 16 |
| 5 | Aminopropyl coated $Fe_3O_4$ | - | RT | 7 min | 87- 89 | 22 |
| 6 | Nano $ZnAl_2O_4$ | - | RT | 2 min | 72 - 97 | present work |

* 1-Butyl-3-methylimidazolium tetrafluoroborate

**Photophysical study of chromeno[2,3-d]pyrimidines**

The spectral properties of the compounds such as absorption ($\lambda_{max}$), emission ($\lambda_{em}$), Stoke's shift and molar extinction coefficient (ε) were measured in tetrahydrofuran, and they are summarized in Table 4. The absorption and fluorescence spectra of all the products dissolved in tetrahydrofuran are shown in Fig. **5a** and **5b** respectively. All the compounds showed absorption with maximum wavelength ranging from 285 to 360 nm. Most of the derivatives displayed two absorption maxima except **4f, 4h** and **4i** which showed single band. Highest energy absorption band I in the region of 280–300 nm and lowest energy absorption band II in the region of 315–360 nm were observed. The lowest energy transition band II could be attributed to the transition from singlet ground ($S_0$) to the first excited state ($S_1$) $S_0 \rightarrow S_1$. The increase in conjugation and increased electron density associated with salicylaldehyde groups and presence of alkyl groups in

**Table 4** Photophysical properties of nano-$ZnAl_2O_4$ catalyzed chromeno [2,3-d]pyrimidine derivatives.




| Entry | Aldehyde | Amine | Product | Yield (%) | Solution $\lambda_{abs}$(nm) | Solution $\lambda_{em}$(nm) | Solid state $\lambda_{em}$(nm) | Δ ($cm^{-1}$) |
|---|---|---|---|---|---|---|---|---|
| 1 | 1a | 3a | 4a | 96 | 290, 320 | 485 | 499 | 10631 |
| 2 | 1b | 3a | 4b | 94 | 300, 355 | 445 | 509, 554 | 10861 |
| 3 | 1c | 3a | 4c | 89 | 290, 325 | 401 | 503 | 5831 |
| 4 | 1d | 3a | 4d | 93 | 295, 315 | 476 | 498 | 10737 |
| 5 | 1f | 3a | 4e | 89 | 295, 330 | 493 | 500 | 10019 |
| 6 | 1e | 3b | 4f | 72 | 295 | 490 | - | 13490 |
| 7 | 1a | 3b | 4g | 97 | 295, 320 | 496 | 491 | 11089 |
| 8 | 1c | 3b | 4h | 93 | 285 | 402 ,457 | 512 | 13206 |
| 9 | 1d | 3b | 4i | 92 | 295 | 478 | 516 | 12978 |
| 10 | 1f | 3b | 4j | 91 | 290, 330 | 496 | 507 | 10142 |
| 11 | 1a | 3c | 4k | 85 | 295, 320 | 498 | 508 | 11170 |
| 12 | 1a | 3d | 4l | 89 | 295, 320 | 501 | 505 | 11290 |
| 13 | 1a | 3e | 4m | 90 | 280, 320 | 496 | 500 | 11089 |
| 14 | 1a | 3f | 4n | 91 | 295, 320 | 470 | 477 | 9973 |
| 15 | 1c | 3f | 4o | 89 | 295, 315 | 499 | 509 | 11706 |
| 16 | 1d | 3f | 4p | 87 | 290, 320 | 494 | 503 | 11007 |
| 17 | 1c | 3g | 4q | 81 | 295, 360 | 474 | 555 | 6681 |
| 18 | 1f | 3g | 4r | 80 | 290, 330 | 495 | 492 | 10101 |
| 19 | 1a | 3h | 4s | nd | - | - | - | - |
| 20 | 1a | 3i | 4t | nd | - | - | - | - |

Yields refer to isolated products after purification by recrystallization.

