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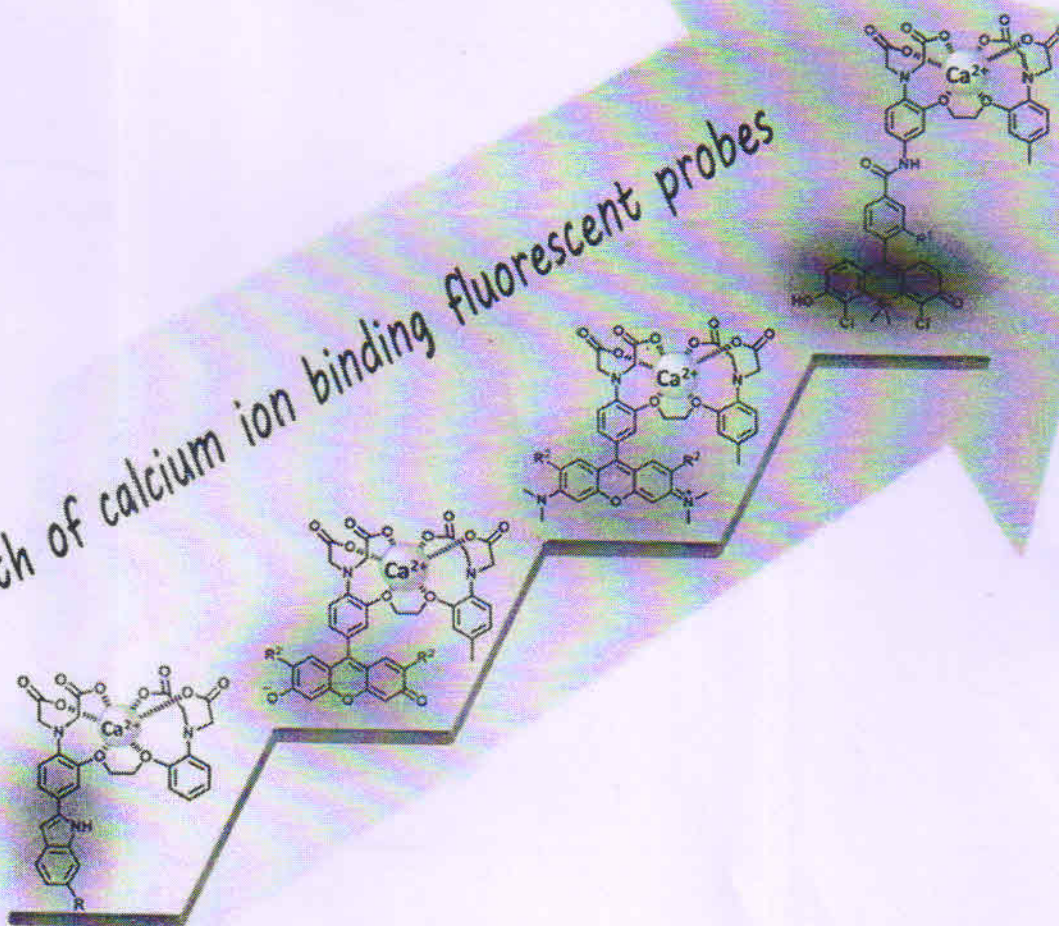


Special  
Issue

# Design and Applications of Small Molecular Probes for Calcium Detection

Roopa,<sup>\*,[a]</sup> Naresh Kumar,<sup>[b]</sup> Manoj Kumar,<sup>[c]</sup> and Vandana Bhalla<sup>\*,[c]</sup>

Growth of calcium ion binding fluorescent probes





PAPER



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# Self-assembled vesicle and rod-like aggregates of functionalized perylene diimide: reaction-based near-IR intracellular fluorescent probe for selective detection of palladium†

Prabhpreet Singh,<sup>a</sup> Lalit Singh Mittal,<sup>a</sup> Vanita Vanita,<sup>b</sup> Kapil Kumar,<sup>a</sup> Amandeep Walla,<sup>c</sup> Gaurav Bhargava<sup>c</sup> and Subodh Kumar<sup>a</sup>

Herein, we report design, synthesis, and self-assembly of perylene diimide (PDI) based near-IR intracellular probe (PS-PDI). PS-PDI molecules undergo aggregation to form self-assembled nanospheres and nanorods morphology in THF : H<sub>2</sub>O (1 : 1) and DMSO : H<sub>2</sub>O (1 : 9), respectively. The nanospheres have an open hole on surface reminiscent of vesicle structure (with a diameter of internal void in the range of 20–25 nm) whereas lengths of the nanorods extended up to few  $\mu\text{m}$  range. The Pd<sup>0</sup> based depropargylation leads to de-aggregation of these PS-PDI aggregates into smaller spherical aggregates as evidenced by DLS, SEM, and TEM studies. Interestingly, these aggregates of PS-PDI in solution show highly sensitive behavior in the presence of Pd<sup>0</sup> showing absorbance changes in NIR region ( $\lambda_{\text{max}} = 710 \text{ nm}$ ) and quenching of emission at  $\lambda_{\text{em}} 630 \text{ nm}$  (DMSO : H<sub>2</sub>O, 1 : 9) with a limit of detection =  $6.6 \times 10^{-6} \text{ M}$  or at  $\lambda_{\text{em}} 564 \text{ nm}$  (THF : H<sub>2</sub>O, 1 : 1) with limit of detection =  $2.1 \times 10^{-6} \text{ M}$ . Time and concentration dependent kinetics profiles of PS-PDI aggregates revealed an impressive rate constant value of  $0.4 \text{ s}^{-1}$  and  $0.21 \text{ s}^{-1}$  (DMSO : H<sub>2</sub>O, 1 : 9), respectively in fluorescence and UV-Vis spectroscopy using  $2 \times 10^{-5} \text{ M}$  concentration of Pd<sup>0</sup>. PS-PDI undergoes rapid internalization into HeLa cells with low cytotoxicity and was successfully used as an intracellular imaging reagent for Pd<sup>0</sup> in live HeLa cells. For practical applications, we exploited these nano-aggregates of PS-PDI for estimation of Pd<sup>2+</sup> in the presence of a NaBH<sub>4</sub>-PPh<sub>3</sub> mixture, Pd<sup>0</sup> in drug and environmental samples, and Pd<sup>2+</sup> in urine samples with excellent selectivity and sensitivity.

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## 1. Introduction

Perylene diimides (PDIs) are a well documented class of functional organic dyes with excellent electronic, optical, and redox properties.<sup>1–5</sup> Due to these properties, PDIs may find applications in dyes and pigments industries,<sup>6</sup> optoelectronic devices,<sup>7–9</sup> and supramolecular chemistry.<sup>10–20</sup> The aggregation and optoelectronic properties of PDIs can be tailored through modification of its  $\pi$ -molecular structure with chemical groups<sup>1,21,22</sup> either or both at the imide or bay positions of the PDIs core. Due to the presence of a planar  $\pi$ -conjugated core, PDI has propensity for

aggregation in an aqueous medium via  $\pi$ - $\pi$  stacking, hydrogen bonding, electrostatic, and solvation interactions. Many reports regarding modification of imide position of PDIs to generate self-assembled nanostructures are being published each year.<sup>23,24</sup> However, little attention has been paid to the self-assembly of bay substituted PDIs.<sup>25,26</sup> Probably, the substitutions at a bay position drastically increase the solubility of PDIs and if substituents are bulky in nature, the perylene backbone deviates from planarity to minimize the strain and this hinders the possibility of  $\pi$ - $\pi$  stacking. Moreover, the application of self-assembled PDIs for molecular recognition of metal ions and anions in water via aggregation or de-aggregation of PDIs has been scarcely reported due to the poor solubility of PDIs in aqueous medium. Earlier we reported (ionic) self-assembly of benzimidazolium, amino acids, and nucleobase-functionalized carbon nanotubes (CNTs)<sup>27–29</sup> and now we envisage that ease in aggregation of perylene chromophore in aqueous medium could be exploited for molecular recognition by using stimuli-based aggregation-disaggregation of PDIs. In this context, we recently synthesized a PDI-based probe and judiciously utilized its aggregation behavior for detection of perchlorate anion in water and C6 glioma cells.<sup>30</sup>

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† Electronic supplementary information (ESI) available: Structural data, self-assembly, spectroscopic and photophysical data of PS-PDI and control molecules with additional information. See DOI: 10.1039/c6tb00512h

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## A facile and chemoselective synthesis of 1,4-benzodiazepin-2-ones and dienyli thiazolidin-4-ones†

Bilash Kula,<sup>a</sup> Yogesh Kumar,<sup>a</sup> Dinesh Mahajan,<sup>b</sup> Kapil Kumar,<sup>c</sup> Prabhpreet Singh<sup>c</sup> and Gaurav Bhargava<sup>\*a</sup>

An efficient protocol for chemoselective synthesis of previously unknown 1,4-benzodiazepin-2-ones and dienyli thiazolidin-4-one carboxylates in excellent yields by ring transformation reactions of functionally decorated 2-azetidin-3-thiazolidin-4-ones is reported.

$\beta$ -Lactams are one of the fascinating heterocyclic systems in organic synthesis. The  $\beta$ -lactam unit is a fundamental structural characteristic in a significant class of antibiotics.<sup>1</sup> Numerous lactam based drugs are commercially used for widespread applications.<sup>2</sup> Literature survey clearly reveals that appropriate functionality around lactams diversified their biological activities.<sup>3</sup> Apart from substitution dependent biological profile, functionalized  $\beta$ -lactams have been extensively explored as versatile synthons and precursors for various heterocyclic systems.<sup>4</sup> The  $\beta$ -lactam synthon methodology has become an important tool in organic synthesis.<sup>5</sup> The key step in  $\beta$ -lactam synthon methodology involves the cleavage of the  $\beta$ -lactam ring. Of the four possible cleavage routes (Fig. 1), the N<sup>1</sup>-C<sup>2</sup> bond cleavage (route-A) has been extensively explored and exploited for the synthesis of biologically relevant molecules such as amino esters, hexahydroisoquinolines, hexahydroisoquinolones, hexahydroisochromones,<sup>6a</sup> thioxo-imidazolidines, imidazolidin-2-ones, piperazine-5,6-diones, dihydroimidazoles,<sup>6b</sup> (*E*)-endo-aldonitrines, hexahydroisoquinolin-1-ylidene, and hydantoins, dihydroquinoline-4-ones.<sup>6c,7</sup>

On the other hand, 1,4-benzodiazepin-2-ones (BZD) are a very successful class of drugs and have been extensively employed as therapeutics since the early 1960s.<sup>8</sup> BZD scaffolds are recurrent templates in the context of their wide range of biological activities such as sedatives, anxiolytics, anticonvulsants or muscle relaxants,<sup>9</sup> antagonists of platelet activating factor,<sup>10a</sup> anti-HIV,<sup>10b</sup> antitumor,<sup>10c,d</sup> and antimalarial.<sup>10e</sup>

There have been significant revelations in the synthesis of C-3 functionalized BZD.<sup>11,12</sup> The substitutions at the C-3 position of BZD are crucial to the possible outcome for the potential biological activities.<sup>10-12</sup> Various BZD with methyl,<sup>12c</sup> acetyl, naphthyl,<sup>12d</sup> and hydrocinnamyl,<sup>12e</sup> groups at its C-3 position have been explored for their applications in many areas of medicinal chemistry; therefore, underlying the importance for the development of new routes for the synthesis of BZD with diverse functionalities at the C-3 position.

As a part of our ongoing interest in the synthesis of a heterocyclic system *via* lactam synthon methodology, we earlier reported the synthesis and subsequent transformation of functionalized lactams for the synthesis of diaza-bicyclo[3.2.0] heptan-7-one,<sup>13</sup> amino-pyrrolidine esters<sup>14</sup> and (2-oxo-4-(styryl) azetidin-3-yl)pyridine.<sup>14</sup> In continuation of this, we herein document a conceptually simple approach that provides an integrated access to pharmacologically useful 1,4-benzodiazepin-2-one or dienyli-thiazolidin-4-one frameworks by careful chemoselective transformation of a bifunctional hybrid, *viz.*, 3-(2-oxo-1-(aryl)-1-styrylazetidin-3-yl)thiazolidin-4-one by ring opening of 2-azetidinones *via* [N<sup>1</sup>-C<sup>2</sup>] bond cleavage using sodium methoxide in methanol and subsequent transformation reactions.

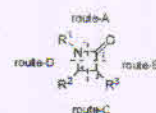
3-Amino-2-azetidinones (**1a-f**) were prepared by reported methods.<sup>15</sup> The variably substituted 3-amino-2-azetidinones **1a-f** used were characterized with the help of analytical data and spectral evidences. These 3-amino-2-azetidinones **1a-f** were explored in three component cyclization reactions with variety

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Fig. 1 Ring opening of the  $\beta$ -lactam ring.


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## Cu(I) mediated Kinugasa reactions of $\alpha,\beta$ -unsaturated nitrones: a facile, diastereoselective route to 3-(hydroxy/bromo)methyl-1-aryl-4-( $\alpha$ -styryl)azetidin-2-ones†

Yogesh Kumar,<sup>a</sup> Prabhpreet Singh<sup>b</sup> and Gaurav Bhargava<sup>\*a</sup>

The manuscript describes a facile and highly diastereoselective synthesis of *cis*-3-(hydroxy/bromo)methyl-1-aryl-4-( $\alpha$ -styryl)azetidin-2-ones via copper(I) mediated Kinugasa reactions of previously unexplored functionalized  $\alpha,\beta$ -unsaturated nitrones. A variety of functionalized acetylenes and  $\alpha,\beta$ -unsaturated nitrones were studied to yield *cis*-3-(hydroxy/bromo)methyl-1-aryl-4-( $\alpha$ -styryl)azetidin-2-ones in good yields (82%).

$\beta$ -Lactams are widely recognized as one of the most significant heterocyclic scaffolds<sup>1</sup> and have maintained a high level of curiosity, both in academia and in industry. The  $\beta$ -lactam ring is the common structural characteristic of a number of broad spectrum  $\beta$ -lactam antibiotics, such as penicillins, cephalosporins, carbapenems, nocardins, monobactams, clavulanic acids as well as inhibitors of HIV-1 protease.<sup>2</sup> In recent years, renewed interest has been paid to the synthesis and modification of the  $\beta$ -lactam ring to obtain compounds with different pharmacological activities such as cholesterol absorption inhibitory activity, human trypsinase, thrombin and chymase inhibitory activity, vasopressin V1a antagonist activity, and antimalarial, antidiabetic, antitubercular, anti-inflammatory, anti-parkinsonian and anti-HIV activity.<sup>3,4</sup>  $\beta$ -Lactams are also increasingly being used as useful synthons for the synthesis of a variety of natural products via  $\beta$ -lactam synthon methodology.<sup>5</sup> The lactams have also been explored for synthesis of variety of non-protein amino acids, oligopeptides, peptidomimetics, and nitrogen-heterocycles,<sup>6,7</sup> as well as biologically active natural and unnatural products of medicinal interest.<sup>8,9</sup>

The common methodologies for the synthesis of functionalized  $\beta$ -lactam include ketene-imine [2+2] cycloaddition reactions<sup>10</sup> and metallo-ester enolate-imine cyclocondensations.<sup>11</sup> However, these

traditional synthetic routes are mostly intolerant to acid or base sensitive moieties. After the advent of the Kinugasa reaction, functionalized lactams were synthesized which were previously inaccessible using traditional synthetic methodologies.<sup>12</sup> The Kinugasa reactions use readily available substrates *viz.* nitrones and acetylenes, and are mild and can tolerate different functional groups (Fig. 1).<sup>13</sup> The Kinugasa cascade provides access to numerous  $\beta$ -lactam compounds with a distinct configuration and potential biological activity.<sup>14</sup>

An early investigation by different research groups on Kinugasa reactions examined the generation of functionalized  $\beta$ -lactams using aliphatic or aromatic substituted nitrones. These Kinugasa reactions are initiated by [3+2] cycloadditions of nitrones with Cu acetylide. These [3+2] cycloadducts (I) usually follow two different pathways: pathway A<sup>17</sup> and pathway B<sup>12b</sup> (Fig. 1). Both pathways A & B have revealed the presence of intermediates  $\beta$ -aminoketene (II) & oxaziridinium (III) respectively, which, eventually, collapse to *cis/trans*- $\beta$ -lactams. The Kinugasa reactions generally afford  $\beta$ -lactams as mixtures of racemic diastereoisomers; however, various stereoselective variants of such transformations with appropriate chiral auxiliaries or chiral Cu(I) ligands have been reported (Fig. 2).<sup>13,14</sup>

Although, in principle, the Kinugasa reaction would provide efficient access to styryl substituted lactam at the C-4 position, to the best of our knowledge, no example of such a process has been

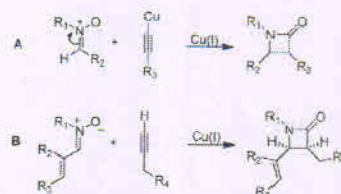


Fig. 1 (A) Previous work on Kinugasa reactions; (B) present work on Kinugasa reactions of  $\alpha,\beta$ -unsaturated nitrones.

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c6nj01747a

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## Highly chemo- and diastereo-selective synthesis of 2,6-diazabicyclo[3.2.0]heptan-7-ones, pyrrolidines and perhydroazirino[2,3-c]pyrroles

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DOI: <http://dx.doi.org/10.3998/ark.5550190.p009.845>

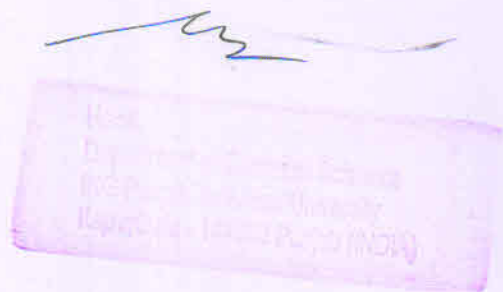
### Abstract

The manuscript describes a simple, convenient and metal-free diastereoselective synthesis of 4-halo-3-aryl/alkyl-6-aryl-2,6-diazabicyclo[3.2.0]heptan-7-ones via intramolecular *endo-trig* haloamination of 3-aminoazetidin-2-ones and its facile transformations to previously unknown methyl 4-halo-3-arylaminopyrrolidine-2-carboxylates and *N*-deprotected diazabicyclo[3.1.0]hexane-2-carboxylic acids in good yields. The synthesis of such heterocyclic system is important in terms of the usefulness as organic synthon as well as their diverse pharmacological profiles.