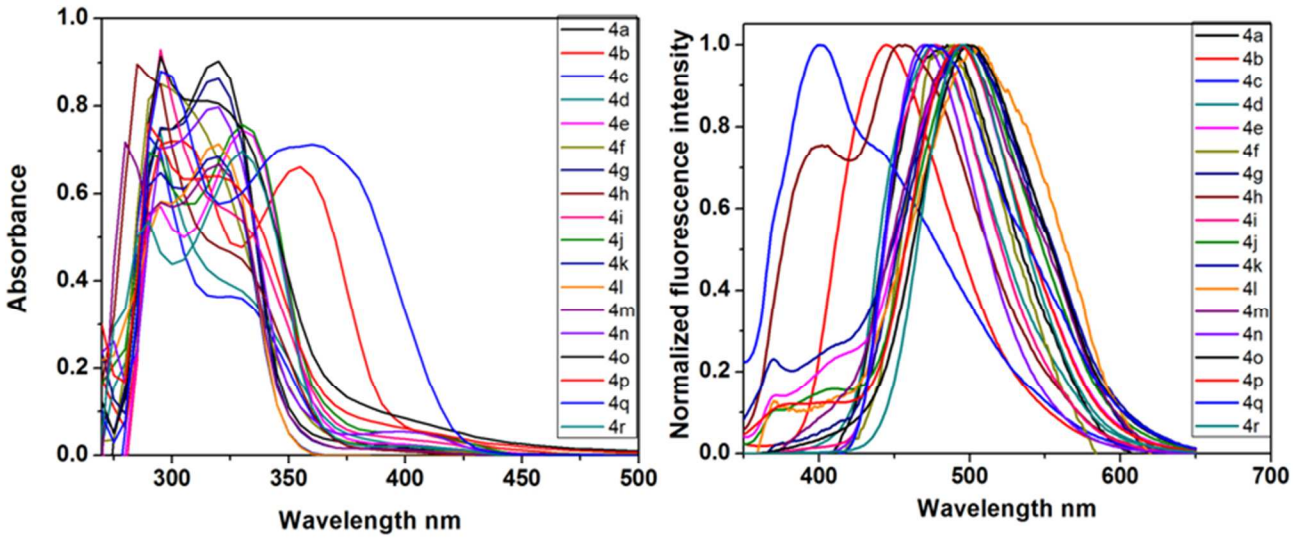



**Fig. 5** (a) UV-vis spectra (b) Fluorescence spectra of compounds 4a–r recorded in tetrahydrofuran solution ($5 \times 10^{-5}$M).

amine moiety in chromeno[2,3-d]pyrimidines led to bathochromic shift of the absorption maxima in compounds **4b**, **4q** and **4r**.

The most notable feature was the exited state intramolecular proton transfer (ESIPT) mechanism that occurred in all the compounds studied, and emission was observed from the excited state of the keto form with fluorescence excitation wavelength ($\lambda_{ex}$) of 330 nm, which is shown in Fig. 6. It can be understood from Fig. 5b that the compounds are fluorescent in solution and most of the compounds displayed almost similar emission spectra in the range of 475–500 nm with the exception of **4b** and **4c** which showed hypsochromic shift of the emission maxima. The compound **4h** showed two emission maxima ranges of 402 nm and 457 nm which was 94 nm blue shifted when compared **4g**. The chromeno[2,3-d]pyrimidines were strongly fluorescent in solid state and the compounds showed strong, bright green emission with a maximum range of 490-510 nm in the solid state. The corresponding solid state fluorescence spectrum is given in Fig. 7. The fluorescence maxima of the derivatives except **4g** and **4r** were bathochromically shifted in solid state when compared to emission maxima in solution. In solid state, compounds **4b** and **4q** bathochromically shifted with the emission maxima of 554, 555 nm respectively and **4n** was hypsochromically shifted with the emission maxima of 477 nm when compared to **4a**. Interestingly, compound **4l** showed high emission maxima in solid state, and donor-acceptor type flurophores based on **4l** were synthesized and detailed photophysical studies are under progress. The compound **4f** was not fluorescent in solid state. The Stoke's shift value was calculated to be 10631 $cm^{-1}$ for molecule **4a**. The higher Stoke's shift and molar extinction coefficient value suggested significant structural changes between the ground and excited states. Further, the large emission shift from absorption maximum may be due to the presence of –OH group connected to quinoline ring at $4^{th}$ position through intervening π–conjugation probably inducing the exited state intramolecular proton transfer character which would also be responsible for the observed larger Stoke's shift values as the characteristic features of ESIPT mechanism.

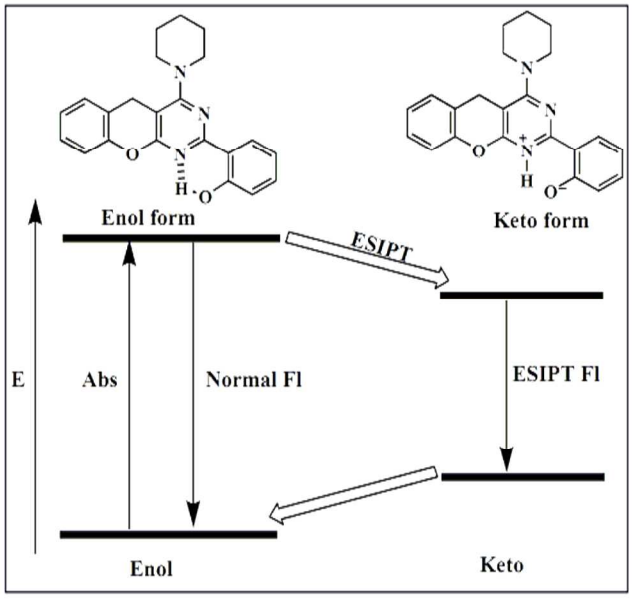



**Fig. 6** The energy diagram of ESIPT process showing tautomeric structures of 4g with normal and ESIPT fluorescence.

## Conclusion

In the current study, we successfully prepared the $ZnAl_2O_4$ nanoparticles with 6-20 nm size. We developed a simple grinding method for the pseudo four component synthesis of chromeno[2,3-d]pyrimidines at room temperature. The advantages of this method are: the catalyst nano $ZnAl_2O_4$ is non-toxic, inexpensive and chemically highly stable, reusable without loss of activity and the method is novel, facile, rapid, green, solvent-free, and a cost effective. Workup is simple and yields are high in short duration. No column chromatography is required. The prepared new chromeno[2,3-d]pyrimidines showed excellent fluorescent properties which can be used in fluorescence based sensor applications.

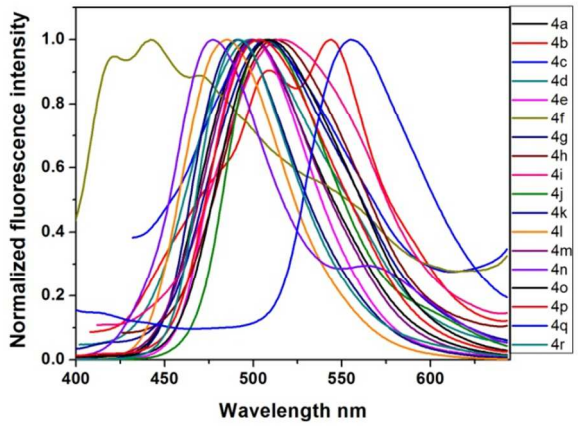



**Fig. 7** Fluorescence spectra of compounds 4a–r recorded in solid state.

## Experimental Section

### General information

Zinc nitrate ($Zn(NO_3)_2.6H_2O$) and Aluminium nitrate ($Al(NO_3)_3.9H_2O$) were purchased from Himedia. Acrylamide ($C_3H_5NO$). N, N'- methylenebisacrylamide ($C_7H_{10}N_2O_2$) and ammonium peroxodisulphate were purchased from Sigma Aldrich. Starch was purchased from SD fine Chemicals. Organic chemicals were purchased from Sigma Aldrich, Merck and Himedia. Purity of all the chemicals was greater than 99%. The phase formation of nano $ZnAl_2O_4$ was inferred by Bruker D8 Advanced powder X-ray diffractometer using Cu Kα (λ = 1.5406 Å) radiation. The diffraction angle 2θ measurements were obtained in the range of 10° - 70° at room temperature. The catalyst was further characterized by Fourier Transformed Infrared Spectra (FTIR) on Shimadzu IR affinity – 1 FTIR spectrometer by KBr disk method. BET surface area of the nano $ZnAl_2O_4$ was found from Nitrogen adsorption desorption isotherms on Micromeritics ASAP 2020 V3.00 H instrument. Elemental analysis of the nano $ZnAl_2O_4$ was performed by Field Emission Scanning Electron Microscope coupled with Energy Dispersive X-ray Analysis (FESEM-EDX) on JEOL JSM 7001F with BRUKER- QUNTAX Version 1.8.2). Transmission Electron microscopic (TEM) images of the catalyst were received on JEOL 3010 instrument with UHR pole piece to find out morphology and particle size. Concentration of leached metal ions of the catalyst after every cycle of the reaction was tested by Atomic Absorption Spectroscopic technique using Varian AA240 instrument. $^1H$ and $^{13}C$ NMR spectra were taken on Bruker 300 MHz using $CDCl_3$ and DMSO-$d^6$ as the solvent with TMS as an internal standard. Melting points were measured on Guna capillary based melting point apparatus and were not corrected. HRMS values were obtained on Joel GC Mate II GC- Mass Spectrometer. FTIR spectra of the synthesized organic compounds were recorded using a Jasco-4100 spectrometer instrument. UV-Visible spectra were taken using Hitachi U-2910 spectrophotometer. Fluorescence spectra in solution and solid were measured using Hitachi F-7000 fluorescence spectrometer.

### Synthesis of $ZnAl_2O_4$

Nano $ZnAl_2O_4$ was synthesized by modifying our previous method[7]. 1:2 molar ratio of aqueous solution of zinc nitrate ($Zn(NO_3)_2.6H_2O$) and aluminium nitrate ($Al(NO_3)_3.9H_2O$) were added drop wise to 25% starch solution followed by 1:1 ratio of acrylamide and N, N'- methylenebisacrylamide under constant stirring and heating. A pinch of ammonium peroxodisulphate was added to the above homogeneous solution when the temperature reached 80 °C. The resulted gel was heated overnight at 80 °C, and the obtained black mass was calcined at 300 °C, 500 °C and 700 °C for 6 h with intermittent grinding. For comparison of activity of catalysts, we prepared bulk $ZnAl_2O_4$ by our previous method[7].

### General procedure for the synthesis of chromeno[2,3-d]pyrimidine derivatives

In a typical synthesis, 20 mol % of nano $ZnAl_2O_4$ was placed in a mortar. To this, salicylaldehyde (1) (2 mmol) was introduced, followed by malononitrile (2) (1 mmol). The entire mixture was well ground at room temperature for 60 sec. A vigorous exothermic reaction took place when the secondary amine (3) (1 mmol) was added to the well ground reaction mixture. Grinding of the mixture for another 60 sec led to the formation of desired products. Completion of the reaction was monitored by TLC. The catalyst was separated using Whatman filter paper by dissolving the reaction mixture in tetrahydrofuran. The solvent was removed by evaporation, and the crude solid product was purified by a recrystallization procedure in tetrahydrofuron and ethanol. In order to reuse the catalyst for the next cycle, the catalyst was washed with chloroform, tetrahydrofuron and acetone (each 5 mL), which was later dried overnight at 60 °C and reused for the next cycle.