**Keywords:** Diazabicyclo[3.2.0]heptanones, pyrrolidines, aziridinopyrrolidines,  $\beta$ -lactams, *endo-trig* haloamination

### Introduction

Over the past decades,  $\beta$ -lactams have emerged as a useful synthon in organic chemistry.<sup>1,2</sup> Numerous researchers have explored the synthesis of a variety of novel heterocyclic systems via  $\beta$ -lactam synthon methodology.<sup>3</sup> Ojima and his co-workers have described the crucial role of  $\beta$ -lactam synthon methodology in the synthesis of paclitaxel, docetaxel and new-generation taxoids viz. C-2- and C-3'-modified taxoids, etc.<sup>4-6</sup> Alcaide *et al.* have utilized a variety of lactams as organic synthons for the construction of various alkaloid skeletons.<sup>7,8</sup> Mahajan *et al.* have explored the  $\beta$ -lactam synthon approach towards the diastereoselective synthesis of functionalized octahydroisoquinolones,<sup>9</sup> pyrroloxazine,<sup>10</sup> tetra/octahydro-isoquinoline<sup>11</sup> and octahydroindole<sup>12</sup> ring systems. Literature survey clearly reveals that  $\beta$ -lactams are important synthons for the synthesis of a variety of useful aza-heterocyclic systems.<sup>4-12</sup> Functionalized proline esters, the five-membered azaheterocyclic systems, are important organocatalysts as well as having vital roles in





## REVIEW

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DOI: 10.1039/c6ra20973d  
www.rsc.org/advancesRecent developments in the synthesis of condensed  $\beta$ -lactamsYogesh Kumar,<sup>a</sup> Prabhpreet Singh<sup>b</sup> and Gaurav Bhargava<sup>\*a</sup>

$\beta$ -Lactams are important heterocycles with diverse pharmacological profiles and have emerged as useful organic synthons. Different variants of  $\beta$ -lactams condensed with carbo-/heterocycles, which have a broad range of antimicrobial activities and other useful pharmacological activities, justify a renewed interest in their synthetic developments. This review embraces an array of different reports on condensed  $\beta$ -lactams dating back to 2000. The aim of this review is to provide practicing and aspiring  $\beta$ -lactam chemists with a survey and flavor of the types of reactions used to prepare nonconventional condensed- $\beta$ -lactams, and an insight into why certain methodologies are advantageous under particular circumstances.

Throughout much of the 20th century,  $\beta$ -lactam antibiotics have been a bastion as therapeutics for treating a wide range of bacterial infections.<sup>1,2</sup>  $\beta$ -Lactams show a broad spectrum of activities on a variety of pathogens and substantial research has been carried out on the synthesis of new potent 2-azetidinone based antibiotics.<sup>3,4</sup> The  $\beta$ -lactam ring is a common structural characteristic of a number of broad spectrum  $\beta$ -lactam antibiotics, i.e. penicillins, cephalosporins, carbapenems, nocardins, monobactams, clavulanic acid, sulbactams and

tazobactams, which have been extensively used as chemotherapeutic agents for the treatment of bacterial infections and microbial diseases.<sup>5-8</sup> Most research up to the early 90's was focused on the synthesis and study of 2-azetidinones and their antibacterial activities.  $\beta$ -Lactam antibiotics have played a fundamental role in the fight against pathogenic bacteria and the subsequent rise in quality of life for the world population as a whole.<sup>9-11</sup> In recent years, there has been a renewed interest in the synthesis and modification of  $\beta$ -lactam rings for their different pharmacological activities, like cholesterol absorption inhibitory activity, human trypsin, thrombin and chymase inhibitory activity, vasopressin V1a antagonist activity, antimalarial, antidiabetic, antitubercular, anti-inflammatory, anti-parkinsonian and anti-HIV activity.<sup>12-17</sup>

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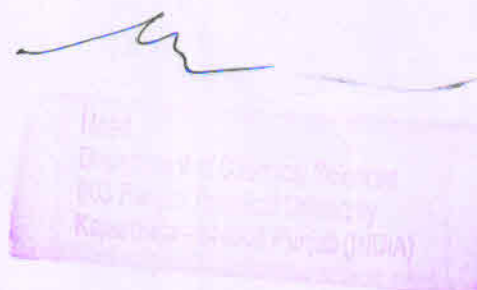
Mr. Yogesh Kumar obtained his B.Sc. degree from DAV College, Jalandhar, India in 2008. He joined Guru Nanak Dev University, Amritsar in 2010 to obtain his M.Sc. in Applied Chemistry with specialization in Pharmaceuticals. After one year as an Assistant Professor at DAV Institute of Engineering and Technology, Jalandhar, he started his Ph.D. in Organic Chemistry under the supervision of Dr

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## A facile and highly chemoselective synthesis of 1-thia-3a,6-diaza-benzo[e]azulen-3-ones by 7-*exo-dig/trig* halocyclizations†

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This manuscript describes a study on relatively unexplored halogen mediated 7-*exo-dig/trig* cyclization reactions of 2-(2-amino-aryl)-3-prop-2-ynyl/allyl-thiazolidin-4-ones for the formation of thiazole condensed 1,4-benzodiazepines in good yields. The reactions are facile, chemoselective and involve the use of simple substrates leading to synthesis of diversely functionalized 1,4-benzodiazepines. The synthesis of such condensed 1,4-benzodiazepines is important in terms of their usefulness as biological active agents.

Halogen mediated cyclizations are gaining increasing importance for the construction of cyclic compounds having variable complexity including medium and large ring sizes.<sup>1</sup> Halocyclizations have been efficiently explored for the synthesis of biologically active heterocyclic molecules.<sup>2</sup> Significant progress has been made in recent years by application of 5-*exo* and 6-*exo-dig/trig* halocyclizations reactions for the synthesis of five or six membered heterocycles.<sup>1–3</sup> There are very limited examples in literature involving construction of seven-membered ring systems by 7-*endo dig/trig* cyclization<sup>4,5</sup> reactions. Recently, Miesch *et al.* explored a silver-catalyzed 7-*exo-dig* cyclization.<sup>3a</sup> Hashmi *et al.* reported gold catalyzed 7-*exo-dig* cyclizations.<sup>3a</sup> However, the synthesis of seven membered carbo/heterocycles involving 7-*exo dig/trig* halocyclization received much less attention in past.<sup>6</sup> Moreover, the bromoamination reaction for the synthesis of seven membered heterocycles is scarcely reported in literature. On the other hand, 1,4-benzodiazepine based structure class holds an important place in drug

discovery because of their diverse pharmacological profiles.<sup>8</sup> 1,4-Benzodiazepines are widely used as analgesic,<sup>9</sup> anti depressive,<sup>9</sup> anticonvulsant,<sup>9</sup> anti-anxiety,<sup>9</sup> sedative and hypnotic agents.<sup>7,8</sup> Olanzapine<sup>9</sup> (I) is an atypical 1,4-benzodiazepines based anti-psychotic drug with a thieno-benzodiazepinyl structure. Olanzapine is approved for the treatment of schizophrenia. It is a selective monoaminergic antagonist with high affinity binding to serotonin 5HT<sub>2A/2C</sub>, dopamine D<sub>14</sub>, muscarinic M<sub>1-5</sub> and adrenergic  $\alpha_1$  receptors. Alprazolam (II) and estazolam (III) have found use as anxiolytic agents,<sup>10a-c</sup> and triazolam (IV) is known as an antidepressant<sup>10a</sup> (Fig. 1). In view of this diverse pharmacological profile of condensed 1,4-benzodiazepines, it was planned to explore a new synthetic route for the formation of 1,4-benzodiazepines having thiazole-benzodiazepinyl structure.

As a part of our ongoing interest in heterocyclic chemistry,<sup>12</sup> we already reported a  $\beta$ -lactam mediated strategy for a facile, chemoselective, economical, as well as short synthetic route to 1,4-benzodiazepin-2-ones.<sup>11</sup> The present manuscript indicates a facile yet high yielding and chemoselective synthesis of functionalized thiazole condensed benzo[1,4]diazepines by relatively unexplored 7-*exo-dig/trig* halocyclization reactions of 2-(2-amino-aryl)-3-prop-2-ynyl/allyl-thiazolidin-4-ones using halogen and a mild base. The developed synthetic methodology can potentially play an important role in synthesis of structurally diverse fused benzo[1,4]diazepines having diverse

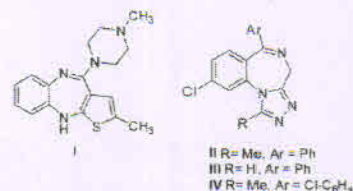


Fig. 1 Some clinically approved condensed 1,4-benzodiazepine based drugs.

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# Diphenylpyrimidinone–salicylideneamine – new ESIPT based AIEgens with applications in latent fingerprinting†

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Diphenylpyrimidinone–salicylideneamine **DPPS-1** undergoes concentration dependent self-assembly to form aggregates with rods – mimicking a ‘coral reef’ superstructure and a spherical morphology evident from dynamic light scattering (DLS), scanning electron microscopy (SEM) and transmission electron microscopy (TEM). **DPPS-1** and **DPPS-2** exhibit weak excited state intramolecular proton transfer (ESIPT) based emission in CH<sub>3</sub>CN and their binary mixtures with water, but in solutions containing > 70% water fraction **DPPS-1** and **DPPS-2** molecules aggregate and ESIPT is facilitated to give a strong green ESIPT emission at 526 nm ( $\phi = 0.273, 0.068$ ). The ESIPT process remains active in the solid state and solid **DPPS-1** and **DPPS-2** appear as fluorescent green under 365 nm light illumination. The AIE-active nature of **DPPS-1** and **DPPS-2** finds applications in the visualization of latent fingerprints on aluminium, steel and glass surfaces. Even 24 h after the placement of the fingerprints, up to the second level of information viz. core, lake, ridge termination and dots, delta and bifurcation in the fingerprints could be identified.

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## 1. Introduction

Organic fluorophores possess a high propensity for aggregation in aqueous solution and in the solid state, which could lead to either ‘aggregation-caused quenching’ (ACQ)<sup>1,2</sup> or ‘aggregation induced emission’ (AIE)<sup>3–5</sup> phenomena. For practical applications in optoelectronics, biomedical research, ecosystem monitoring and environmental protection, the majority of organic fluorophores are used as thin films or in the aggregate form, and probably at this juncture, the AIE fluorophores provide an edge over the ACQ fluorophores.<sup>1–5</sup> Fluorophores with AIE properties remain non-fluorescent in the molecularly dissolved state owing to the dissipation of the absorbed energy through non-radiative decay channels, whereas in the aggregated form close packing imposes restrictions to non-radiative decay channels and strong fluorescence is observed.<sup>6–17</sup> In light of the bright prospects of AIE fluorophores in various applications,<sup>4</sup> researchers

have embarked upon the development of new AIE fluorophores to be included in the AIE family.

The excited state intramolecular proton transfer (ESIPT) process is an intriguing phenomenon<sup>4,18</sup> which provides a large Stoke’s shift via alteration in the conjugation through proton transfer. ESIPT based fluorophores can show two emission bands termed as normal emission from the enol-form (high energy and a low stokes shift) and ESIPT emission due to the keto-form (low energy and a large stokes shift). However, if the ESIPT process is allowed to happen, proton transfer usually takes place from the hydroxyl group (proton donor) to nitrogen (proton acceptor) through a cyclic transition state resulting in an energy gap much lower than that of a non-ESIPT state and consequently red-shifted emission is observed. Therefore, the fluorescence of ESIPT fluorophores can be quenched in the molecularly dissolved state (via blocking of the hydroxyl group) or can become AIE-active in the aggregated state either due to restriction in the motion process or through isolation from the bulk solvent system due to aggregation (unblocking of the hydroxyl group). In recent years, the combination of AIE and ESIPT has provided new dimensions and functions to bioimaging, self-assembly and disassembly based on the detection of analytes<sup>19–24</sup> in water.

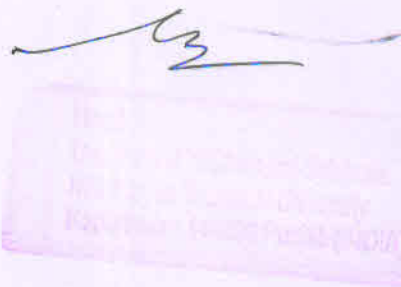
The development of LFPs with a high efficiency and selectivity, and with low background interference is one of the major challenges in the identification of an individual for security and forensic reasons. Fingerprints contain a unique pattern of

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## Organic &amp; Supramolecular Chemistry

Nanomolar  $\text{Cu}^{2+}$  Detection in Water Based on Disassembly of AIEgen: Applications in Blood Serum, Cell Imaging and Complex Logic CircuitsPrabhpreet Singh,<sup>[a]</sup> Harminder Singh,<sup>[a]</sup> Vanita Vanita,<sup>[b]</sup> Rashmi Sharma,<sup>[c]</sup>  
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Here in, we report self-assembled aggregates of AIEgen 1, which exhibits excited state intramolecular proton transfer (ESIPT) coupled aggregation induced emission (AIE) with intense green fluorescence ( $\lambda_{\text{em}} = 526 \text{ nm}$ ) in aqueous solution as well as in solid state. AIEgen 1 behaves as disassembly based fluorescent probe for selective and sensitive detection of  $\text{Cu}^{2+}$  in drinking water with lowest limit of detection of 0.261 ppb (4.13 nM) (much lower than recommended by EPA). AIEgen 1 finds applications for the detection of  $\text{Cu}^{2+}$  in blood serum, environmental (tap, pond and industrial waste water) samples. Probably the interaction of  $\text{Cu}^{2+}$  ions at Schiff-base unit of AIEgen 1 via metal chelation disrupts the self-assembled aggregates and results in disassembly of the nanorods into

smaller spherical nanostructures as also evidenced in DLS, SEM and TEM studies. Incubation of HeLa cells with AIEgen 1 results in fluorescence 'switch-on' showing cell internalization of AIEgen 1 with low cytotoxicity and thus establishes the potential of AIEgen 1 in cell imaging. The reversibility of fluorescence / absorbance of 1- $\text{Cu}^{2+}$  complex with EDTA helps in elaboration of various reconfigurable and superposed logic gates such as NOT (at  $F_{425}$ ,  $A_{360}$ ), INH (at  $A_{360}$ ), IMP<sub>1</sub> (at  $A_{360}$ ) and IMP<sub>2</sub> (at  $F_{425}$ ). By observing the output switching in absorbance and fluorescence channels on addition of  $\text{Cu}^{2+}$  (In1) and EDTA (In2) as inputs, 'set-reset' flip-flop memory element and complementary IMP/INH logic circuits have been elaborated.

## Introduction

Aggregation induced emission (AIE) is a phenomenon which is associated with abrupt increase in fluorescence intensity on aggregation of organic molecules in water or in solid state and has been exceedingly explored in last few years.<sup>[1–6]</sup> Organic molecules which are non-emissive in the molecularly dissolved state but strongly emit light in the aggregate form (achieved by addition of poor solvent or analyte complexation), are known as AIEgens. Up to now, AIEgens' family includes siloles,<sup>[7–10]</sup> tetraphenylethenes,<sup>[11–12]</sup> salicylaldehyde azines,<sup>[13–16]</sup> pyrrole and diketopyrrolopyrroles,<sup>[15–16]</sup> cyanostilbenes,<sup>[17–18]</sup> pyr-

azine,<sup>[19]</sup> diphenyldibenzofulvenes,<sup>[21–25]</sup> and other derivatives.<sup>[21–25]</sup> The AIE fluorophores are beneficial in the fields of organic light emitting diode (OLED), cell staining and drug delivery by virtue of high emission in the solid state and in aqueous environment.<sup>[1]</sup> For practical applications in the domain of molecular recognition, AIE fluorophores provide the liberty of working in solvent systems with water content as high as > 95% and allow analyte detection even in the solid state.<sup>[9]</sup>

Copper, an essential nutrient, is third most abundant transition metal in the body. The deficiency of copper in diet associated with neurodegenerative diseases viz. Alzheimer's, Minke and Wilson's disease. On the other hand, the high concentrations of copper prove to be toxic to the body and have high environmental hazards.<sup>[26–28]</sup> Therefore, in order to early diagnosis and treatment of these aforesaid diseases, the development of copper sensors with high sensitivities and low detection limits with ability to work in aqueous conditions is crucial.<sup>[26]</sup> The detection of copper in water using AIE based chemosensors has been scarcely reported with only limited number of reports in literature<sup>[22–25]</sup> with lowest detection limit of 160 nM.

On the other hand molecular computing<sup>[29–40]</sup> or molecular logic gates could provide alternate of silicon-based computer. Molecular logic gates provide possibility of reconfigurability (wavelength-based) and superposition (functioning of different logic simultaneously) of logic gates. After pioneering work in molecular logic gates by Aviram and then de Silva, researchers are in progress of developing more organic molecule for addressing complex molecular logic gates.<sup>[41–43]</sup>

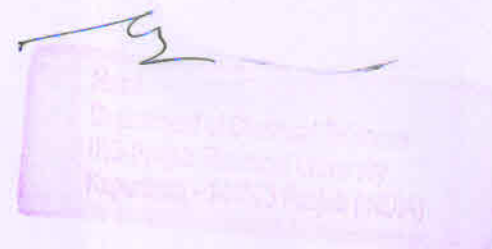
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# ‘To kill many birds with one stone’: Addressing half-adder, half-subtractor, demultiplexer, 2-to-4 decoder, comparator, keypad lock with unimolecular system

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## ABSTRACT

Unimolecular system SBU shows multiple output responses on interaction with  $\text{Cu}^{2+}/\text{F}^{-}$  ions individually and simultaneously. The complexation of  $\text{Cu}^{2+}$  with imine ( $-\text{C}=\text{N}$ ) and  $-\text{OH}$  groups results in blue-shift from 332 to 303 nm and de-protonation of  $-\text{OH}$  group with  $\text{F}^{-}$  ions causes red-shift of the absorption maxima from 332 to 405 nm. The addition of  $\text{F}^{-}$  to  $\text{SBU}/\text{Cu}^{2+}$  solution or addition of  $\text{Cu}^{2+}$  to  $\text{SBU}/\text{F}^{-}$  solution shifts the absorption maxima from 303 to 374 nm or 405–303 nm, respectively. Similarly, the complexation of  $\text{Cu}^{2+}$  ions inhibits the ESIPT emission at 512 nm with concomitant release of emission at 425 nm, whereas  $\text{F}^{-}$  results in quenching of emission at 512 nm up to 10  $\mu\text{M}$ . Followed by blue-shift to 425 nm at  $>10 \mu\text{M}$   $\text{F}^{-}$  ions. The addition of  $\text{F}^{-}$  to  $\text{SBU}/\text{Cu}^{2+}$  solution causes quenching of emission at 512 and 425 nm, whereas addition of  $\text{Cu}^{2+}$  to complex  $\text{SBU}/\text{F}^{-}$  solution revives the emission at 425 nm considerably. These multiple output response leads to elaboration of YES, NOT, NOR, INH, AND, XOR and XNOR logic gates and Half-adder, Half-subtractor, 2-to-4 decoder, 1:2 demultiplexer, Magnitude Comparator, complimentary OR/NOR circuit and molecular keypad lock logic circuits.