### 2-(4-morpholino-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4a)

Yellow solid; Melting point: 197-199 °C: IR (KBr): 3375, 3024, 2949, 2779, 1753, 1708, 1560, 1388, 1246, 1209, 1161, 1118, 1008, 920, 767, 671 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.46-3.43 (t, *J* =6.0 Hz, 4H), 3.74-3.72 (t, *J* =8.0 Hz, 4H), 3.94 (s, 2H), 6.87-6.83 (t, *J* =8.0 Hz, 2H), 7.13-7.07 (m, 2H), 7.24-7.20 (t, *J* =8.0 Hz, 2H), 7.33-7.29 (q, *J* =4.0 Hz, 2H), 8.20-8.18 (d, *J* =2.0 Hz, 1H), 13.03 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.6, 48.0, 65.9, 97.6, 116.3, 117.3, 118.0, 118.8, 119.8, 124.5, 128.1, 128.6, 129.0, 132.9, 149.7, 159.7, 160.5, 163.1, 164.0; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 361.1426, Found 361.1420.

### 1-(11-morpholino-12H-benzo[5,6]chromeno[2,3-d]pyrimidin-9-yl)naphthalen-2-ol (4b)

Brown solid; Melting point: 180-182 °C: IR (KBr): 3377, 3051, 2970, 2845, 1737, 1622, 1588, 1537, 1425, 1404, 1365, 1228, 1111, 925, 821, 746, 518 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.65 (s, 4H), 3.88 (s, 4H), 4.36 (s, 2H), 7.24-7.22 (d, *J* =8.0 Hz, 1H), 7.36-7.32 (t, *J* =8.0 Hz, 1H), 7.43-7.41 (d, *J* =8.0 Hz, 1H), 7.59-7.48 (m, 3H), 7.70-7.66 (t, *J* =8.0 Hz, 1H), 7.84-7.82 (d, *J* =8.0 Hz, 1H), 7.98-7.89 (m, 5H), 8.08-8.06 (d, *J* =8.0 Hz, 1H), 9.00-8.98 (d, *J* =8.0 Hz, 1H), 12.96 (s, 1H); HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 461.1739, Found 461.1741.

### 2-methoxy-6-(9-methoxy-4-morpholino-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol (4c)

Pale yellow solid; Melting point: 198-200 °C: IR (KBr): 3311, 3023, 2848, 1737, 1546, 1435, 1369, 1273, 1240, 1203, 1078, 1016, 742, 737, 665 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.50-3.49 (m, 4H), 3.91-3.89 (m, 4H), 3.94-3.93 (m, 8H), 6.79-6.77 (d, *J* =8.0 Hz, 1H), 6.88-6.84 (t, *J* =8.0 Hz, 1H), 6.98-6.96 (d, *J* =8.0 Hz, 1H), 7.07-7.03 (t, *J* =8.0 Hz, 1H), 8.10-8.08 (d, *J* =8.0 Hz, 1H), 13.67 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 25.7, 30.9, 48.7, 56.0, 56.1, 66.6, 97.8, 110.7, 114.1, 117.9, 118.5, 119.8, 119.9, 121.1, 124.3, 140.0, 148.2 ,148.7, 150.7, 162.4, 164.4; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 421.1638, Found 421.1640.

**2-ethoxy-6-(9-ethoxy-4-morpholino-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol (4d)**

Yellow solid; Melting point: 120-122 °C: IR (KBr): 3247, 3037, 2978, 2922, 2893, 284, 2183, 1714, 1649, 1579, 1544, 1438, 1394, 1271, 1238, 1111, 1008, 732 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.42-1.38 (t, *J* =8.0 Hz, 3H), 3.51 (s, 2H), 3.81 (s, 2H), 4.05-4.00 (m, 6H), 7.09-6.75 (m, 6H), 7.86-7.84 (d, *J* =8.0 Hz, 1H), 13.35 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 14.6, 14.8, 24.8, 38.8, 39.0, 39.2, 39.4, 39.7, 39.9, 40.1, 48.1, 97.5, 111.8, 116.0, 117.9, 118.1, 120.0, 120.7, 124.3, 139.1, 146.6, 147.7, 150.4, 160.8, 163.31, 163.8; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 449.1951, Found 449.1958

**4-bromo-2-(7-bromo-4-morpholino-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4e)**

Yellow solid; Melting point: 194-196 °C: IR (KBr): 3333, 3015, 2970, 2850, 1737, 1541, 1477, 1417, 1352, 1273, 1244, 1116, 1068, 956, 867, 731, 626 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.52 (m, 4H), 3.82 (m, 4H), 4.03 (s, 2H), 6.88-6.86 (d, *J* =8.0 Hz, 1H), 7.15-7.13 (d, *J* =8.0 Hz, 1H), 7.48-7.41 (m, 2H), 7.56 (s, 1H), 8.31-8.30 (d, *J* =4.0 Hz, 1H), 13.08 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.5, 48.0, 65.9, 97.5, 109.9, 116.1, 118.4, 119.7, 122.3, 130.4, 130.7, 131.4, 135.1, 148.9, 158.9, 159.4, 162.8, 163.9; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 516.9637, Found 516.9639.

**4-nitro-2-(7-nitro-4-(piperidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4f)**

Yellow solid; Melting point: 262-264 °C: IR (KBr): 3346, 3071, 2927, 2858, 2677, 1708, 1602, 1517, 1336, 1244, 1182, 1064, 842, 742, 688 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.76 (s, 6H), 2.51 (s, 2H), 3.53 (s, 4H), 4.10 (s, 2H), 7.03-7.00 (t, *J* =8.0 Hz, 1H), 7.35-7.33 (d, *J* =8.0 Hz, 1H), 7.98-7.97 (d, *J* =8.0 Hz, 1H), 8.26-8.10 (m, 3H), 9.10 (s, 1H), 14.19 (s, 1H); HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 449.1335, Found 449.1333.

**2-(4-(piperidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4g)**

Yellow solid; Melting point: 166-168 °C: IR (KBr): 3373, 3045, 2926, 2852, 2229, 1722, 1602, 1588, 1446, 1257, 1186, 1051, 970, 758, 690, 582 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.78-1.75 (m, 6H), 3.45-3.42 (t, *J* =6.0 Hz, 4H), 3.92 (s, 2H), 6.93-6.89 (t, *J* =8.0 Hz, 1H), 6.98-6.96 (d, *J* =8.0 Hz, 1H), 7.12-7.08 (t, *J* =8.0 Hz, 1H), 7.26-7.18 (m, 3H), 8.36-8.32 (t, *J* =8.0 Hz, 1H), 8.43-8.41 (d, *J* =8.0 Hz, 1H), 13.45 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.3, 25.6, 25.9, 49.5, 97.5, 117.1, 117.5, 118.6, 118.8, 119.5, 124.4, 128.2, 128.5, 129.2, 132.8, 150.6, 160.4, 162.0, 164.4, 165.2; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 359.1634, Found 359.1632.

**2-methoxy-6-(9-methoxy-4-(piperidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4h)**

Pale yellow solid; Melting point: 181-183 °C: IR (KBr): 3345, 3043, 2931, 2841, 1570, 1541, 1438, 1394, 1365, 1276, 1234, 1099, 1062, 954, 740, 682 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.71 (m, 2H), 1.76 (m, 4H), 3.42 (m, 4H), 3.91 (s, 2H), 3.93 (s, 6H), 6.78-6.76 (d, *J* =8.0 Hz, 1H), 6.86-6.81 (m, 2H), 6.97-6.95 (d, *J* =8.0 Hz, 1H), 7.05-7.01 (t, *J* =8.0 Hz, 1H), 8.11-8.09 (d, *J* =8.0 Hz, 1H), 14.00 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.3, 25.7, 25.9, 49.5, 56.0, 56.0, 97.5, 110.5, 113.8, 117.7, 118.7, 119.8, 120.5, 121.1, 124.1, 140.2, 148.1, 148.7, 150.7, 162.2, 164.5, 164.9; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 419.1845, Found 419.1849.

**2-ethoxy-6-(9-ethoxy-4-(piperidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4i)**

Yellow solid; Melting point: 100-102 °C: IR (KBr): 3273, 3041, 2976, 2929, 2848, 1722, 1588, 1544, 1471, 1440, 1387, 1273, 1219, 1199, 1070, 1020, 897, 777 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.70 (t, 6H), 3.49 (m, 4H), 3.81 (m, 4H), 3.95 (s, 4H), 3.99 (s, 2H), 6.94-6.83 (m, 3H), 7.00-6.98 (d, *J* =8.0 Hz, 1H), 7.12-7.05 (m, 2H), 8.90-8.88 (d, *J* =8.0 Hz, 1H), 13.52 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 23.8, 24.9, 25.4, 48.7, 55.7, 55.7, 97.1, 114.8, 117.8, 118.1, 120.0, 120.0, 120.8, 124.3, 139.1, 147.4, 148.5, 150.3, 160.7, 164.1; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 447.2158, Found 447.2157.

**4-bromo-2-(7-bromo-4-(piperidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4j)**

Yellow solid; Melting point: 226 °C: IR (KBr): 3310, 3062, 2937, 2848, 2320, 1541, 1438, 1421, 1367, 1348, 1213, 1182, 1060, 971, 817, 744, 665, 623 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.71 (m, 6H), 3.48 (s, 4H), 4.00 (s, 2H), 6.88-6.86 (d, *J* =8.0 Hz, 1H), 7.15-7.13 (d, *J* =8.0 Hz, 1H), 7.48-7.42 (m, 2H), 7.58 (s, 1H), 8.31-8.30 (d, *J* =4.0 Hz, 1H), 13.28 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 23.7, 24.6, 25.4, 48.7, 78.5, 78.9, 79.2, 97.2, 116.0, 118.4, 119.7, 119.8, 122.6, 130.4, 130.7, 131.4, 135.1, 149.1, 158.9, 159.3, 162.9, 164.1; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 514.9844, Found 514.9848.

**2-(4-(4-phenylpiperazin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4k)**

Yellow solid; Melting point: 212-214 °C: IR (KBr): 3337, 3031, 2885, 2833, 2731, 1737, 1597, 1577, 1490, 1429, 1365, 1247, 1180, 1012, 950, 815, 758, 695 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.41 (s, 4H), 3.71 (s, 4H), 4.03 (s, 2H), 6.93-6.86 (m, 3H), 7.01-6.99 (d, *J* =8.0 Hz, 2H), 7.16-7.12 (m, 2H), 7.36-7.25 (m, 5H), 8.38-8.36 (d, *J* = 8.0 Hz, 1H), 13.13 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 25.0, 47.6, 48.5, 97.3, 115.7, 116.3, 117.1, 118.0, 118.3, 118.9, 119.6, 124.1, 127.8, 128.4, 128.6, 128.7, 132.4, 149.8, 150.4, 159.8, 161.1, 163.5, 164.2; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 436.1899, Found 436.1896.