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## 1. Introduction

Information technology (IT) has helped the mankind in developing fast computation techniques that could be used in communication, aeronautical-space science, robotics, medical diagnostics, data storage and even programmed activation of prodrug [1,2]. At present, IT systems have been sculptured from electronic logic gates developed by means of silicon-based-semiconductor materials [3]. However, these are plagued with lack of reconfigurability, size  $>100 \text{ nm}$ , excessive heat generation and load of data [4]. The molecular computing provides promising alternate to silicon computers due to ease in chemical modification in the molecular structure, high level of information storage and bottom-up approaches to control the dimensions and properties of the molecules [5–10]. The molecular computing or molecular logic gates [7,8] can be elaborated at  $<1 \text{ nm}$  scale.

In parallel to huge array of binary logic gates, which are operational components in computer, Aviram [11] in 1988 first proposed molecular logic and later on de Silva reported molecule based AND logic gate [12]. This was followed by plethora of reports describing molecular logic systems by modulating the input signals such as laser at different wavelengths, chemical stimuli or proton concentration and receiving the outputs in terms of changes in absorption, emission and redox properties [13–16]. Molecular logic gates can be re-configured [17], by using different output signals at different wave-

lengths (wavelength-reconfigurable logic gate) and also provide opportunity to look into functioning of different logics simultaneously with a given set of inputs (super-position of logic) [18]. Also, with molecular logic systems, multiple optical signals can be instantaneously transmitted by virtue of an optical fibre cable with high travelling speeds [19]. In literature the execution of complex molecular analogues such as half-adder, half-subtractor, full-adder, full-subtractor, encoder, decoder, multiplexer, demultiplexer, molecular key pad lock and other such complex systems are quite tedious [20–29] and involve simultaneous use of more than one molecule in the solution to read different logic gates or need great attention to choose between positive and negative logic convention [30]. So, there is a need to develop unimolecular systems to address complex molecular logic gates [26,27,30].

Dual chemosensor bearing pockets for cation and anion separately can perform supramolecular recognition via colorimetrically or fluorescent-based response through modulation of different signaling mechanisms [31–34]. Such dual chemosensors could be foreseen as potential candidates to develop unimolecular system to address multiple logic gates. In our previous works, we have developed tetrapodal and dipodal systems based molecular switches and logic gates [35,36]. Recently, we designed perylene-3,4,9,10-tetracarboxylic diimide based chemosensor which shows self-assembled nanorod [37,38] and nanovesicle [39] morphology and utilized its  $\text{Cu}^{2+}/\text{Pd}^{0}$  based response for mimicking several logic gates [37]. We also reported dipod based dual chemosensor which offered possibility for INH, IMP, AND logic gate via triple signalling mechanism [31].

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## Biosensors

## Ionic Self-Assembled Platform of Perylenediimide–Sodium Dodecylsulfate for Detection of Spermine in Clinical Samples

Prabhpreet Singh,<sup>[a]</sup> Lalit Singh Mittal,<sup>[a]</sup> Gaurav Bhargava,<sup>[b]</sup> and Subodh Kumar<sup>[a]</sup>

**Abstract:** The detection and quantification of spermine in clinical practice is important for early diagnosis of many diseases. Chromatographic and immunoassay-based methods are commonly used. However, a fluorescence-based assay could provide real-time detection. Herein, the synthesis and aggregation properties of a dicationic perylene probe (N<sup>1</sup>-dodecyl-N<sup>3</sup>-(4-phenyl)benzimidazolium-functionalized perylenediimide (DAB-PDI)) used to develop a fluorescent “turn-on” ensemble for the detection of spermine are discussed. The fluorescence of DAB-PDI (10  $\mu$ M,  $\Phi=0.55$ ) is efficiently quenched by negatively charged sodium dodecylsulfate (SDS) through the formation of ionic self-assembled aggregates (charge ratio of negative (N) in SDS to positive (P) in

DAB-PDI (N/P = 9)). This negatively charged ionic self-assembly between DAB-PDI and SDS has been characterized by using photophysical, microscopic, dynamic light scattering, isothermal titration calorimetry, and HRMS techniques. The addition of spermine to this ensemble solution results in the breakdown of the DAB-PDI–SDS ensemble owing to strong binding of spermine with SDS and, as a result, the fluorescence of DAB-PDI is recovered. This ensemble exhibits high sensitivity and selectivity for spermine detection in water, urine, and blood serum. The lowest limit of detection is 27.5 nM, which is at least about 36 times lower than that required for early diagnosis of cancer (1 to 10  $\mu$ M for urinary spermine).

## Introduction

Spermine, a biogenic aliphatic tetraamine, is found in eukaryotic cells and body fluids. Owing to its polycationic nature, spermine plays an important role in cell growth and proliferation, and is involved in various stages of protein synthesis and stabilization of nucleic acid conformations.<sup>[1–3]</sup> Elevated spermine concentrations in urine and blood could be related to the presence of malignant tumors or cancer. Thus, the detection of spermine in physiological samples can be regarded as an excellent tool for early diagnosis and to assess the effectiveness of cancer therapy.<sup>[4,5]</sup> Traditional methods, such as chromatographic techniques, immunoassays, and mass spectrometry, are time consuming, require tedious procedures, and expensive instrumentation.<sup>[6]</sup> On the contrary, fluorescence-based

methods are more selective, approach ultratrace-level sensitivity, and involve simple operation with real-time detection. However, to date, few reports on fluorescence-based assays with “turn-on” responses in the nanomolar range for spermine are available in the literature.<sup>[7]</sup> Therefore, there is a need to develop methods with satisfactory sensitivity and selectivity for the detection of spermine.

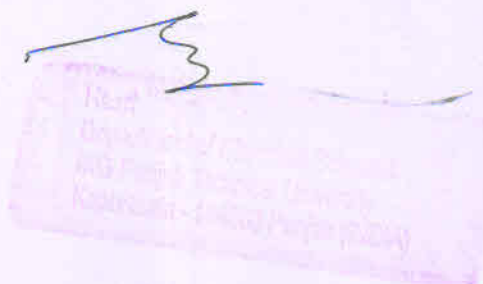
Sodium dodecylsulfate (SDS), owing to its amphiphilic nature, is known to form supramolecular aggregates, such as micelles and vesicles in aqueous solution.<sup>[8]</sup> Owing to extensive industrial and domestic use of SDS, its presence in natural waters has caused serious environmental problems by inhibiting biological activity.<sup>[9]</sup> It also helps in the transfer of other pollutants, namely, petroleum products, oil, and pesticides, into water because of its foam formation property. Therefore, apart from creating a supramolecular self-assembly, we also need effective fluorescence-based methods that enable the analysis of SDS from water because it can be used as a masking agent in drug abuse and food preparations.

Perylene diimides (PDIs), which form an interesting class of functional organic dyes, have been used as high-performance pigments,<sup>[10,11]</sup> supramolecular hosts,<sup>[12–17]</sup> and in optoelectronic devices.<sup>[18,19]</sup> The functionalization of PDIs at bay-, peri-, ortho-, and N-terminal positions is being performed to increase the solubility of PDIs in organic solvents. However, the poor solubility of PDI derivatives in aqueous media remains one of the most detrimental factors in the development of PDI-based receptors for the recognition of cations and anions in water. In recent years, the groups of Hirsch and Würthner have used

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Supporting information for this article can be found under:  
<http://dx.doi.org/10.1002/asia.201700120>. It contains experimental procedures and characterization data for PDI 3 and DAB-PDI; additional microscopic and spectroscopic data for the DAB-PDI–SDS ensemble; and spectroscopic and DLS data of titration for spermine with the ensemble.





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## Perylene diimide-based organic $\pi$ -motif for differentiating $\text{CN}^-$ and $\text{F}^-$ ions by electron-transfer and desilylation mechanisms: applications to complex logic circuits†

Prabhpreet Singh,<sup>a,\*</sup> Lalit Singh Mittal,<sup>a</sup> Harminder Singh,<sup>a</sup> Gaurav Bhargava<sup>c</sup> and Subodh Kumar<sup>a</sup>

In this work, we have designed and synthesized a perylene diimide based derivative **PDI-SiHQ** having an *O*-silylated-8-hydroxyquinoline group at the bay position. **PDI-SiHQ** is able to detect and differentiate  $\text{CN}^-$  from  $\text{F}^-$  in the presence of other anions. The electron transfer from cyanide ions to **PDI-SiHQ** leads to the emergence of panchromatic and NIR absorption bands due to the formation of a **PDI-SiHQ**<sup>•−</sup> radical anion. In contrast, fluoride induced desilylation of **PDI-SiHQ** coupled with  $\pi$ - $\pi$  aggregation results in a red-shifted absorption band at 730 nm. <sup>1</sup>H NMR and cyclic voltammetry combined with the reversal of the **PDI-SiHQ**<sup>•−</sup> radical anion to the **PDI-SiHQ** neutral form in the presence of  $\text{NOBF}_4$  or  $\text{Cu}^{2+}$  ions confirm the formation of the radical anion in **PDI-SiHQ**. Multi-channel UV-Vis-NIR absorption and emission bands and their reversibility with  $\text{NOBF}_4/\text{Cu}^{2+}$  ions offer the possibility for fabrication of complex logic circuits such as complementary IMP/INH logic circuits, magnitude comparators and 'set–reset' flip flop memory elements

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### 1. Introduction

Perylene diimides (PDIs)<sup>1,2</sup> are a valued class of *n*-type dye which are highly colored (with broad color range), fluorescent (quantum yield is near unity) and possess a high absorption coefficient and good redox, electron acceptor and light harvesting properties. Moreover, PDIs offer wide freedom of functionalization (at bay-, imide-, *peri*- and *ortho*-positions)<sup>3–5</sup> of their  $\pi$ -backbones for modulation of optical and electronic properties for possible applications in photonic materials<sup>6</sup> (as chemosensors and molecular logic gates) and optoelectronic materials (as field effect transistors, organic light emitting diodes and dye sensitizers in solar cells).<sup>7–9</sup> In our endeavor towards exploiting self-assembled materials<sup>10–13</sup> for applications in biosensing and bioimaging, we have reported a library of PDI based derivatives for molecular recognition of metal ions, anions and biogenic amines in aqueous/organic–aqueous solvents.<sup>10,11</sup> Within this framework, we recently reported a PDI derivative for the

detection of  $\text{ClO}_4^-$  via encapsulation in the cavity<sup>14</sup> and sodium dodecyl sulphate (SDS) anion via ionic self-assembly<sup>10</sup> in water and live cells. In these cases, the binding between the anion and PDI based receptor relies on non-covalent forces such as hydrogen bonding and hydrophobic and electrostatic interactions.

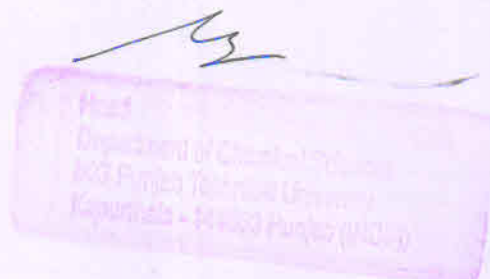
In recent years, the concept of anion- $\pi$  interactions,<sup>14–16</sup> so called electronic interactions between electron-rich anions and electron-deficient  $\pi$  systems, began to emerge as a novel method to generate radical anions which offer applications in supramolecular and material chemistry combined with multi-channel and panchromatic-NIR detection of anions.<sup>17–20</sup> From a series of recent literature, it is clear that the position of charge-transfer bands varied with the nature of electron-donors (*viz.* nature of the anion and use of reducing agents such as dithionite and ascorbate ions)<sup>21–23</sup> and electron-acceptors (arylenediimide,  $\text{HAT}(\text{CN})_6$ , binary complex of arylenediimide and macrocyclic supramolecular host *viz.* cucurbit[4]uril).<sup>17–19,24</sup> Mechanistically, when an acceptor molecule (such as PDI, NDI and  $\text{HAT}(\text{CN})_6$ ) having a low lying LUMO level comes in contact with the HOMO of  $\text{CN}^-$ ,  $\text{F}^-$  or  $\text{OH}^-$  (strong basic anions), a facile single electron-transfer (SET) mechanism involving HOMO–LUMO rapidly forms a stable radical anion *via* single electron transfer. Usually, all strong Lewis basic anions ( $\text{CN}^-$ ,  $\text{F}^-$  and  $\text{OH}^-$ ) trigger thermal electron transfer (ET) processes and thus it is difficult to differentiate between these basic anions. In this context, many efforts are undertaken to develop arylenediimide based derivatives

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† Electronic supplementary information (ESI) available: Experimental details, and additional photophysical and spectroscopic characterization of **PDI-SiHQ** and **PDI-SiHQ**<sup>•−</sup> radical anion. See DOI: 10.1039/c7nj02580d





## Catalysis

## Copper(I)-Catalyzed Regioselective C-H Amination of N-Pyridyl Imines Using Azidotrimethylsilane and TBHP: A One-Pot, Domino Approach to Substituted Imidazo[4,5-b]pyridines

Nisha,<sup>[a]</sup> Gaurav Bhargava,<sup>[b]</sup> and Yogesh Kumar<sup>\*,[b, c]</sup>Dedicated to Prof. M. P. Mahajan on the occasion of his 70<sup>th</sup> birthday

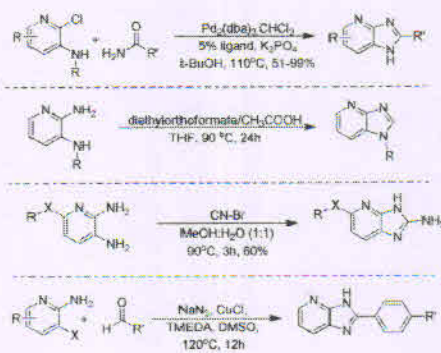
A novel, efficient and one-pot multicomponent copper-catalyzed amination of N-pyridyl imines is described. This, one-pot, multicomponent reaction, in which imine acts as a directing group by chelating to the metal core, affords a domino approach for the transformation of the commercial pyridine-amines, aldehydes and azide into valuable imidazo[4,5-b]pyridines with wide substrate extent and diversity.

Advances in transition-metal catalysis have led to the progress of valuable methods for regioselective carbon-carbon, carbon-nitrogen, carbon-oxygen, and carbon-sulfur bond formations.<sup>[1,2]</sup> The carbon-nitrogen bond formation has attracted significant interest since nitrogen-containing heterocycles have extensive applications in the biological and medicinal chemistry.<sup>[1,3]</sup> Among first-row transition metals (Mn, Fe, Co and Cu), copper is well considered as a catalyst with various amine ligands, additives, and under various conditions for coupling reactions. But, there are very few reports on the copper-catalyzed systems, which are particularly striking because of its high abundance and low toxicity.<sup>[3]</sup> Copper-catalyzed C-H amination is one of the most fundamental and significant reactions as it provide a straightforward and inexpensive protocol to synthesize a wide range of nitrogen heterocycles.

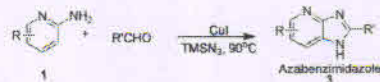
On the other hand, imidazo[4,5-b]pyridines scaffold represent a nucleus skeleton of various heterocyclic analogues of purine with biological activities<sup>[4]</sup> which depend on the

substituents on the pyridine ring. These medicinal important imidazo[4,5-b]pyridines<sup>[5]</sup> has been evaluated as an antagonist of different biological receptors, including platelet-activating factor (PAF),<sup>[7]</sup> angiotensin-II<sup>[6]</sup> and metabotropic glutamate subtype V.<sup>[8]</sup> Recently, these are also reported as anticancer,<sup>[9]</sup> inotropic,<sup>[10]</sup> and selective antihistamine (H1) agents<sup>[11]</sup> aurora kinases<sup>[12]</sup> and cyclic phosphodiesterase inhibitors.<sup>[13]</sup> But only a few approaches were reported for the regioselective synthesis of imidazo[4,5-b]pyridines via metal-catalyzed cascade reactions and C-H functionalization/activation reactions. An attempt has been recently made on the expansion of new strategies to build the imidazo[4,5-b]pyridine structural motifs using Pd-catalyzed amide coupling reaction of chloro-amino-pyridines (Scheme 1, a), acid catalyzed cyclization of diamino-

## Previous Reports



## Present Work



Scheme 1. Main strategies for imidazo[4,5-b]pyridine syntheses.

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Invited paper

Fluorometric differential detection of  $\text{Zn}^{2+}$  and  $\text{Cu}^{2+}$  by picolylamine appended pyrimidinone-based receptor: Application in mimicking TRANSFER and INH logic gatePrabhpreet Singh<sup>a,\*</sup>, Harminder Singh<sup>a</sup>, Rashmi Sharma<sup>b</sup>, Sanjeev Dhawan<sup>c</sup>,  
Parvesh Singh<sup>c</sup>, Gaurav Bhargava<sup>d</sup>, Subodh Kumar<sup>a</sup><sup>a</sup> Department of Chemistry, UGC-Centre of Advance Studies-II, Guru Nanak Dev University, Amritsar, 143 005, India<sup>b</sup> Department of Chemistry, Trinity College, Jalandhar, 144009, Punjab India<sup>c</sup> School of Chemistry and Physics, University of KwaZulu Natal, Pietermaritzburg, 4000, South Africa<sup>d</sup> Department of Chemical Sciences, IK Gujral Punjab Technical University, Kapurthala, 144 601, Punjab, India

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## ABSTRACT

Herein, we have designed and synthesized pyrimidinone-based dual chemosensor (DPPA) containing picolylamine moiety as binding unit. Investigation on the optical property of DPPA revealed fluorescence enhancement at 435 nm with  $\text{Zn}^{2+}$  ion through binding with picolylamine and carbonyl moieties, while  $\text{Cu}^{2+}$  ion was detected through fluorescence quenching at 425 nm and colorimetric changes at 350 nm due to complexation with picolylamine and deprotonation of amide  $-\text{NH}$  group. The detection limit of  $\text{Zn}^{2+}$  and  $\text{Cu}^{2+}$  was calculated to be 10.04 nM and 34.1 nM, respectively. The Job's plot showed formation of 1:2 and 2:1 binding stoichiometry of DPPA with  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$ , respectively.  $^1\text{H}$  NMR titration in  $\text{CD}_3\text{CN}$  revealed downfield shift in methyl groups of  $\text{N}(\text{CH}_3)_2$  and methylene ( $-\text{CH}_2$ ) protons of picolylamine chain due to formation of coordinate bonds between  $\text{Cu}^{2+}$  and DPPA, whereas only downfield shift of methylene ( $-\text{CH}_2$ ) protons of picolylamine were responsible for complexation with  $\text{Zn}^{2+}$  ions. The complexation mechanisms of DPPA with  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  were also supported by detailed theoretical calculations.