**2-(4-(4-benzylpiperazin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4l)**

White solid; Melting point: 136-138 °C: IR (KBr): 3357, 3012,

2926, 2808, 2736, 1708, 1579, 1529, 1436, 1253, 997, 835, 748, 695. $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 2.58 (s, 4H), 3.54 (s, 4H), 3.58 (s, 2H), 3.99 (s, 2H), 6.95-6.92 (t, *J* =6.0 Hz, 2H), 7.20-7.14 (m, 2H), 7.30-7.27 (t, *J* =6.0 Hz, 2H), 7.39-7.34 (m, 6H), 7.28-7.26 (d, *J* = 8.0 Hz, 1H), 13.16 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.7, 25.1, 47.7, 52.4, 61.9, 66.9, 97.4, 116.3, 117.3, 118.1, 118.8, 119.9, 124.5, 127.0, 128.1, 128.2, 128.6, 128.9, 129.0, 132.8, 137.8, 149.8, 159.7, 160.5, 163.2, 163.9; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 450.2056, Found 450.2054.

**2-(4-(4-benzhydrylpiperazin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4m)**

Pale yellow solid; Melting point: 198-200 °C: IR (KBr): 3367, 3024, 2954, 2877, 2841, 2382, 1735, 1597, 1546, 1489, 1429, 1384, 1284, 1217, 1138, 997, 956, 742 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.59 (s, 8H), 3.96 (s, 2H), 4.40 (s, 1H), 6.93-6.89 (t, *J* = 8.0 Hz, 2H), 7.38-7.12 (m, 12H), 7.51-7.49 (m, 4H), 7.26-7.24 (d, *J* = 8.0 Hz, 1H), 13.16 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.7, 47.7, 51.4, 74.9, 97.4, 116.3, 117.3, 118.0, 118.8, 119.9, 124.57, 126.9, 127.6, 128.1, 128.6, 129.0, 132.9, 142.6, 149.7, 159.7, 160.5, 163.2, 163.9; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 526.2369, Found 526.2369.

**2-(4-(pyrrolidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4n)**

Yellow solid; Melting point: 186-188 °C: IR (KBr): 3317, 3043, 2968, 2870, 1602, 1543, 1448, 1436, 1390, 1259, 1134, 958, 839, 748 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.94 (m, 4H), 3.80 (s, 4H), 4.32 (s, 2H), 6.92-6.88 (t, *J* =8.0 Hz, 2H), 7.14-7.12 (d, *J* =8.0 Hz, 2H), 7.29-7.25 (m, 2H), 8.37-8.33 (t, *J* =8.0 Hz, 1H), 8.30-8.28 (d, *J* =8.0 Hz, 1H), 13.53 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.3, 24.9, 46.0, 49.3, 91.8, 116.1, 117.2, 118.2, 118.5, 119.8, 124.2, 128.0, 128.5, 129.2, 132.5, 149.5, 159.9 ; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 345.1477, Found 345.1478.

**2-methoxy-6-(9-methoxy-4-(pyrrolidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4o)**

Yellow solid; Melting point: 158-160 °C: IR (KBr): 3369, 3051, 2968, 1737, 1548, 1536, 1435, 1396, 1240, 1211, 1138, 983, 777 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.72 (s, 6H), 3.83-3.79 (m, 8H), 4.18 (s, 2H), 6.70-7.11 (m, 5H), 7.80-7.78 (d, *J* =8.0 Hz, 1H), 13.85 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.8, 25.1, 40.1, 49.2, 55.4, 55.6, 79.0, 110.2, 118.2, 120.0, 138.8, 147.1, 150.4, 160.6; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 405.1689, Found 405.1698.

**2-ethoxy-6-(9-ethoxy-4-(pyrrolidin-1-yl)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4p)**

Yellow solid; Melting point: 178-180 °C: IR (KBr): 3367, 3031, 2974, 2927, 2868, 1717, 1598, 1579, 1537, 1444, 1242, 1211, 1112, 1060, 929, 773, 675 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 3.03 (m, 6H), 3.57 (m, 6H), 3.91 (s, 4H), 4.17 (s, 2H), 7.11-7.10 (d, *J* =4.0 Hz, 1H), 7.31-7.27 (t, *J* =8.0 Hz, 2H), 7.81.7.56 (m, 4H), 9.43-9.41 (d, *J* =8.0 Hz, 1H), 13.94 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 22.3, 48.2, 66.2, 76.9, 77.2, 77.5, 110.9, 116.9, 119.2, 121.7, 122.5, 124.6, 125.5, 126.7, 126.8, 128.0, 128.4, 128.6, 133.1, 159.7; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 433.2002, Found 433.2010.