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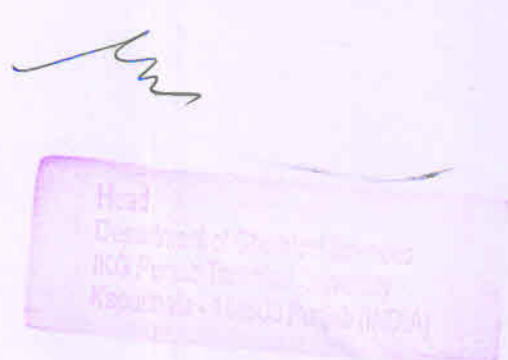
## 1. Introduction

Dual chemosensors [1–3] are capable of detecting two analytes simultaneously and thus provide an edge over the chemosensors (which can detect only one analyte) in terms of cost-effectiveness and efficient analysis in fields and contaminated sites [4]. Among the different detection approaches reported so far for analyte using dual chemosensors includes either simultaneous detection of two analytes at the same time independent of each other (*simultaneous approach*) [5]; or detection of second analyte achieved through breaking of complex between chemosensor and first analyte in a sequential manner (*displacement approach*) [6]. The sequential detection of two metal ions or metal ion and anion can be easily achieved using metal ( $\text{Zn}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Hg}^{2+}$ ) bound receptor followed by displacement of either metal ion with another metal ion due to higher binding constant or displacement of metal ion with anion

via strong binding of these metals with target anions. However, design strategy of dual chemosensor for simultaneous detection of two metal ions or metal ion and anion required incorporation of differential binding domain for both analytes in unimolecular system [7,8]. The binding of these analytes at their respective binding domain would produce differential color or fluorescence response due to change in signalling mechanism such as CHEF (chelation induced fluorescence enhancement), ESIPT (excited state intramolecular proton transfer), CHEQ (chelation induced fluorescence quenching), PET (photoinduced electron transfer), ICT (internal charge transfer), PCT (photoinduced charge transfer) and FRET (fluorescence resonance energy transfer) [9]. Moreover, in last few years we have witnessed that organic molecules, having dimension in nanometer scale and variability in properties through chemical functionalization, are extensively employed for mimicking logic gates and circuits. In this context, dual chemosensor showing multiple outputs in absorbance or fluorescence mode could be used to fabricate logic gates and circuits [10–17].

$\text{Zn}^{2+}$  is the second most abundant transition metal ion and plays an important role in many biological processes such as apoptosis,

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## Research Paper

## Self-assembled small molecule based fluorescent detection of serum albumin proteins: Clinical detection and cell imaging

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## ABSTRACT

We report perylenediimide-benzimidazolium based fluorescent 'turn-on' probe **BIM-PDI** for selective detection of human serum albumin (HSA) and bovine serum albumin (BSA) proteins. In HEPES buffer (0.1% DMSO), **BIM-PDI** self-assembles into aggregates and shows absorption maxima at 500 nm and weak fluorescence centered at 577 nm. The addition of HSA or BSA ( $1 \times 10^{-9}$ – $5 \times 10^{-8}$  M) to the solution of **BIM-PDI** results in decrease in the emission intensity at 577 nm. However, further increase in concentration of HSA/BSA results in appearance of new blue shifted emission band at 540 nm. The minimum detection limit for HSA/BSA is  $3.01 \times 10^{-10}$  M at 577 nm and  $4.2 \times 10^{-8}$  M at 540 nm. On addition of BSA to the solution of **BIM-PDI**, the size of the aggregates decreased from 100 to 250 nm to <10 nm assigned to microencapsulation driven disassembly of **BIM-PDI** aggregates responsible for 'turn-on' response in fluorescence spectrum. Site-selective experiments using warfarin and diazepam drugs show that **BIM-PDI** preferably binds at site-I of HSA/BSA proteins. In clinical application of **BIM-PDI**, we estimated HSA content in blood serum and urine samples. **BIM-PDI** showed potential application in serum albumin protein tracking and imaging.

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## 1. Introduction

Perylenediimide (PDI) is an important scaffold and well documented class of functional organic dyes for developing supramolecular nanostructures for applications in molecular recognition [1–8]. The perylenediimide core can be modified through functionalization at *-bay*, *-peri*, *-ortho* and N-terminal positions [1,9,10]. The functionalization of PDIs at N-terminal positions are being done to increase the solubility of the PDIs in organic solvents without affecting the optical properties of PDIs, whereas bay functionalization dramatically changes the photophysical properties of PDIs. The poor solubility of *-bay* and N-terminal functionalized PDIs in aqueous medium results in self-aggregation of PDIs through short-range non-covalent forces such as  $\pi$ - $\pi$  stacking, H-bonding or van der Waal's forces to produce either *H*-aggregates [11] or *J*-aggregates [12] and thus greatly hampers the exploitation of PDIs in supramolecular chemistry.

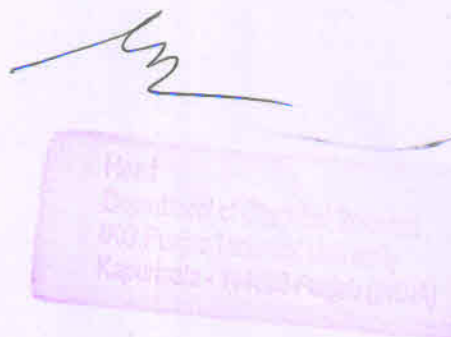
However, if the interaction of a specific stimulant with these aggregates of PDIs in water occurs, it would result in change of fluorescence and morphology of the aggregates to mark the molecular recognition process in real time. In this context, recently we have reported library of 1- or 1,7- substituted perylenediimide derivatives to achieve self-assembled morphology of nano-spheres, vesicles or rods and utilized these supramolecular aggregates to develop fluorescent probes for  $\text{ClO}_4^-$ ,  $\text{Pd}^0/\text{Pd}^{2+}$ , sodium dodecyl-sulfate (SDS), spermine, trivalent metal ions in water and live cells; detection of  $\text{Cu}^{2+}$  and  $\text{CN}^-$  in organic media [3–5].

Concept of using self-assembled aggregates of small molecules as fluorescent bio-probes for the detection and imaging of protein has attracted much attention in recent years [13–25]. Amongst different thiol-containing proteins, the serum albumins (SA) – human serum albumin (HSA) in human and bovine serum albumin (BSA) in animals, play important roles in maintaining oncotic pressure of the blood, transporting and deposition of various endogenous and exogenous molecules to specific sites, scavenging free radicals and in preventing protein aggregation [26–28]. HSA and BSA are structurally similar and have two major sites for non-covalent binding of ligands namely site-I, where binding is primarily driven by hydrophobic interactions, and site-II, where both hydrophobic

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## Controllable supramolecular self-assemblies (rods–wires–spheres) and ICT/PET based perylene probes for palladium detection in solution and the solid state†

Kapil Kumar,<sup>a</sup> Gaurav Bhargava,<sup>b</sup> Subodh Kumar<sup>b</sup> and Prabhpreet Singh<sup>a\*</sup>

Control over the self-assembly of bay functionalized perylene diimides and the response of these self-assembled materials towards analytes in mixed aqueous–organic media is important to consider the potential of this intriguing dye family in supramolecular chemistry. Herein, we have designed and synthesized allylcarbonate-functionalized perylene diimide AC-PDI which shows solvent dependent supramolecular nanostructures and could readily self-assemble into nanorods of tens of  $\mu\text{m}$  in length in  $\text{CH}_3\text{CN}$ , but the length of the rods dramatically decreased to 0.8–1.2  $\mu\text{m}$  in a  $\text{H}_2\text{O}:\text{CH}_3\text{CN}$  (1:1, v/v) mixture. Interestingly, AC-PDI self-assembles into nanowires of several tens of  $\mu\text{m}$  in length in a 30%  $\text{H}_2\text{O}:\text{DMSO}$  mixture and forms only nanospheres in ethyl acetate. AC-PDI can be used as a near-infrared (NIR) colorimetric ( $\lambda_{\text{abs}}$  685 nm) and fluorescent ( $\lambda_{\text{em}}$  530/570 nm) probe for selective detection of  $\text{Pd}^{2+}$  [LOD = 39 nM (UV); 45 nM (FI)]. Furthermore, TLC strips coated with the AC-PDI probe could detect 0.58  $\text{pg cm}^{-2}$  of  $\text{Pd}^{2+}$  in the solid state. The mechanism of interaction of AC-PDI with  $\text{Pd}^{2+}$  has been confirmed by  $^1\text{H}$  NMR titration, kinetic and morphological studies.

## Introduction

Controlled self-assemblies of  $\pi$ -conjugated molecules have drawn much attention in the last decade due to their potential applications in photovoltaic and optoelectronic devices.<sup>1–4</sup> Among various  $\pi$ -conjugated molecules, perylene diimides (PDIs) are one of the most studied classes of functional dyes with excellent electronic, optical and redox properties.<sup>2,3</sup> PDIs have been widely utilized as an active component of organic field-effect transistors (n-type), light emitting diodes, solar cells and sensors<sup>4–10</sup> because of their strong absorption combined with high fluorescence quantum yield, low reduction potential, good electron acceptor properties and broad colour range properties.<sup>2,3</sup> The aggregation (self-assembly) and optoelectronic properties of PDIs primarily depend on the local arrangement of their  $\pi$ -stacked array, which can be tuned through modification of their  $\pi$ -molecular structure at the bay, *peri*, *ortho*- and *N*-imide positions with organic chemical groups.<sup>3–4</sup> Many reports regarding modification of the

*N*-imide position of PDIs to generate self-assembled nanostructures including fibers, ribbons, rods, tubes *etc.* are being published each year. However, little attention has been paid to the self-assembly of bay substituted PDIs in an aqueous medium.<sup>11</sup> Probably, substitutions at a bay position drastically increase the solubility of PDIs and if the substituents are bulky in nature, the perylene backbone deviates from planarity to minimize the strain and this hinders the possibility of  $\pi$ - $\pi$  stacking and so the examples of self-assembled bay functionalized PDIs are less known.

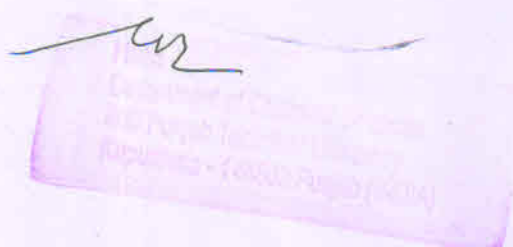
Palladium is one of the most important transition metals, extensively exploited in modern organic chemistry and industrial production. Moreover, the high affinity of Pd species towards thiol containing biomolecules such as amino acids and proteins may cause their denaturation and Pd can also bind effectively to DNA which may disrupt a number of cellular processes in the human body.<sup>12–16</sup> Henceforth, it is prerequisite to establish fast and effective techniques for the detection of palladium with high sensitivity and selectivity. Due to the heavy cost factor and tedious operational procedures involved in conventional analytical methods, appreciable attention has been paid to the establishment of fluorescent probes for the detection of Pd species ( $\text{Pd}^0$  or  $\text{Pd}^{2+}$ ).<sup>5,6,17</sup>

In the last decade, successful efforts have been made to explore *N*-imide functionalized PDIs as photoinduced electron-transfer (PET) based chemosensors for metal ions in mixed

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† Electronic supplementary information (ESI) available: Experimental details, and additional photophysical, spectroscopic and microscopic characterization of AC-PDI and AC-PDI +  $\text{Pd}^{2+}$ . See DOI: 10.1039/c7nj03751a





## Cycloadditions

# Transition-Metal-Catalyzed [3+2+2] Cycloaddition Reactions

Bilash Kuila,<sup>[a]</sup> Maninderjeet Kaur,<sup>[a]</sup> Prabhpreet Singh,<sup>[b]</sup> and Gaurav Bhargava<sup>\*[a]</sup>

**Abstract:** [3+2+2] Cycloaddition reactions are of key importance in organic chemistry for the synthesis of seven-membered mono- and condensed carbocycles. This review article summarises the different reports on transition-metal-catalysed [3+2+2] cycloaddition reactions since 2000. Different transition-metals, such as Ni, Rh, Pd, Co, or Ru, which have been earlier reported for higher order [3+2+2] cycloaddition reactions are

summarized in this article. The [3+2+2] cycloadditions of different functionalized substrates afford cycloheptane derivatives, 6-7,5-7 condensed bicyclic carbocycles, or 5-7-5 or 6-7-5 condensed tricyclic carbocycles. These higher order cycloaddition reactions may provide an easy route for the total synthesis of natural products, or as a preferable key synthetic step leading to final structure.

## 1. Introduction

Cycloaddition reactions are the most powerful method for the construction of a complex structure in a single step.<sup>[1]</sup> Although two component [4+2] and [3+2] cycloaddition reactions are synthetically the most explored reactions for the synthesis of six- and five-membered carbo-/heterocycles, respectively, but the comparable methodology for higher-membered carbo-/heterocycles are still in the process of development. The higher-order [m+n+o] cycloaddition reactions are emerging as useful synthetic tools for the synthesis of higher order mono or condensed carbo/heterocyclic ring systems.<sup>[2-3]</sup> The transition-metal-catalyzed [m+n+o] reactions provide useful carbo-/heterocycles from relatively inactive substrates, such as alkenes and alkynes.<sup>[4,5]</sup>

Of different variants of [m+n+o] cycloadditions reactions, [3+2+2] is an important synthetic tool for the synthesis of functionalized mono- or condensed cycloheptanes. The importance of atom-economical [3+2+2] cycloadditions lies in the fact that cycloheptanes and their analogues have played vital role as functionalized biomolecules in food, pharmaceutical, and natural products.<sup>[6-8]</sup> Methylene-cyclopropanes as a 3 $\pi$  component has been utilized as an important synthon in organic synthesis.<sup>[9-14]</sup> Methylene- and vinyl-cyclopropane as organic synthons have been successfully explored for [m+n] and [m+n+o] cycloaddition reactions with a variety of alkenes and alkynes using different metal complexes as catalysts.<sup>[15]</sup> For example, cyclopropyl ketones, alkylidenecyclopropanes (ACP) and vinylcyclopropanes (VCP) have been shown to participate in several transition-metal-catalyzed [3+2], [4+3], [3+2+2] and [5+2] cycloaddition reactions.<sup>[16-19]</sup>

Different researchers have successfully explored functionalized cyclopropanes as 3 $\pi$  components with various alkenes, alkynes, diynes, among others, as 2 $\pi$  components in [3+2+2] cycloaddition reactions using Ni, Pd, Rh and Ru metal complexes as catalysts.<sup>[20-27]</sup> The present review summarizes various reports on [3+2+2] cycloaddition reactions with not only products arising from the activity of the key players (different metal complexes) but also those from proton-based chemistry for the synthesis of mono-and/or condensed cycloheptadiene derivatives, since 2000.

## 2. Nickel-Catalyzed [3+2+2] Cycloaddition Reactions

In this section, we have summarized the various nickel-catalysed inter- and intramolecular [3+2+2] cycloaddition reactions. A majority of the reports on [3+2+2] cycloadditions involve the use of functionalized cyclopropanes as 3 $\pi$ -components in cycloadditions with a variety of alkenes and alkynes as 2 $\pi$ -components.

### 2.1 Nickel-Mediated [3+2+2] Cycloadditions of Alkenyl Fischer Carbene Complexes

One of the first reports on [3+2+2] cycloaddition reactions was described by Barluenga et al. It involves the nickel-mediated [3+2+2] cycloaddition reaction of chromium carbene complexes **1** with various terminal alkynes **3** (Scheme 1) to afford a variety of cycloheptatrienes in fair yields.<sup>[28]</sup>

Nickel-mediated [3+2+2] cyclizations of Fischer-carbene complexes and alkynes take place with complete regio- and stereoselectivity, with the formation of an *endo* isomer. Electron-poor alkynes such as methyl propiolate also undergo [3+2+2] cyclizations to afford functionalized cycloheptatrienes in good yields.<sup>[28]</sup>

A pathway for the formation of **6** and **7** involves the initial chromium-nickel exchange to yield the nickel species **2** (where

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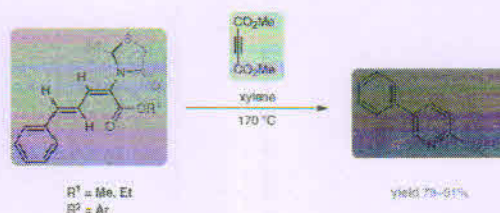
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**Abstract** Acetylenic ester promoted ring opening of dienyli-thiazolidin-4-ones and subsequent electrocyclicization affords 5-phenyl-6-aryl pyridine-2-carboxylates in good to excellent yields.

**Key words:** pyridine-2-carboxylate, dienyl-thiazolidin-4-one, acetylenic ester, cyclization, 5,6-diarylpyridine

Functionalized pyridines having ester substituents at their 2-position i.e., pyridine-2-carboxylates, are prominent in biologically active molecules.<sup>1-3</sup> Functionalized pyridine-2-carboxylates have been identified as cholecystokinin (CCK1) receptors, cannabinoid receptor type 1 (CB1), and telomerase inhibitors.<sup>4</sup> Similarly, 5,6-diaryl-2-pyridine-carboxamides have been used as urotensin II receptor antagonists and sphingosine-1-phosphate (S1P) receptor agonists.<sup>5,6</sup>

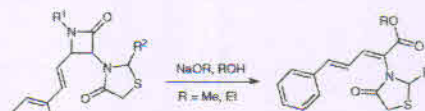
Traditionally, [4+2] cycloadditions of acyclic 2-azadienes have been used as a versatile method for the formation of functionalized pyridines, dihydropyridines, and tetrahydropyridines.<sup>7-17</sup> Barluenga et al. have explored the synthesis of functionalized pyridines utilizing ethoxycarbonyl 2-aza-1,3-butadienes as starting materials.<sup>12</sup> Meurer et al. have reported the synthesis of different 5,6-diarylpyridine carboxylates and carboxamides via cycloaddition of azadiene phosphazene moieties and subsequently studied their human CB1 inverse agonist activity.<sup>13</sup> However, most 2-azadienes are found to be quite unstable and their synthesis requires cumbersome experimental procedures. Moreover, synthesis and cycloadditions of conjugated 2-azadienes have been little explored.

Thiazolidin-4-ones represent an important class of heterocyclic compounds due to their diverse biological activities.<sup>14</sup> Thiazolidin-4-ones have activity profiles, acting

as inhibitors of COX-1,<sup>15</sup> HIV-RT,<sup>16</sup> aldose reductase,<sup>17,18</sup> bacterial enzyme MurB and YycG histidine kinase,<sup>19,20</sup> as well as having antidiabetic activity,<sup>21</sup> antitubercular, antifungal, and antihelminthic activities.<sup>21</sup> Thiazolidin-4-ones have also been explored as useful organic synthons of different heterocycles.<sup>22</sup>

There are numerous reports on the acetylenic ester-mediated synthesis of thiazolidin-4-ones using a variety of thioamides and thioureas.<sup>22</sup> However, there are few reports exploring acetylenic ester mediated ring opening/transformations of 4-thiazolidinones. The present manuscript demonstrates acetylenic ester mediated synthetic transformations of dienyl-thiazolidinones<sup>23</sup> leading to a facile synthesis of functionalized pyridine-2-carboxylates. In this transformation, the dienyl-thiazolidinones **1a-h** behave as masked conjugated 2-azadienes and afford a facile and chemoselective formation of pyridine-2-carboxylates mediated by acetylenic esters in good to excellent yields.

The dienyl thiazolidin-4-ones **1a–h** were prepared by amidolytic ring opening of 2-azetidinones-3-thiazolidin-4-ones with sodium alkoxide in the corresponding alcohols (Scheme 1).<sup>23</sup> Crystallography data for **1a** established the *trans* conformation of the dienyl thiazolidin-4-one moiety.<sup>23</sup>



**Scheme 1** Synthesis of dienyli thiazolidin-4-ones<sup>22</sup>

We started our investigations by attempting Diels–Alder reactions of dienylium thiazolidin-4-one **1a** with electron-deficient dienophiles (such as methyl acrylate, methyl vinyl

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# Quadruple-signaling (PET, ICT, ESIPT, —C=N— rotation) mechanism-based dual chemosensor for detection of $\text{Cu}^{2+}$ and $\text{Zn}^{2+}$ ions: TRANSFER, INH and complimentary OR/NOR logic circuits

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Logic gate

Complementary logic circuit

## ABSTRACT

Herein, we have designed and synthesized o-phenylenediamine-based 4-in-1 dual chemosensor DAU, for simultaneous detection of  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  through modulation of PET, ICT, ESIPT and —C=N— rotation mechanisms. The binding of first  $\text{Cu}^{2+}$  ion with —NEt<sub>2</sub> group causes red shift of absorption band from 372 nm to 420 nm and fluorescence enhancement due to keto- form at 480 nm (~20 fold). When concentration of  $\text{Cu}^{2+}$  further increased from 1 to 10 equivalents, it results in decrease in absorption intensity at 420 nm and increase in absorption intensity at 300 nm and fluorescence quenching at 480 nm followed by enhancement due to enol- form at 410 nm. In contrary higher concentrations of  $\text{Zn}^{2+}$  causes only red shift from 372 to 420 nm however fluorescence remained low due to PET quenching effect. Significantly, when  $\text{Cu}^{2+}$  is added to DAU- $\text{Zn}^{2+}$  (1:5) complex, it results in decrease of absorption intensity at 420 nm and increase in fluorescence at 480 nm followed by a 7-fold increase of the emission intensity at 410 nm. The multiple outputs of DAU can be used for fabrication of INHIBIT, TRANSFER logic devices and complementary OR/NOR logic circuit.

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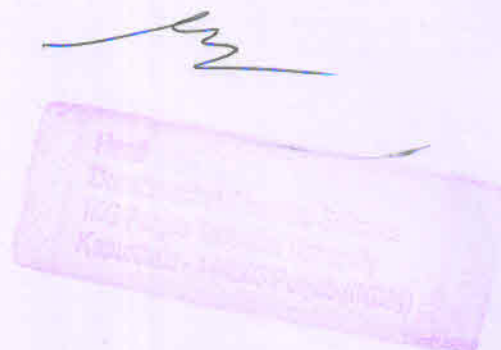
## 1. Introduction

Dual chemosensors [1–3], which may or may not possess two separate binding sites, can be useful for detection of two or more analytes through modulation of different signaling mechanisms such as PET (photo-induced electron transfer), ICT (intramolecular charge transfer), FRET (fluorescence resonance energy transfer), AIE (aggregation induced emission), ESIPT (excited state intramolecular proton transfer), blocking of —CH=N— rotation, excimer or exciplex formation, CHEF (chelation enhanced fluorescence effect), TBET (through bond electron transfer) and CHEQ (chelation enhancement quenching effect) [4–9]. In literature, the design of dual chemosensor allows the detection of two analytes at the same time independent of each other (*simultaneous approach*) [10] or detection of second analyte achieved after breaking of complex between chemosensor and first analyte (*displacement approach*) [11] (Fig. 1). However, currently the majority of literature reports

are on the dual chemosensors which shows modulation in single-signaling mechanism for binding of one or two analytes and perhaps, this limits the use of such chemosensors in the fields of multiple ion sensing and molecular computing (fabrication of molecular scale logic devices) [12,13].

In this context, multiple-signaling mechanisms-based dual chemosensor would definitely provide an edge over the single-signaling mechanism-based dual chemosensor in terms of cost effectiveness, efficient analysis in contaminated sites and application in molecular computing [14–16]. Therefore, the control and understanding of relationship between different signaling mechanisms, which are responsible for change in absorbance/emission intensities and wavelengths on coordination with the analyte, would be important in designing the multiple-signaling mechanisms-based dual chemosensor for one or two analytes. Some examples are known where dual signaling mechanism-based chemosensor are used for sensitive and selective detection of one or two analytes [17–23]. These dual-signaling mechanism-based chemo-sensors can be grouped based on the combination of signaling mechanism such as ICT-FRET, PET-FRET, TBET-PET, ICT-PET, ESIPT-AIE or ESIPT-PET, through which they respond to the

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# Microstructural (self-assembly) and optical based discrimination of $\text{Hg}^{2+}$ , $\text{CN}^-$ and $\text{Hg}(\text{CN})_2$ ion-pair; $\text{Hg}^{2+}$ promoted-ESIPT assisted guanylation of thiourea

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## ARTICLE INFO

**Keywords:**  
Dual chemosensor  
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ESIPT  
Intramolecular guanylation  
Self-assembly

## ABSTRACT

A multifunctional self-assembled dual-chemosensor DTS was synthesized and used for optical and microstructural based discrimination of  $\text{Hg}^{2+}$ ,  $\text{CN}^-$  ions and  $\text{Hg}(\text{CN})_2$  ion-pair. The addition of  $\text{Hg}^{2+}$  ions to the  $\text{CH}_3\text{CN}$  solution of DTS promotes the ESIPT phenomena (emission peak at 458 nm red shifted to 510 nm; increase in absorption between 400 and 480 nm), followed by cyclization (guanylation) reaction with concomitant desulfurization (decrease of emission intensity at 510 nm and minor increase at 410 nm; increase and decrease in absorbance intensity at 270 and 325 nm, respectively). In contrast,  $\text{CN}^-$  induced deprotonation in DTS results in simultaneous decrease in absorbance at 310 nm and increase in absorbance at 385 nm and 425–475 nm and fluorescence enhancement at  $\lambda_{\text{em}}$  453 nm. On the addition of  $\text{Hg}(\text{CN})_2$  ion pair, DTS shows apparent effect of both  $\text{Hg}^{2+}$  and  $\text{CN}^-$  ions. The mechanism of interaction of DTS with  $\text{Hg}^{2+}$ ,  $\text{CN}^-$  and  $\text{Hg}(\text{CN})_2$  has been established by detailed  $^1\text{H}$  NMR and ESI-MS studies. DTS in  $\text{CH}_3\text{CN}$  shows flake like morphology which undergoes analyte induced self-assembly to form a bunch of nanorods with  $\text{Hg}^{2+}$ ; segregated nanorods with curly ends with  $\text{CN}^-$  and spherical structures with  $\text{Hg}(\text{CN})_2$  ion pair.

## 1. Introduction

Molecular recognition of toxic metal ions and anions using chromofluorescent methods has received great attention for the past decade because of their involvement in biological, environmental and chemical processes [1,2].  $\text{Hg}^{2+}$  is considered as significant pollutant due to its toxic nature to both animals and plants [3]. The most devastating effect of mercury on aquatic life is due to bacteria mediated conversion of inorganic  $\text{Hg}^{2+}$  into methylmercury (II) which has neurotoxic and neurodegenerative effects on human health [4,5]. The  $\text{Hg}^{2+}$  contamination in water and soil even at low concentrations, can lead to problems in digestive system, central nervous system, brain and kidneys [6–8]. Cyanide is a highly toxic anion as its 0.5–3.5 mg/kg body weight is sufficient to cause death in human due to its strong interaction with a heme unit at the active site of cytochrome C and this, interferes with the oxygen supply in the body [9,10]. In recent years, many different strategies for detection of  $\text{CN}^-$  have been developed in the literature which include hydrogen bonding interactions, metal coordination (due to strong affinity of  $\text{CN}^-$  towards  $\text{Hg}^{2+}$  and  $\text{Cu}^{2+}$  etc.) and nucleophilic addition of  $\text{CN}^-$  towards  $-\text{C}=\text{C}-$ ,  $-\text{C}=\text{N}-$  and  $-\text{C}=\text{O}$  [11–14]. On the other hand, many fluorescent chemosensors that bind  $\text{Hg}^{2+}$  ions

have been developed based on the mechanisms which include  $\text{Hg}^{2+}$ -induced desulfurization followed by guanylation, hydrolysis, ring opening reactions and chelation via S atoms [15–22].

The majority of current literature reports are based on single target of interest such as  $\text{Hg}^{2+}$  or  $\text{CN}^-$  ions [11–22]. However, simultaneous detection of multiple targets such as  $\text{Hg}^{2+}$  and  $\text{CN}^-$  ions using chromofluorescent probe is of prime importance in supramolecular chemistry. In this context, dual chemosensors, which possess two different binding sites, could be used for individual or simultaneous detection of two analytes at the same time independent of each other [23–25]. Dual chemosensors, which show responses for multiple targets at different wavelengths through the modulation of multiple-signaling mechanisms are still in demand [26–30]. Moreover, if the interaction of a specific single or multiple analyte with self-assembled aggregates of dual chemosensor occurs, it would also result in change of microstructural features (morphology) of the aggregates to mark the molecular recognition process [31–33].

Recently, our group produced first report of triple-signaling mechanisms-based 3-in-1 multichannel chemosensor for recognition of  $\text{Cu}^{2+}$ ,  $\text{AcO}^-$  and  $\text{Cu}(\text{OAc})_2$  ion pair [34]; individual and simultaneous detection of  $\text{Cu}^{2+}$  and  $\text{F}^-$  ions [35]. The multi outputs were further

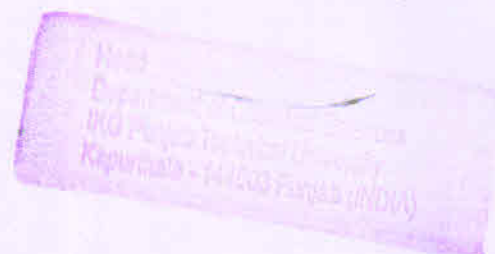
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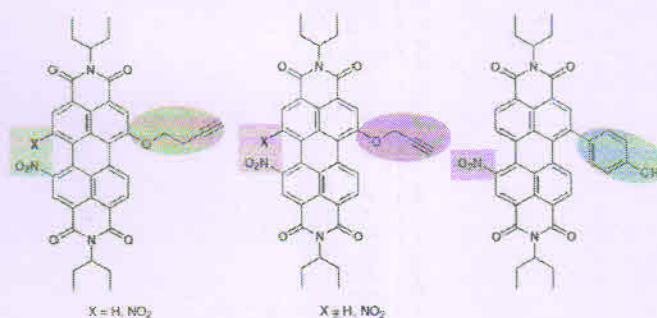
# Dissymmetric Bay-Functionalized Perylenediimides

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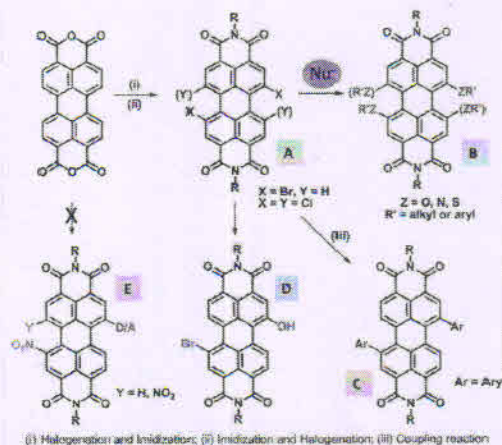
**Abstract** We report the synthesis of perylenediimide (PDI)-based donor-acceptor hybrids through dissymmetric bay functionalization of PDIs. The dissymmetric bay-functionalized di- and trisubstituted PDIs were characterized by using one- and two-dimensional NMR spectroscopy. Density functional theory calculations revealed (i) an energy gap between the HOMO and LUMO in the range 2.14–2.34 eV, beneficial for charge-transfer properties; and (ii) a twist angle between the two naphthalene units in the range 17–26°, which might be beneficial for disruption of co-facial stacking of the PDI.

**Key words** perylenediimide, dissymmetric functionalization, bay functionalization, nitration, density functional theory

Perylenediimide<sup>1–4</sup> (PDI), an important member of the rylene family, is a promising scaffold owing to the prominent features of PDIs such as their excellent optical, chemical, and thermal robustness; high fluorescence quantum yield; high electron mobility; and high molar absorptivity. Moreover, the optical, electronic, and aggregation properties of PDIs can be modified by judicious selection of functional groups at the *N*-imide, *bay*, *ortho*, or *peri* positions of the PDI core.<sup>2–6</sup> Therefore, PDIs have been explored for various applications in the dye and pigment industries<sup>5</sup> and in optoelectronic devices.<sup>6–10</sup> Recently, *bay*- and *N*-terminal-functionalized PDIs have been explored in supramolecular chemistry.<sup>11–17</sup> In this context, PDI-based chromophores with attached donor and acceptor substituents (D–A hybrids) might be potential candidate for use as reaction-based probes for producing long-wavelength-absorbing dyes<sup>18</sup> and in the field of organic photovoltaic devices.<sup>19</sup>

In literature reports, basically, either two (1,7-) or four (1,6,7,12-) positions of the *bay* area of PDIs (**A**, Scheme 1) have been extensively used for homogeneous functionalization through nucleophilic substitution or Suzuki/Sonogas-

hira coupling reactions of di- or tetrahalogenated derivatives in the presence or absence of a catalyst, to attach various aryl or alkyl groups to the PDI core (**B** and **C**; Scheme 1).<sup>1–6</sup> PDIs with two different functional groups in the *bay* positions can be prepared by multiple stepwise substitution reactions of halogenated PDIs, but these syntheses involve cumbersome purification procedures and give the desired product in low to moderate yield (**D**; Scheme 1).<sup>20</sup> Few reports have appeared that discuss halogenated or non-halogenated routes for the synthesis of dissymmetric bay-functionalized di- or trisubstituted PDIs (**E**; Scheme 1). We therefore proposed that PDI-based D–A hybrids might be synthesized by dissymmetric bay functionalization of the PDI core.<sup>21</sup>



**Scheme 1** General approaches for the synthesis of dissymmetric functionalized PDIs reported in the literature





Journal Name

ARTICLE

## AIE+ESIPT based red fluorescent aggregates for visualization of latent fingerprints

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Fluorescent molecules are extensively employed in (bio)sensing and bioimaging but their applications in visualization of fingerprints are less reported due to their inherited aggregation-caused quenching (ACQ) mechanism in solid state (aggregated form). DPSA undergoes self-assembly to form aggregates with rod-like structures in 90% H<sub>2</sub>O:CH<sub>3</sub>CN mixture evident from dynamic light scattering (DLS) and scanning electron microscopic (SEM) techniques. Self-assembled diphenylpyrimidinone derivative (DPSA) shows aggregation-induced emission (~24 fold) in >90% H<sub>2</sub>O:CH<sub>3</sub>CN mixture with orange-red fluorescence ( $\lambda_{\text{max}}$  564 nm). The red fluorescent aggregates of DPSA show applications in visualization of latent fingerprints on aluminium, stainless steel and metal currency coin substrates. In addition, we established the individuality of three subjects based on information gathered at level one (pattern of arch, loop or whorl) and level two (minute details of dots, bifurcation, ridge ending, core and delta).

### Introduction

The papillary ridges and furrows present on fingers and palms offer a unique identity to every individual. The papillary ridges are a fine network of minute ridges formed by skin folding whereas depression between adjacent ridges is known as furrow. These papillary ridges have small apertures at their surface which are connected to sweat glands existing underneath the skin and these glands persistently secrete sweat with 99.5% of its volume being water and rest (0.5%) being organic (mainly consists of sebum) and inorganic substances.<sup>1</sup> However, the sebum content of these papillary ridges is escalated if we make contact of fingers on face, neck and hair follicles. Afterwards, if contact of these sebum rich papillary ridges be made with any surface (aluminium, mica, coins, tiles etc.), it could leave a pattern (mirror image) of fine ridges of fingers on that surface. This pattern of fine ridges is called latent (invisible) fingerprints.

Latent fingerprints (LFPs) collected from crime scenes are considered as very useful evidence in forensic investigations. The routinely used procedures for the visualization of latent fingerprints includes powder dusting<sup>2</sup>, vacuum metal deposition<sup>3</sup>, dye adsorption on nanoparticles<sup>4-6</sup>, quantum dots (QDs)<sup>7</sup> and staining using chemicals such as iodine, ninhydrin and cyanoacrylate<sup>8</sup>. Presently, development of fingerprints

using powder dusting is widely used method in forensic analysis. However, these techniques have limitations such as destruction of LFPs during washing or cleaning of LFP impressed surfaces, high toxicity of used chemicals and low resolution of the developed LFPs. Recently, spectroscopic techniques such as Raman<sup>9,10</sup>, FT-IR<sup>11,12</sup> and mass<sup>13</sup> are also used for visualisation of fingerprints but requirement of heavy instrumentation limits the scope of their use.

In recent years, combination of aggregation induced emission (AIE) and excited state intramolecular proton transfer (ESIPT) mechanisms provided a new paradigm for developing application based fluorescent materials. Both AIE and ESIPT process are important phenomena and the participation of both in a molecule can provide high fluorescence in solid/aggregate state. Therefore, fluorescence based methods involving use of molecules possessing AIE+ESIPT could be more useful for visualisation of LFPs on wet non-porous surfaces. Probably, these hydrophobic aggregates of AIE+ESIPT fluorophores could bind preferentially to the sebum rich papillary ridges of fingerprints by virtue of hydrophobic interactions. On illumination with 365 nm UV lamp, the hydrophobic aggregates would light up and minute details of papillary ridges can be visualised.<sup>14-19</sup> However, this field is still growing and to the best of our knowledge, only few reports are available in the literature<sup>14,20-21</sup>.