**2-(4-(diethylamino)-9-methoxy-5H-chromeno[2,3-d]pyrimidin-2-yl)-6-methoxyphenol(4q)**

Yellow solid; Melting point: 170-172 °C: IR (KBr): 3377, 3045, 2977, 2322, 2212, 1726, 1637, 1595, 1489, 1371, 1255, 1197, 1149, 1118, 1049, 923, 752, 615 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.77-1.72 (m, 6H), 3.42 (s, 4H), 3.93 (s, 8H), 6.82-6.79 (d, *J* =8.0 Hz, 1H), 6.87-6.85 (t, *J* =4.0 Hz, 2H), 6.97-6.95 (d, *J* =8.0 Hz, 1H), 7.06-7.04 (t, *J* =8.0 Hz, 1H), 8.12-8.10 (d, *J* = 8.0 Hz, 1H), 14.0 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.3, 25.7, 25.9, 29.7, 49.6, 56.0, 56.1, 97.5, 110.5, 113.8, 117.7, 118.7, 119.8, 120.5, 121.1, 124.1, 140.2, 148.2, 148.7, 150.7, 162.2, 164.6, 165.0; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 407.1845, Found 407.1847.

**4-bromo-2-(7-bromo-4-(diethylamino)-5H-chromeno[2,3-d]pyrimidin-2-yl)phenol(4r)**

Yellow solid; Melting point: 180-182 °C: IR (KBr): 3329, 3059, 2964, 2864, 1737, 1595, 1539, 1481, 1421, 1377, 1257, 1214, 1103, 966, 812, 731, 628, 538 $cm^{-1}$: $H^1$NMR (400 MHz, $CDCl_3$)$^{TM}$ ppm: 1.96 (s, 6H), 3.79 (s, 4H), 4.03 (s, 2H), 6.87-6.85 (d, *J* =8.0 Hz, 1H), 7.10-7.08 (d, *J* =8.0 Hz, 1H), 7.49-7.39 (m, 3H), 8.28 (s, 1H), 13.54 (s, 1H); $C^{13}$NMR (100 MHz, $CDCl_3$)$^{TM}$ ppm: 24.6, 48.0, 65.9, 97.6, 116.3, 117.3, 118.0, 118.8, 119.8, 124.6, 128.1, 128.6, 129.0, 132.9, 149.7, 159.7, 160.5, 163.1, 164.0; HRMS for $C_{27}H_{21}N$ Calculated [$M^+$] m/z 502.9844, Found 502.9856.

## Acknowledgements

Balijapalli Umamahesh and Triveni Rajashekhar Mandlimath thank CSIR for providing Senior Research Fellowship. The DST-FIST NMR facility at VIT University and VIT management are duly acknowledged.

## Notes and references

1 (a) M. Bakthadoss, D. Kannana and R. Selvakumar, *Chem. Commun*., 2013, **49**, 109471; (b) K.V.V. Satyanarayana, A. P. Ramaiah, Y. L. N. Murty, R. M. Chandra and S. V. N. Pammi, *Catal. Commun*., 2012, **25**, 50; (c) N. P. Eagalapati, A. Rajack and Y. L. N. Murthy, *J. Mol. Catal. A: Chem*., 2014, **381**, 126; (d) S. Ramesh and R. Nagarajan, *Tetrahedron*., 2013, **69**, 4890.

2 (a) S. K. Kundu, J. Mondal and A. Bhaumik, *Dalton Trans*., 2013, **42**, 10515; (b) I. A. Azath, P. Puthiaraj and K. Pitchumani, *ACS Sustainable Chem. Eng*., 2013, **1**, 174.

3 (a) J. A. Mondal, A. Modak, M. Nandi, H. Uyamab and A. Bhaumik, *RSC Adv*., 2012, **2**, 11306; (b) M. B. Teimouri, P. Akbari-Moghaddam and G. Golbaghi, *ACS Comb. Sci*., 2011, **13**, 659; (c) V. G. Ramu, A. Bordoloi, T. C. Nagaiah, W. Schuhmann, M. Muhler, and C. Cabrele, *App. Catal., A*., 2012, **431–432**, 88.

4 (a) R. Roy, S. Rakshit, T. Bhowmik, S. Khan, A. Ghatak and S. Bhar, *J. Org. Chem*., 2014, **79**, 6603; (b) N. M. Evdokimov, A. S. Kireev, A. A. Yakovenko, M. Y. Antipin, I. V. Magedov and A. Kornienko, *J. Org. Chem*., 2007, **72**, 3443.

5 (a) J. S. Ghomi, B. K. Koopaei and H. S. Alavi, *RSC Adv*., 2014, **4**, 46106; (b) P. P. Ghosh and A. R. Das, *J. Org. Chem*., 2013, **78**, 6170.

6 (a) S. Santra, M. Rahman, A. Roy, A. Majee and A. Hajra, *Catal. Commun*., 2014, **49**, 52; (b) J. K. Rajput and G. Kaur, *Catal. Sci. Technol*., 2014, **4**, 142.

7 (a) T. R. Mandlimath, B. Umamahesh and K. I. Sathiyanarayanan, *J. Mol. Catal. A: Chem*., 2014, **391**, 198; (b) A. F. Shojaei, K. Tabatabaeian, F. Shirini and S. Z. Hejazi, *RSC Adv*., 2014, **4**, 9509.

8 U. C. Rajesh, J. Wang, S. Prescott, T. Tsuzuki and D. S. Rawat, *ACS Sustainable Chem*., Eng, dx.doi.org/10.1021/sc500594w.