In last few years, we explored perylenediimide, peptides and CNTs based self-assembled materials for application in biosensing, bioimaging, molecular computing and catalysis.<sup>14, 23-33</sup>

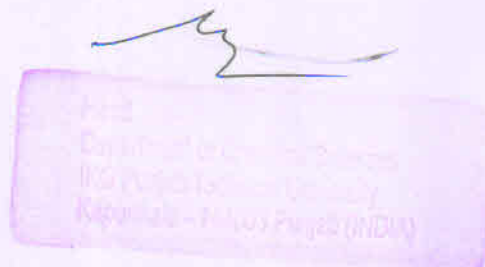
Recently, we have shown that the attachment of salicylideneamine can make the diphenylpyrimidinone (an interesting class of heterocyclic derivative based on pyrimidine nucleobase) be AIE-active, for example, DPPS-1 (Fig. 1). It

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## Multifunctional metallo-supramolecular interlocked hexagonal microstructures for the detection of lead and thiols in water†

Prabhpreet Singh,<sup>a,\*</sup> Lalit Singh Mittal,<sup>a</sup> Kapil Kumar,<sup>b</sup> Poonam Sharma,<sup>a</sup> Gaurav Bhargava<sup>b</sup> and Subodh Kumar<sup>b</sup>

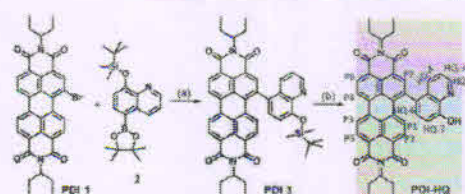
We report  $Pb^{2+}$ -mediated interlocked hexagonal self-assembly associated with the near-IR (660 nm) 'turn-on' detection of  $Pb^{2+}$  ions (LOD = 25 nM) in water using a perylene diimide derivative (PDI-HQ). The PDI-HQ- $Pb^{2+}$  complex was further used to develop a fluorescent NIR ensemble for the detection of thiols.

Metallo-supramolecular self-assembly is a term used to describe metal-mediated self-assembly.<sup>1</sup> In this area, the emphasis is on the design and synthesis of receptors which possess the correct number and spatial arrangement of coordination (donor) sites, whereas the metal ions which are being used as a template must have the correct coordination number and stereochemical preference. This metal-directed self-assembly has led to the development of fascinating architectures of boxes, triangles, grids and helicates.<sup>2,3</sup> The metal-directed self-assembly of bay functionalized perylene diimide (PDI) dyes has been only recently investigated.<sup>4</sup> PDIs and their derivatives have been valued for a long time due to their unique properties and ease of functionalization at the so called bay-, N-terminal-, *ortho*- and *peri*- positions.<sup>5</sup> Current available literature has shown that N-terminal substituted PDIs resulted in the formation of self-assembled nanostructures<sup>6</sup> including fibers, ribbons, rods and tubes. However, the main challenge is to control the self-assembly of bay substituted PDIs and exploration of the molecular recognition properties of these self-assembled PDIs in water.<sup>7–9</sup>

Heavy metal ions ( $Pb^{2+}$ ,  $Hg^{2+}$  and  $Cd^{2+}$ ) have non-degradable nature and possess detrimental effects and become a threat to global sustainability if accumulated in the ecosystem (air, water and soil) over the permissible limits.<sup>10,11</sup> Lead ( $Pb^{2+}$ ) is an environmental pollutant and can cause physical growth impairments, irritability in children and reduced IQ levels<sup>12,13</sup> and can

have adverse effects on human organs. Thiol-containing amino acids such as cysteine (Cys) and homocysteine (HCy) play important roles in biological processes such as protein synthesis, metabolism and growth of cells and tissues. The alteration of Cys levels in living systems can cause hair de-pigmentation, weakness, lethargy, skin lesions and slow growth rates.<sup>14–16</sup> Traditional methods<sup>17,18</sup> involve the usage of ionic solvents, heavy instrumentation, trained operators and lack of portability. Therefore, fluorescence based methods for the detection of  $Pb^{2+}$  ions and thiols are highly demanded.<sup>19</sup>

Herein, we have designed and synthesized PDI-HQ (Scheme 1) and Fig. 1 shows the overall detection strategy of  $Pb^{2+}$  and thiols using PDI-HQ. (1) In an aqueous solution, PDI-HQ forms H-aggregates of diameter 50–160 nm and these aggregates are non-fluorescent due to the combined effect of H-aggregation and PET from the 8-hydroxyquinoline moiety. (2) When the  $Pb^{2+}$  ions are added to the aqueous solution of PDI-HQ, strong interaction between 8-HQ and  $Pb^{2+}$  results in the formation of metallo-supramolecular aggregates having interlocked hexagonal self-assembly with diameter in the range of 0.5–1.7  $\mu$ m and thickness ~250 nm. As a result of binding of  $Pb^{2+}$  with PDI-HQ, the PET process is effectively inhibited and a consequent increase in the fluorescence intensity of aggregated species is observed at 660 nm. (3) When a thiol is added to the PDI-HQ- $Pb^{2+}$  ensemble,



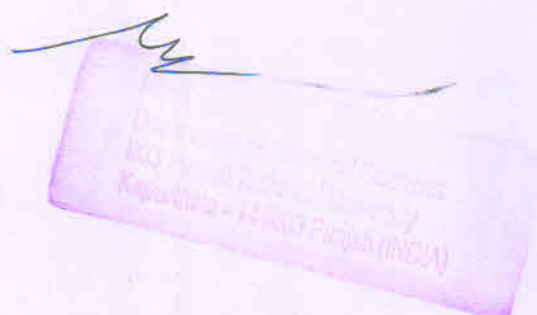
**Scheme 1** Synthesis and chemical structure of PDI-HQ (also showing the arbitrary designation of protons). Reagents and conditions: (a)  $Pd(PPh_3)_4$ ,  $Na_2CO_3$ , Toluene:  $H_2O$  (2:1 v/v), 70 °C, 10 h; (b) 10 M solution of tetrabutylammonium fluoride (TBAF), THF, RT, 24 h.

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† Electronic supplementary information (ESI) available: Synthesis, spectral data, and photophysical data of PDI-HQ with  $Pb^{2+}$  and Cys. See DOI: 10.1039/C8CC05814H





## Organic &amp; Supramolecular Chemistry

**[2+2] Cycloadditions of Sorbyl Tosylate with Imines/1-Azadienes: A One-Pot Domino Approach for  $\alpha$ -Alkylidene- $\beta$ -lactams and Their Computational Studies and Antimicrobial Evaluation**Yogesh Kumar,<sup>[a, b]</sup> Preet Mohinder Singh Bedi,<sup>[c]</sup> Prabhpreet Singh,<sup>[d]</sup> Adebayo A. Adeniyi,<sup>[e]</sup> Ashona Singh-Pillay,<sup>[f]</sup> Parvesh Singh,<sup>[f]</sup> and Gaurav Bhargava<sup>\*,[a]</sup>(Dedicated to Prof. M. P. Mahajan on the occasion of his 71<sup>st</sup> Birthday)

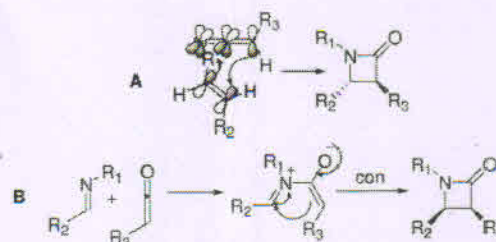
The manuscript describes a straightforward and atom-efficient method for the synthesis of  $\alpha$ -alkylidene- $\beta$ -lactams using sorbyl tosylate and imines/1-azadienes at high temperature (80 °C). The Density functional theory calculations have shown the prevalence of the first order kinetics in these [2+2] cyclo-

additions to produce mixture of 3-butadienyl-azetidin-2-ones and 3-but-2-enylidene-azetidin-2-ones in good yields. The 3-but-2-enylidene-azetidin-2-ones have also shown antimicrobial activity against the *E. coli*, *S. aureus*, *P. aeruginosa*, *B. cereus* and *B. subtilis*.

## Introduction

Ketenes are versatile intermediates in organic synthesis.<sup>[1]</sup> There are numerous reports on synthesis and cycloadditions of functionalized ketenes for the synthesis of heterocyclic systems of biological relevance.<sup>[2–3]</sup> The [2+2] cycloadditions of ketenes with alkenes or iminic systems have widespread been utilized for the synthesis of carbo- and heterocyclic systems respectively.<sup>[3]</sup> There has been significant interest and controversies over the mechanism of ketene-imines cycloadditions. Experimental work as well as theoretical studies have been made on the reactions of the imines with simple ketenes.<sup>[4]</sup> It is well understood that the Staudinger reactions involving [2+2]

cycloadditions of ketene and imines are proceeded via zwitterionic intermediates as shown in the Figure 1.<sup>[5]</sup>



**Figure 1.** (A) Orbital interactions in concerted cycloaddition. (B) Stepwise mechanism. con = conrotatory

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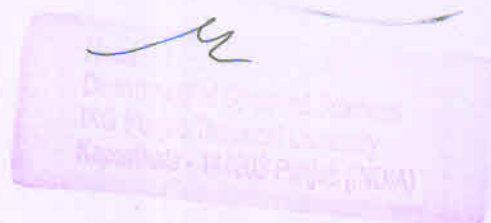
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However, the corresponding studies on [2+2] cycloaddition reactions involving conjugated ketene such as butadienylketene still need to be explored. Earlier Mahajan et. al. have explored the [2+2] and [4+2] cycloaddition reactions of butadienylketene generated *in situ* from sorbyl chloride and triethylamine, with imines and 1,3-diazabuta-1,3-dienes respectively.<sup>[6]</sup> The reaction resulted in the formation of *cis*- and *trans*-butadienyl-azetidin-2-ones. However, studies on cycloaddition reactions involving butadienylketene with iminic systems at high temperature and using alternative methods for *in situ* generation of butadienylketene still need to be studied. On the other hand,  $\alpha$ -alkylidene- $\beta$ -lactams are known structural units found in several potent  $\beta$ -lactamase inhibitors such as Ro 15-1903, asprenomycins, 6-(2'-pyridyl)methylene penem sulfone,







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## Coronene diimide-based self-assembled (fibre-to-disc) fluorescent aggregates for visualization of latent fingerprints

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Powder dusting  
Biotabling

### ABSTRACT

Coronenediimide (CDI 3) forms long fibrillar nanostructure when dissolved in DMF. On addition of > 70% water in DMF, CDI 3 undergo fibre-to-disc morphological transformation alongside onset of different emission colors in water-DMF binary mixtures. These self-assembled red emitting aggregates of CDI 3 applied for visualization of latent fingerprints using solution spray and powder dusting methods on porous and non-porous surfaces commonly found in home such as aluminium, stainless steel, glass, metal coins, compact discs (CDs), OHP films, ceramic tiles and paper sheets. In an attempt to explore the application of CDI 3 in the forensic cases, 2<sup>nd</sup> level of information was used for distinguishing different fingerprints from different subjects. These disc-like fluorescent red aggregates of CDI 3 were also used for staining of HeLa cells.

### 1. Introduction

Many  $\pi$ -conjugated molecules with extended polycyclic framework have been developed by research groups [1–4]. Among them, coronene diimides (CDIs), [5] which can be considered as bay-extended perylene diimides (PDIs), [3–4] have gained interest due to their excellent thermal and oxidative stabilities, high molar extinction coefficient, fluorescence quantum yields and self-organization properties [6–13]. The benzene and heterocycle ring annulation at the bay-region of the perylene core leads to coronenediimide derivatives which offers applications in optoelectronics such as organic field effect transistors (OFETs), fluorescent solar collectors, organic light emitting diodes (OLEDs) and optical lasers [6–13]. Despite many synthetic efforts of modification in CDIs, little progress has been made in making CDIs water soluble [1–2] and preserving its fluorescence (far-red to near-infrared region) [1–2] in solid and solution state for application in the fields of designing AIEgens, visualization of latent fingerprints and biotabling.

Latent (invisible) finger prints (LFPs), which are made up of papillary ridges and furrows present on fingers and palm offer a unique identity to each individual [14–15]. Such LFPs collected from crime scenes are considered as useful physical evidence and cornerstone to

identify individuals. Currently, powder dusting method, quantum dots, nanoparticles and chemical methods were applied in visualization of LFPs, however potential toxicity and destructive nature, short preservation time, low resolution and expensive procedures limit their wider applications [16–17].

In continuation of our interest in PDIs, [18–27] herein, we report CDI 2 and CDI 3 as new additions in the rylene family. Due to onset of aggregation of molecules of CDI 3 with increasing water fraction ( $f_w$ ), the nano-fibres of CDI 3 in DMF are eventually transformed into disc-like aggregates in > 70% water-DMF mixtures. These disc-like aggregates of CDI 3 both in water-dispersed and solid-state are fluorescent red and were used for visualization of LFPs imprinted on common household items and for staining HeLa cells.

### 2. Experimental section

#### 2.1. Materials and methods

Chemicals and solvents were of reagent grade and used without further purification unless otherwise stated. Chromatographic purification was done with silica gel 60–120 mesh. TLC was performed on aluminium sheets coated with silica gel 60 F254 (Merck, Darmstadt).

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## REVIEW



## Transition metal catalyzed [6 + 2] cycloadditions

Amit Anand,<sup>a</sup> Prabhpreet Singh,<sup>b</sup> Vipin Kumar<sup>ab</sup> and Gaurav Bhargava<sup>ac</sup>Cite this: *RSC Adv.*, 2019, 9, 25554Received 15th April 2019  
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## Introduction

Cycloaddition reactions are considered to be one of the most powerful methods for the construction of cyclic skeletons<sup>1</sup> with atom economy. There are ample reports on different variants of [4 + 2] and [3 + 2] cycloadditions which provide an easy access to a variety of five or six membered carbo-/heterocycles.<sup>2,3</sup> However, the parallel methodologies such as [5 + 2],<sup>4</sup> [6 + 2],<sup>5</sup> [8 + 2]<sup>6</sup> etc. for the synthesis of seven, eight or ten membered carbo-/heterocycles are still uncommon in the literature. Eight-membered rings are found in a wide variety of natural products and are useful ring systems available in variety of drugs, drug leads, or biological probes.<sup>6</sup> Taxol, the well-known natural product in this family, is now among the most potent anticancer drug in clinical use. In 2008, another member of this family, pleuromutilin was approved for use as an antibiotic by Food and Drug Administration (FDA)<sup>7</sup> (Fig. 1). Several methods<sup>8–12</sup> including ring-closing metathesis and Cope rearrangement have been reported for the synthesis of eight-membered carbocycles.<sup>13</sup> However, the intolerance to substrate substituent in conventional procedures along with complexities observed in natural products makes these techniques ineffective and instigated the development of alternate protocols. Recent years have seen a significant upsurge in this direction with relatively few reports appearing on the synthesis of eight membered carbocycles using [6 + 2]<sup>14</sup> and [4 + 2 + 2]<sup>15</sup> cycloaddition reactions. Concerted [6 + 2] cycloaddition reactions are forbidden thermally as per Woodward–Hoffmann rules, when the two reacting  $\pi$ -systems add in a suprafacial fashion. However, transition metal-catalyzed [6 + 2] cycloadditions constitute one such

protocol for the synthesis of monocyclic or condensed functionalized cyclooctadienes. The present review summarizes various reports on the transition metal catalyzed inter- and intra-molecular [6 + 2] cycloaddition reactions appeared in literature since 2000.<sup>14</sup>

## Rhodium catalyzed [6 + 2] cycloadditions

Rhodium complexes plays a pivotal role in organic synthesis as major catalytic contributors to C–C bond formation reactions.<sup>16</sup> A number of carbo-/heterocyclic systems have been generated employing rhodium complexes as efficient catalyst in a variety of cycloaddition/cyclization reaction<sup>16</sup>. Literature rationale suggests an inspiring advancement in this field and many research groups are extensively using rhodium complexes to efficiently conceive these reactions.<sup>17</sup> Considering the importance of rhodium catalysed cycloadditions, there should have been a number of reports on generation of eight membered carbo-/heterocycles engaging rhodium complexes in [6 + 2] cycloadditions, however only a few reports are available which successfully comprehends [6 + 2] cycloadditions. Till now, different substrates such as cycloheptatriene, 2-vinylcyclobutanones, allenals, allenylcyclobutanes, cyclooctatrienes etc. have been reported as 6 $\pi$ -components in Rh(I) catalysed [6 +



Fig. 1 Carbocycles in natural products.

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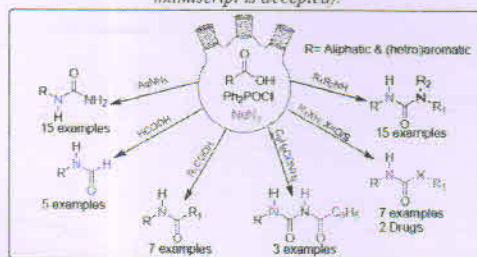
# Direct Conversion of Carboxylic Acids to Various Nitrogen Containing Compounds in One-Pot Exploiting Curtius Rearrangement

Arun Kumar<sup>1</sup>, Naveen Kumar<sup>1</sup>, Ritika Sharma<sup>2</sup>, Gaurav Bhargava<sup>2</sup> and Dinesh Mahajan<sup>1\*</sup>

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<sup>2</sup>Department of Chemical Sciences, I. K. Gujral Punjab Technical University, Kapurthala, Punjab-144603, India

RECEIVED DATE (will be automatically inserted after manuscript is accepted).



**ABSTRACT:** Herein we report, a single pot multi-step conversion of inactivated carboxylic acids to various N-containing compounds using a common synthetic methodology. The developed methodology rendered the use of carboxylic acids as direct surrogate of primary amines, for the synthesis of primary ureas, secondary/tertiary ureas, O/S-carbamates, benzoyl ureas, amides and N-formyls, exploiting Curtius reaction. This approach has a potential to provide a diversified library of N-containing compounds starting from a single carboxylic acid, based on selection of the nucleophile.

Nitrogen containing compounds such as amines, amides, ureas, acyl ureas, and carbamates are ubiquitous in natural products, agrochemicals as well as pharmaceutical agents or molecules of biological and commercial interests. Hence, synthesis of these various N-containing compounds is an important objective in organic synthesis. Carboxylic acids are favorable substrates because of their broad structural diversity, ease in availability, high stability, low toxicity along with ease in storage and handling.<sup>1</sup> Curtius rearrangement of acyl azides is a powerful method for construction of a new C-N (sp<sup>2</sup>C-N or sp<sup>3</sup>C-N) bond using azide as a source of nitrogen and carboxylic acid as source of carbon.<sup>2</sup> The conversion of carboxylic acids to nitrogen containing compounds, avoiding use of any organic amine as a primary source of nitrogen is very alluring. In a typical Curtius reaction, an acyl azide is thermally degraded to rearrange as an isocyanate.<sup>3</sup> The acyl azide is often synthesized in a different pot as a separate step from a pre-activated carboxylic acid and sodium azide.<sup>2-4</sup> The isocyanate thus formed can be reacted with water, alcohol or amine as one of the nucleophile to yield corresponding amine, carbamate or urea as a final product. This makes whole process multi-pot and practically cumbersome, if one aims for conversion of carboxylic acids to N-containing compounds. One pot multi-step conversion provides an effective approach

to infuse economic and environmental efficiencies because several synthetic transformations and bond-forming steps can be carried out in a single pot.<sup>5</sup> Yamada et al.,<sup>6</sup> reported the first one-pot conversion of inactivated carboxylic acids to urethanes involving Curtius reaction using DPPA (diphenyl phosphoric azide). The generation of DPPA needs an additional step in a different pot involving sodium azide and diphenyl phosphoryl chloride.<sup>7</sup> Recently, Lebel et al.<sup>8</sup> reported one-pot conversion of carboxylic acids employing either chloroformate or di-*tert*-butyl dicarbonate along with sodium azide as a replacement of DPPA. However, these methodologies are confined to conversion of carboxylic acids to corresponding amines, ureas or carbamates only.

Herein, we want to report a direct, multi-step, single pot conversion of carboxylic acids to corresponding primary ureas, mixed ureas (secondary/tertiary), O-carbamates, S-carbamates, acyl ureas, N-formyls and amides exploiting a single methodology.

Initial optimization efforts were focused on conversion of benzoic acid to corresponding 1-phenylurea (Table 1). Primary ureas are not only found to be bioactive molecules but they also serve as starting materials for molecules of biological and commercial interests.<sup>9</sup> Often, primary ureas are synthesized from corresponding organic amines and ammonia involving phosgene, carbamoyl chloride or isocyanates.<sup>9</sup> Interestingly, there is no report for direct conversion of carboxylic acids to corresponding primary ureas in one pot. This instigated us to start our optimization efforts for synthesis of 1-phenylurea (1b), as a model reaction from corresponding benzoic acid (1). In a typical procedure, benzoic acid was mixed with DPPA (entry 1, Table 1) at 0°C, using toluene as a solvent. An equivalent amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was added and reaction was stirred for 30 minutes at room temperature to facilitate the formation of acyl azide. The conversion of the acyl azide was monitored as well as quantified, before heating the reaction to 90°C. Aqueous ammonium hydroxide was added to this heated solution and reaction was monitored by TLC and <sup>1</sup>H NMR for the formation of 1-phenylurea as a final product. Use of DPPA as a reagent of choice provided 32% isolated yield of 1-phenylurea, albeit corresponding benzoyl azide intermediate was formed in reasonably good amount (Entry 1, Table 1). DPPA is a commercial grade reagent which is generally obtained by vacuum distillation of the crude product obtained after a reaction of diphenyl phosphoryl chloride with sodium azide.<sup>7</sup> We tried to replace DPPA by *in situ* use of diphenyl phosphoryl chloride and sodium azide (entry 2). The reaction of benzoic acid was repeated and replacement of DPPA was compensated by *in situ* addition of diphenyl phosphoryl chloride, sodium azide (as a solution in dry DMF) and catalytic amount of DMAP. In new reaction involving sodium azide, the conversion to corresponding benzoyl azide was less, however it was pleased to see similar isolated yield for final product 1b (entry 2 vs entry 1). As clear from data tabulated in table 1, a quick screening of few other similar reagents concluded, diphenyl phosphinic chloride (Ph<sub>2</sub>POCl) as a reagent of choice for better yields of benzoyl azide as well as 1-phenylurea (entry 3). Decent success in overall conversion with methanesulfonyl chloride (entry 5) and reaction feasibility with POCl<sub>3</sub> (entry 4) needs special mention as these two are common reagents in organic chemistry laboratories. Ammonium chloride or ammonium formate (entry 6 and 7) were also found to be two other potential sources of ammonia for the desired conversion. Influenced by the outcome of this





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## Transition metal catalyzed [6 + 2] cycloadditions

Amit Anand,<sup>a</sup> Prabhpreet Singh,<sup>b</sup> Vipin Kumar<sup>c,\*</sup> and Gaurav Bhargava<sup>c,\*</sup>

The [6 + 2] cycloaddition reactions are one of the important synthetic transformations to construct eight membered carbo-/heterocyclic systems. The present review is an attempt to update readers on transition metal catalyzed [6 + 2] cycloaddition reactions of various 6 $\pi$ -contributing substrates such as cycloheptatrienes (CHT), cyclooctatetraenes (COT), allenals, vinylcyclobutanones, fulvene etc. employing rhodium, cobalt, titanium, copper, platinum, ruthenium, rhenium and diphenylprolinolsilyl ethers etc. as catalysts. The transition metal catalyzed [6 + 2] cycloaddition reactions with a variety of functionalized substrates provide straightforward access to eight membered cyclic and/or 5/8, 6/8 etc. condensed carbo-/heterocyclic molecules in moderate to good yields.

## Introduction

Cycloaddition reactions are considered to be one of the most powerful methods for the construction of cyclic skeletons<sup>1</sup> with atom economy. There are ample reports on different variants of [4 + 2] and [3 + 2] cycloadditions which provide an easy access to a variety of five or six membered carbo-/heterocycles.<sup>2,3</sup> However, the parallel methodologies such as [5 + 2],<sup>4</sup> [6 + 2],<sup>5</sup> [8 + 2]<sup>6</sup> etc. for the synthesis of seven, eight or ten membered carbo-/heterocycles are still uncommon in the literature. Eight-membered rings are found in a wide variety of natural products and are useful ring systems available in variety of drugs, drug leads, or biological probes.<sup>6</sup> Taxol, the well-known natural product in this family, is now among the most potent anticancer drug in clinical use. In 2008, another member of this family, pleuromutilin was approved for use as an antibiotic by Food and Drug Administration (FDA)<sup>7</sup> (Fig. 1). Several methods<sup>8–12</sup> including ring-closing metathesis and Cope rearrangement have been reported for the synthesis of eight-membered carbocycles.<sup>13</sup> However, the intolerance to substrate substituent in conventional procedures along with complexities observed in natural products makes these techniques ineffective and instigated the development of alternate protocols. Recent years have seen a significant upsurge in this direction with relatively few reports appearing on the synthesis of eight membered carbocycles using [6 + 2]<sup>14</sup> and [4 + 2 + 2]<sup>15</sup> cycloaddition reactions. Concerted [6 + 2] cycloaddition reactions are forbidden thermally as per Woodward–Hoffmann rules, when the two reacting  $\pi$ -systems add in a suprafacial fashion. However, transition metal-catalyzed [6 + 2] cycloadditions constitute one such

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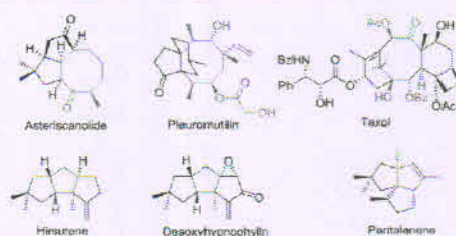


Fig. 1 Carbocycles in natural products.

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## Perylene diimide–Cu<sup>2+</sup> based fluorescent nanoparticles for the detection of spermine in clinical and food samples: a step toward the development of a diagnostic kit as a POCT tool for spermine†

Kapil Kumar,<sup>a</sup> Sandeep Kaur,<sup>b</sup> Satwinderjeet Kaur,<sup>b</sup> Gaurav Bhargava,<sup>c</sup> Subodh Kumar<sup>b</sup> and Prabhpreet Singh<sup>b,\*</sup>

The sustainable development of point-of-care testing (POCT) for spermine detection is important to check for food spoilage, early diagnosis of various malignancies and diminished anticonvulsant drug carbamazepine response in chronic epilepsy. Herein, the synthesis, characterization and spectroscopic properties of perylene diimide EA-PDI/Cu<sup>2+</sup> complex based nanoparticles towards spermine were studied in detail. This EA-PDI/Cu<sup>2+</sup> complex can be used for the ultrasensitive detection of spermine as low as 86.3 nM (UV-vis) and 90 pM (fluorescence) in aqueous medium, in urine and blood serum samples (recovery 99 ± 3) and in the solid state (0.1 µg L<sup>-1</sup>), and EA-PDI shows minimal cytotoxicity to cells and can easily enter into Human Osteosarcoma MG-63 cells for bio-imaging of Cu<sup>2+</sup> and spermine. This EA-PDI/Cu<sup>2+</sup> complex can be established as a cost-effective method to develop a diagnostic kit for POCT of spermine in terms of a solution-based test kit for real time detection of spermine in vapor and solution form released from fermented food samples.

## Introduction

Supramolecular synthetic receptors having molecular bio-recognition properties are important in biology for monitoring enzymatic activity, signaling and regulation.<sup>1,2</sup> In this context, perylene diimide (PDI),<sup>3,4</sup> which was first synthesized in 1913 by Kardos<sup>5</sup> as an industrial colorant, is now-a-days attracting increasing research attention as a key chromophore for applications in the field of fluorescent sensors and bio-imaging<sup>6–12</sup> besides its application in organic electronic devices.<sup>13,14</sup> The wide spread applications of PDIs may be attributed to their strong absorption and fluorescence properties, and chemical, thermal and photochemical stability. One of the main obstacles in exploring PDIs for sensing applications seems to be poor solubility, however their optical properties and solubility can be readily tuned through functionalization at the bay-, N-terminal-,

ortho- and peri-positions.<sup>3,4,15</sup> To circumvent the solubility issues, ionic PDIs were studied as fluorescent sensors, whereas to achieve sensing properties using neutral PDI derivatives in > 50% water is still a challenging task.<sup>6–12</sup>

Biogenic polyamines such as putrescine, spermidine and spermine, essentially found in all eukaryotic cells, play many crucial roles in cellular growth and proliferation, transcription, translation and modulation of gene expression.<sup>16,17</sup> Spermine detection in biofluids such as urine and blood serum is clinically used for diagnosis of early stages of various types of malignancies, to determine the efficiency of long term cancer chemotherapy and to check the development of anticonvulsant carbamazepine (CBZ)-resistant Na<sup>+</sup> currents in chronic epilepsy.<sup>18,19</sup> Biogenic polyamines have also been produced as a physiological component in many protein rich food products by microbial proteolysis followed by decarboxylation of amino acids.<sup>20,21</sup> They can lead to production of nitrosoamines in meat products by reacting with nitrites<sup>22</sup> and high levels of biogenic amines in spoiled food can cause headaches, nausea and changes in blood pressure.<sup>21</sup> Therefore, the detection of spermine has become highly paramount as it is directly linked with food safety and human health.

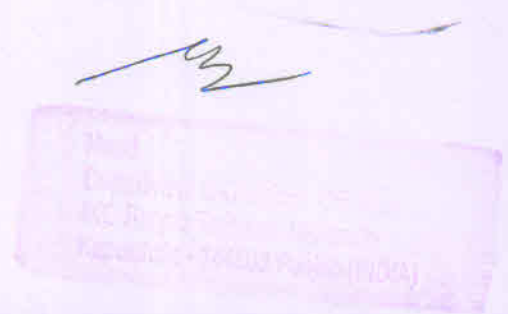
Now-a-days, point of care testing (POCT), which involves diagnostic testing at the time and place of patient care, is in

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c9tb02039j





**Near-IR discriminative detection of H<sub>2</sub>S and Cysteine with 7-nitro-2,1,3-benzoxadiazole-perylenediimide conjugate in water, live cells and solid state: Mimicking IMP, INH and NOR/OR complimentary logic**

Poonam Sharma,<sup>a</sup> Kapil Kumar,<sup>a</sup> Sandeep Kaur,<sup>b</sup> Satwinderjeet Kaur,<sup>b</sup> Gaurav Bhargava,<sup>c</sup> Subodh Kumar<sup>a</sup> and Prabhpreet Singh,<sup>\*a</sup>

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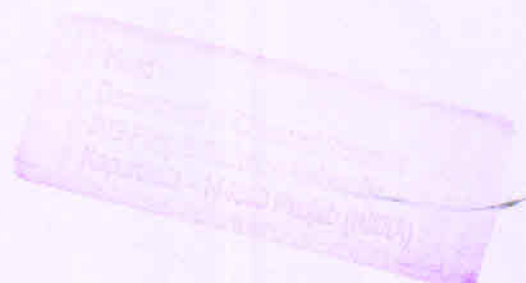
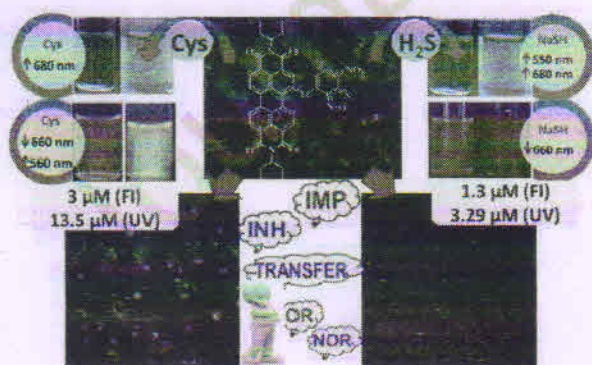
<sup>c</sup>Department of Chemical Sciences, IK Gujral Punjab Technical University, Kapurthala-144601, Punjab, India.

\*Corresponding author. Tel: +91-84271-01534

Email: prabhpreet.chem@gndu.ac.in;

**Graphical abstract**

Near-IR ratiometric chromo-fluorescent probe for detection of H<sub>2</sub>S and Cys was developed based on differential optical response in water and live cells.





# A multifunctional perylenediimide-based dual-analyte chemodosimeter for specific and rapid detection of H<sub>2</sub>S and Pd<sup>0</sup> in water, biofluids, live cells and solid state

Kapil Kumar<sup>a</sup>, Sandeep Kaur<sup>b</sup>, Satwinderjeet Kaur<sup>b</sup>, Gaurav Bhargava<sup>c</sup>, Subodh Kumar<sup>a</sup>, Prabhpreet Singh<sup>a\*</sup>

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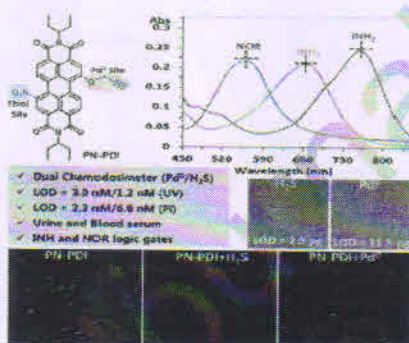
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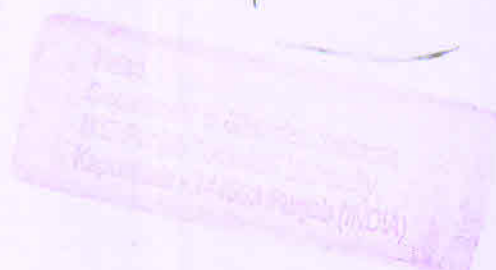
## Graphical abstract

A fast-responsive, near-IR colorimetric fluorescent chemodosimeter for individual and simultaneous detection of H<sub>2</sub>S and Pd<sup>0</sup> at nanomolar level in water, biofluids and A549 cells is reported.



## Highlights

- A novel perylenediimide-based dual-analyte chemodosimeter PN-PDI have been synthesized.





## Rhodium-catalysed chemo- and regio-selective [3 + 2 + 2] cycloadditions of bis(methylenecyclopropanes) and alkynes: Synthesis of spirocyclic 5–7 condensed cycloheptenes

Bilash Kuila<sup>a</sup>, Priyanka Sharma<sup>a</sup>, Dinesh Mahajan<sup>b</sup>, Prabhpreet Singh<sup>c</sup>, and Gaurav Bhargava<sup>a</sup>

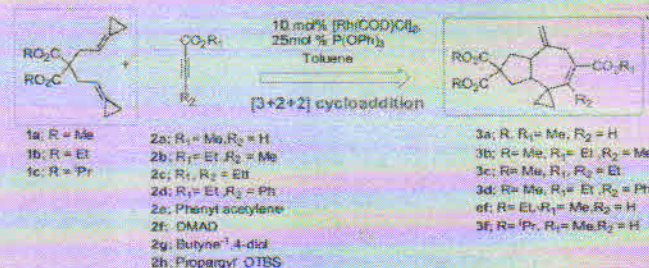
<sup>a</sup>Department of Chemical Sciences, I. K. Gujral Punjab Technical University, Kapurthala, India; <sup>b</sup>Drug Discovery Research Center, Translational Health Science and Technology Institute, Faridabad, India;

<sup>c</sup>Department of Chemistry, Guru Nanak Dev University, Amritsar, India

### ABSTRACT

Rhodium-catalyzed intermolecular [3 + 2 + 2] cycloaddition reactions of bis(methylenecyclopropanes) with different alkynes are described. The rhodium-catalyzed [3 + 2 + 2] cycloadditions resulted in the formation of functionalized 5–7 spirocyclic carbocycles in moderate yields with excellent regio- and chemo-selectivity.

### GRAPHICAL ABSTRACT



### ARTICLE HISTORY



Received 10 October 2019

### KEYWORDS

[3 + 2 + 2] Cycloadditions; [Rh(COD)Cl]<sub>2</sub>; bis(methylene-cyclopropanes); multicomponent reaction; spirocyclic cycloheptenes

### Introduction

Transition metal-catalyzed cycloaddition reactions are one of the few sustainable methods which lead to synthesis of complex molecules with high atom economy exploiting simple synthetic precursors.<sup>1,2</sup> The two-component cycloadditions such as [4 + 2] or [3 + 2] transformations are synthetically most explored reactions for the synthesis of six and five-membered carbo-/heterocycles.<sup>3–5</sup> Contrary to this, synthesis of higher-membered carbo-/heterocycles using [m + n + o] cycloadditions still is infancy and needs the attention of synthetic chemists.<sup>6–8</sup> The [3 + 2 + 2] cycloadditions of functionalized methylenecyclopropanes and alkenes and/or alkynes provide an easy access to functionalized cycloheptanes and their analogs.<sup>9–11</sup> Functionalized cycloheptanes are key structural

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8, 125

## Self-assembled nanofibers of perylene diimide for the detection of hypochlorite in water, bio-fluids and solid-state: exogenous and endogenous bioimaging of hypochlorite in cells†

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Subodh Kumar<sup>a</sup> and Prabhpreet Singh<sup>a,\*</sup>

A fluorescent probe **PDI-DAMN** based on perylene diimide containing diaminomaleonitrile at the bay-position was designed and synthesized for the detection of  $\text{ClO}^-$ . **PDI-DAMN** self-assembled as nanofibers with diameters in the range of 100–200 nm in  $\text{H}_2\text{O}:\text{CH}_3\text{CN}$  (1:1). The addition of  $\text{ClO}^-$  into **PDI-DAMN** resulted in the disintegration of nanofibers into flake-like aggregates of smaller size (50–80 nm) as supported by SEM and DLS data. The addition of  $\text{ClO}^-$  to HEPES buffer– $\text{CH}_3\text{CN}$  solution (1:1 v/v, pH 7.4) of **PDI-DAMN** caused a hypochromic effect on the ICT band at 528 nm and ‘turn-on’ fluorescence enhancement at 508/554 nm due to the oxidative cleavage of  $-\text{C}=\text{N}-$  bond. A linear correlation plot between the concentration of  $\text{ClO}^-$  versus fluorescence intensity ( $R^2 = 0.9968$ )/absorbance ( $R^2 = 0.9988$ ) in the concentration range 0–7 nM (fluorescence)/0–90 nM (absorbance) could determine  $\text{ClO}^-$  with the detection limits of 1 and 10 nM, respectively. Optical studies performed on spiked urine and blood serum samples showed good estimation and recovery of  $\text{ClO}^-$  (100  $\pm$  5%). TLC-based test-strips coated with **PDI-DAMN** changed colour upon the addition of  $\text{ClO}^-$  with detection as low as 7.44 ng  $\text{cm}^{-2}$ . The application of **PDI-DAMN** for the bio-imaging of both exogenous and endogenous  $\text{ClO}^-$  in MG-63 cells with good biocompatibility has also been demonstrated. The detailed mechanism of the interactions of  $\text{ClO}^-$  with **PDI-DAMN** using  $^1\text{H}$  NMR titration, DFT studies and response mechanism of pH are also discussed.