9 (a) H. Naeimi, Z. Rashid, A. H. Zarnani and R. Ghahremanzadeh, *New. J. Chem*., 2014, **38**, 348; (b) S. Rostamnia, A. Nuri, H. Xin, A. Pourjavadi and S. H. Hosseini, *Tetrahedron Lett*., 2013, **54**, 3344.

10 (a) J. Zhang, Z. Zhang, Y. Wang, X. Zheng and Z. Wang, *Eur. J. Org. Chem*., 2008, 5112; (b) C. Dong, M. Zhong, T. Huang, M. Ma, D. Wortmann, M. Brajdic and I. Kelbassa, *ACS Appl. Mater. Interfaces*., 2011, **3**, 4332.

11 (a) F. Liu, Y. Yu and H. He, *Chem. Commun*., 2014, **50**, 8445; (b) D. Kumar and A. Ali, *Energy Fuels*., 2013, **27**, 3758.

12 (a) P. Das, A. Dutta, A. Bhaumik and C. Mukhopadhyay, *Green Chem*., 2014, **16**, 1426; (b) H. Zhao, Y. Dong, G. Wang, P. Jiang, J. Zhang, L. Wu and K. Li, *Chem. Eng. J*., 2013, **219**, 295; (c) L. Y. Gan and Y. J. Zhao, *J. Phys. Chem. C*., 2012, **116**, 16089.

13 L. Liu, Z. Ji, W. Zou, X. Gu, Y. Deng, F. Gao, C. Tang and L. Dong, *ACS Catal*., 2013, **3**, 2052.

14 (a) P. Bandyopadhyay, G. K. Prasad, M. Sathe, P. Sharma, A. Kumar and M. P. Kaushik, *RSC Adv*., 2014, **4**, 6638; (b) M. Raula, Md. D. Rashid, S. Lai, M. Roy and T. K. Mandal, *ACS Appl. Mater. Interfaces*., 2012, **4**, 878.

15 (a) L. Zhang, L. Shi, L. Huang, J. Zhang, R. Gao and D. Zhang, *ACS Catal*., 2014, **4**, 1753; (b) R. Easterday, C. Leonard, O. S. Felix, Y. Losovyj, M. Pink, B. D. Stein, D. G. Morgan, N. A. Lyubimova, L. Zh. Nikoshvili, E. M. Sulman, W. E. Mahmoud, A. A. Al-Ghamdi, and L. M. Bronstein, *ACS Appl. Mater. Interfaces*., 2014, **6**, 21652.

16 (a) S. Farhadi and S. Panahandehjoo, *Appl. Catal., A*., 2010, ***382***, 293; (b) M. Gopiraman, R. Karvembu and I. S. Kim, *ACS Catal*., 2014, **4**, 2118.

17 A. Dandia, A. K. Jain and S. Sharma, *RSC Adv*., 2013, **3**, 2924.

18 J. A. Hadfield, V. H. Pavlidis, P. J. Perry and A. T. McGown, *Anti-cancer drugs*., 1999, **10**, 591.

19 (a) N. M. Sabry, H. M. Mohamed, E. S. A. E. H. Khattab, S. S. Motlaq and A. M. E. Agrody, *Eur. J. Med. Chem*., 2011, **46**, 765; (b) S. Kanakaraju, B. Prasanna, S. Basavoju and G. V. P. Chandramouli, *J. Mol. Struct*., 2012, **1017**, 60.

20 (a) A. Zonouzi, F. Hosseinzadeh, N. Karimi, R. Mirzazadeh and S. Weng Ng, *ACS Comb. Sci*., 2013, **15**, 240; (b) N. Azizi, M. Mariami and M. Edrisi, *Dyes and Pigm*., 2014, **100**, 215; (c) H. R. Tavakoli, S. M. Moosavi, and A. Bazgir, *J. Korean Chem. Soc*., 2013, **57**, 260.

21 (a) C. N. O'Collaghan, *Proc. R. Ir. Acad*., 1973, **73**, 291; (b) C. N. O'Collaghan, J. *Chem. Soc. Perkin. Trans*., 1980, **1**, 1335.

22 (a) L. Moafi, S. Ahadi and A. Bazgir, *Tetrahedron Lett*., 2010, **51**, 6270; (b) R. Ghahremanzadeh, T. Amanpour and A. Bazgir, *Tetrahedron Lett*., 2010, **51**, 4202.

23 A. Zonouzi, M. Biniaz, R. Mirzazadeh, M. Talebi and S. Weng Ng, *Heterocycles*., 2010, **81**, 1271.

24 (a) A. K. Gupta, K. Kumari, N. Singh, D. S. Raghuvanshi and N. K. N. Singh, *Tetrahedron Lett*., 2012, **53**, 650; (b) H. R. Shaterian, M. Aghakhanizadeh, *Res Chem Intermed*, 2013, **39**, 3877.

25 S. Amirnejat, F. Movahedi, H. Masrouri, M. Mohadesi and M. Z. Kassaee, *J. Mol. Catal. A: Chem*., 2013, **378**, 135.

26 H. R. Shaterian and M. Aghakhanizadeh, *Catal. Sci. Technol*., 2013, **3**, 425.

27 D. L. Ge, Y. J. Fan, C. L. Qi and Z. X. Sun, *J. Mater. Chem. A*., 2013, **1**, 1651.