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### 1. Introduction

Hypochlorous ( $\text{HOCl}$ ) or hypochlorite ( $\text{ClO}^-$ ; conjugate base), besides being a bioactive molecule, is an important reactive oxygen species (ROS), which can be endogenously generated by the reaction of  $\text{H}_2\text{O}_2$  and chloride ion catalyzed by myeloperoxidase (MPO) enzyme in leukocytes.<sup>1</sup> Hypochlorous acid helps the human immune system by killing the invading bacteria and pathogens.<sup>2</sup> At physiological pH,  $\text{HOCl}$  could partially dissociate to hypochlorite ( $\text{ClO}^-$ ) in water and can be used as a bleaching agent and as a disinfectant for drinking water.<sup>3</sup> The uncontrolled level of hypochlorous acid (oxidative agent) can lead to the oxidation of proteins, cholesterol, DNA and RNA in living

cells, resulting in pathological diseases such as atherosclerosis, cardiovascular disease, osteoarthritis, cystic fibrosis cancers and pulmonary lesions.<sup>4</sup> Therefore, real-time direct visualization or *in situ* cellular imaging of  $\text{ClO}^-$  in a living system is highly desirable to better understand its role in the biological system.

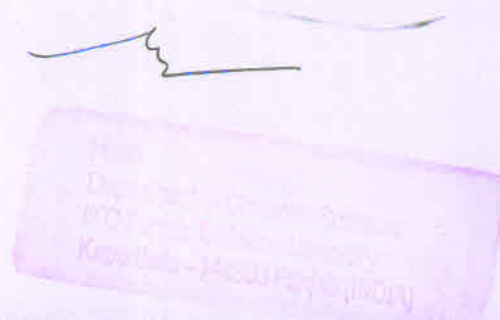
Many detection techniques such as electrochemical, electron paramagnetic resonance (EPR),<sup>5</sup> chromatographic methods,<sup>6</sup> and chemiluminescence,<sup>7</sup> are available in the literature. However, fluorescence and colorimetry-based methods offer several advantages in comparison to other analytical techniques such as non-destructive nature, sensitivity, selectivity, chemical modification and spatiotemporal resolution in living cells. In recent years, many fluorescent probes have been designed for the detection of  $\text{ClO}^-$  with an underlying mechanism involving the oxidation of oxime,<sup>8</sup> acyl nitroso group,<sup>9</sup> *p*-methoxyphenol,<sup>10</sup> selenide,<sup>11</sup> arylboronate,<sup>12</sup> thioester/thioether<sup>13</sup> and  $-\text{C}=\text{N}-$  bond.<sup>14</sup> In this context, fluorescent probes based on a red-to-NIR dye such as cyanine,<sup>15</sup> rhodamine,<sup>16</sup> BODIPY,<sup>17</sup> porphyrin<sup>18</sup> have been reported. However, their use is often limited due to fast photobleaching, low quantum yield, interference from other ROS, incompetency in detecting of  $\text{ClO}^-$  in

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c9tb01902b





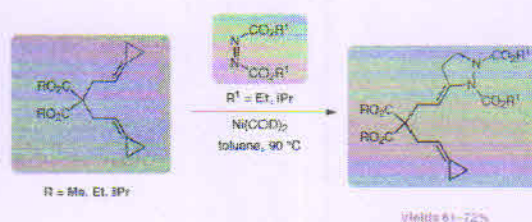
# Nickel(0)-Catalyzed [3+2] Cycloadditions of Bis(alkylidenecyclopropanes) with Diazenes: A Facile Synthesis of Functionalized Pyrazolidine-1,2-dicarboxylates

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**Abstract** A nickel(0)-catalyzed intermolecular [3+2] cycloaddition of bis(alkylidenecyclopropanes) with diazenes such as diethyl or diisopropyl azodicarboxylate gave pyrazolidine-1,2-dicarboxylates in moderate to good yields (61–72%).

**Keywords** bis(alkylidenecyclopropanes), diazenes, pyrazolidine-1,2-dicarboxylates, [3+2] cycloaddition, nickel catalysis

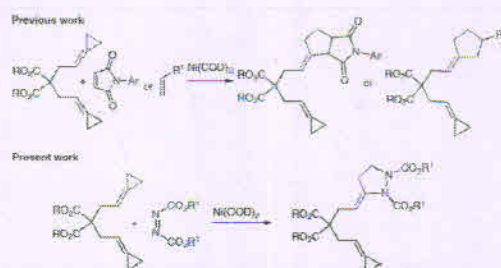
Metal-catalyzed  $[m+n]$  cycloaddition reactions are effective tools for the synthesis of carbo- and heterocyclic systems.<sup>1</sup> Functionalized cyclopropanes have been exploited in metal-catalyzed  $[m+n]$  cycloadditions for the synthesis of monocyclic or condensed carbocycles.<sup>2–4</sup> There are also reports on cycloadditions of activated cyclopropanes with heterodienophiles for the synthesis of monocyclic or condensed carbo- and heterocycles.<sup>2–4</sup> De Meijere and co-workers explored the Lewis acid-catalyzed [3+2] cycloadditions of 2-arylcylopropane-1,1-dicarboxylates with diazenes to afford functionalized pyrazolidines.<sup>5</sup> However,  $[m+n]$  cycloadditions of functionalized nonactivated cyclopropanes, especially with heterodienophiles, have rarely been reported in the literature.<sup>2c,4,6,7</sup>

Pyrazolidines have been evaluated as antibacterial, antifungal, anticancer, antidepressant, antiinflammatory, antituberculosis, antioxidant, and antiviral agents in various pharmacological studies.<sup>8</sup> Several pyrazolidine-based drugs have been marketed, including the antiinflammatory drug celecoxib, rimonabant for the treatment of obesity, fomepizole as an effective alcohol dehydrogenase inhibitor, and sildenafil as a phosphodiesterase inhibitor.<sup>9</sup> Pyrazolidines are also useful as chiral auxiliaries and as synthetic re-

agents in multicomponent reactions.<sup>10</sup> In addition, natural products containing pyrazolidine moieties have been shown to have pharmacological properties.<sup>11</sup>

Conventional approaches, such as the condensation of 1,3-dicarbonyl compounds with hydrazines or [3+2] cycloadditions of 1,3-dipoles have been used in syntheses of simple pyrazolidines.<sup>12</sup> However, there are few reports on synthesis of functionalized pyrazolidines. Chaudhry et al. recently reported acid-catalyzed cyclizations using allylic hydrazines for the synthesis of pyrazolidines.<sup>13</sup>

In view of these results and our ongoing interest in the cycloaddition chemistry of functionalized cyclopropanes, we wish to report an extension of our nickel(0)-catalyzed [3+2]-cycloadditions of bis(alkylidenecyclopropanes) to the preparation of pyrazolidines by using diazenes (Scheme 1).<sup>7</sup>



**Scheme 1** [3+2]-Cycloadditions of bis(alkylidenecyclopropanes)

In the present work, we examined the [3+2] cycloadditions of bis(alkylidenecyclopropanes) with diazenes such as diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD) as dienophiles (Scheme 1). The reaction



## 3-Butadienyl- $\beta$ -lactams: A useful synthon for functionalized heterocycles

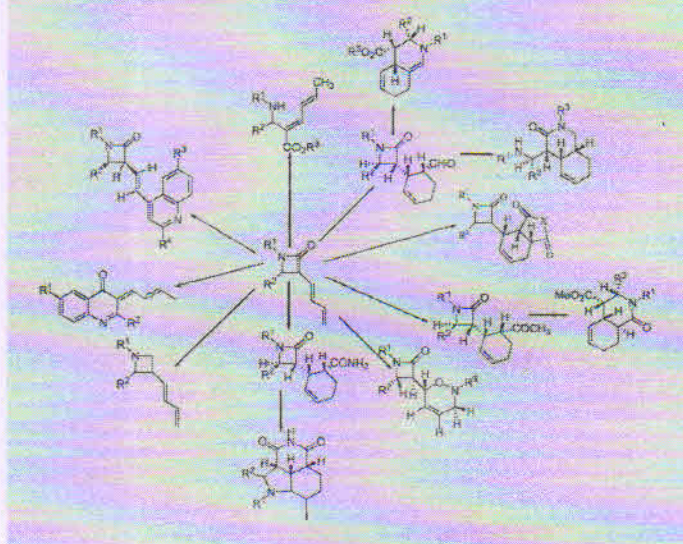
Gaurav Bhargava, Maninderjeet K. Mann, and Rayees Ahmad Naikoo

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### ABSTRACT

3-Butadienyl- $\beta$ -lactams are useful organic synthon which have efficiently been explored for the synthesis of a variety of heterocyclic systems. The present review compiles the various reports on the synthesis of 3-butadienyl- $\beta$ -lactams and their explorations in the development of variety of monocyclic as well as condensed heterocyclic systems.

### GRAPHICAL ABSTRACT



### ARTICLE HISTORY



Received 6 July 2020

### KEYWORDS

amidic bond hydrolysis;  
Diényl- $\beta$ -Lactam; cycloadditions;  
 $\beta$ -lactams;  $\beta$ -lactam  
synthon methodology

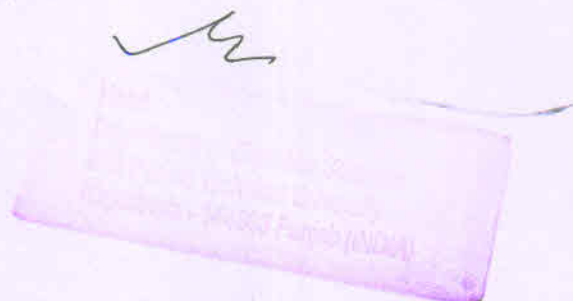
### Introduction

$\beta$ -Lactams are versatile synthons in organic synthesis.<sup>[1–5]</sup> Functionalized lactams have also been explored as important pharmacophore having plethora of biological applications<sup>[1–10]</sup>  $\beta$ -lactam based antibiotics, such as penicillins, cephalosporins, carbapenems, nocardicins, monobactams, clavulanic acid are used therapeutically for controlling

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Dedicated to Professor M. P. Mahajan for his work on 3-butadienyl- $\beta$ -lactams

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## 7-Endo-trig Pictet–Spengler type cyclization of 5-alkylidene/arylidene-amino-3H-pyrimidin-4-ones: An efficient and diastereoselective synthesis of pyrimido[4,5-b][1,4]benzodiazepines

Rayees Ahmad Naikoo<sup>a</sup>, Rupesh Kumar<sup>a</sup> , Parvesh Singh<sup>b</sup>, and Gaurav Bhargava<sup>a</sup>

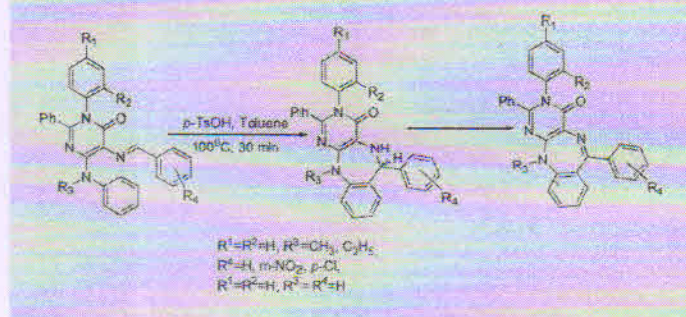
<sup>a</sup>Department of chemical sciences, I. K. Gujral Punjab Technical University Kapurthala, Punjab, India;

<sup>b</sup>School of Chemistry and Physics, University of KwaZulu Natal, Durban, South Africa

### ABSTRACT

The manuscript describes an efficient, atom economical synthesis of pyrimido[4,5-b][1,4]benzodiazepin-4-ones by relatively unexplored 7-endo-trig Pictet–Spengler type cyclisations. The synthetic methodology involves the synthesis of different variants of 5-arylidene-amino-3H-pyrimidines and their *p*-toluene sulfonic acid mediated 7-endo-trig Pictet–Spengler type cyclisations to afford biologically relevant functionalized benzodiazepine condensed pyrimidinones such as pyrimido[4,5-b][1,4]benzodiazepines in good to excellent yields (82–94%).

### GRAPHICAL ABSTRACT



### ARTICLE HISTORY



Received 4 December 2020


### KEYWORDS

Pictet–Spengler; 7-endo-trig cyclization; benzodiazepine; pyrimidinones; benzodiazepines condensed pyrimidinones

### Introduction

Pictet–Spengler cyclizations are among the useful synthetic methodologies for the synthesis of a variety of heterocycles.<sup>[1]</sup> There are ample reports on the synthesis of biologically relevant heterocycles using 5/6-endo-dig Pictet–Spengler cyclisations.<sup>[1]</sup> However, the reports on the synthesis of corresponding seven-membered heterocycles via 7-endo-trig Pictet–Spengler cyclizations are still scarce in the literature.<sup>[2]</sup> Hence, exploration on atom economical Pictet–Spengler cyclizations using appropriately

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## Recent development in synthesis of pyrrolin-4-ones/pyrrolin-3-ones

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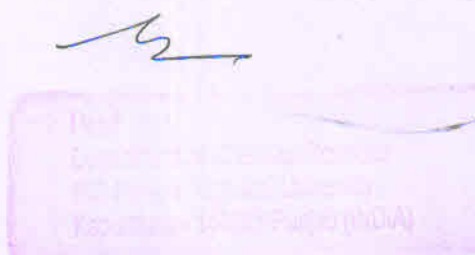
**Abstract:** Pyrrolin-4-ones/Pyrrolin-3-ones and its derivatives are important heterocyclic systems which are observed in vast variety of natural products, pharmaceuticals and biologically important compounds. Different researchers all across the world have developed different synthetic methodologies for the construction of functionalized pyrrolin-4-ones/Pyrrolin-3-ones scaffolds such as the transition-metal catalyzed/mediated cycloisomerizations of 1-amino ynones and dimerization of enaminones or  $\alpha$ -diazo- $\beta$ -oxoamides etc. The present review article summarizes the various reports on the synthesis of various simple and functionalized pyrrolin-4-ones/ pyrrolin-3-ones from 2000 onwards.

**Keywords:** Pyrrolin-4-ones, Pyrrolin-3-ones, Enaminones, Ynones, Diketones, Acetylenic esters, Diazadienes, Formyl-2H-azirines.

### 1. INTRODUCTION

Pyrrolin-4-ones/Pyrrol-3-ones are prevalent in a vast variety of pharmaceutical active molecules, biologically important natural products, and a variety of vital materials having immense applications.<sup>[1-3]</sup> Functionalized pyrrolin-3/4-ones have received incredible attention, as privileged N-heterocycles, in the development of various molecules having anticancer, antithrombotic, and antimalarial activities.<sup>[4-5]</sup> The pyrrolin-4-ones are also valuable intermediates in the development of functionalized pyrrolidines and other natural products. Pyrrol-3/4-ones occur extensively in natural products as fundamental units with useful biological activities (**Figure-1**).<sup>[6-8]</sup>

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## Recent developments in the synthesis of tricyclic condensed pyrimidinones

Rayees Ahmad Naikoo<sup>a</sup>, Rupesh Kumar<sup>a</sup> , Vipin Kumar<sup>b</sup>, and Gaurav Bhargava<sup>a</sup>

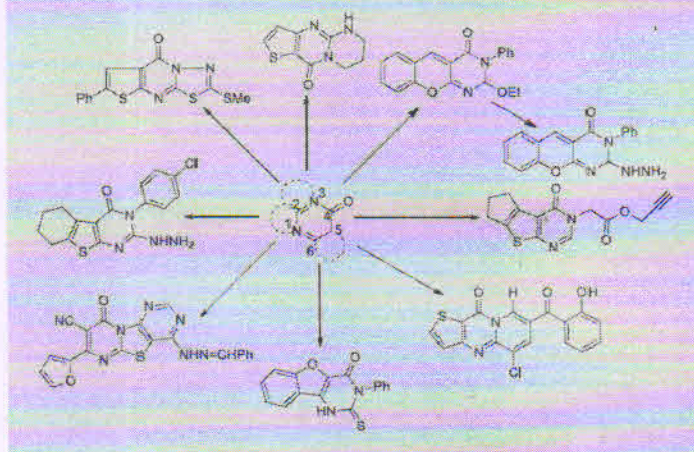
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<sup>b</sup>Department of Chemistry, Guru Nanak Dev University, Amritsar, Punjab, India

### ABSTRACT

Functionalized tricyclicpyrimidinones, a class of condensed heterocyclic systems, are found in numerouspotentially active molecules having both innate as well as synthetic origin. Different researchers across the world have explored different synthetic methods for the construction of appropriately functionalized tricyclicpyrimidinones. The present review article recapitulates various reports pertaining to substituted and functionalized tricyclic pyrimidinones reported since 2000.

### GRAPHICAL ABSTRACT



### ARTICLE HISTORY



Received 7 January 2021

### KEYWORDS

Condensed pyrimidinones;  
fused pyrimidinones;  
tricyclic pyrimidinones

### Introduction

Pyrimidinones are important heterocyclic compounds which are predominant in numerous biologically active molecules. Functionalized pyrimidinones have been employed as a useful template in the exploration of therapeutically active molecules.<sup>[1]</sup> The synthetic explorations for devising new routes for the formation of condensed pyrimidinones have been made comprehensively due to their wide spectrum of biological activity.<sup>[2]</sup> Pyrimidinones and its derivatives are prevalent in DNA, RNA, vitamins, coenzymes and

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BRIEF REPORT



## Solvent-free mechanochemical synthesis of bisthioglycolic acid derivatives: an efficient and versatile strategy for carbon–sulfur bond formation

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<sup>a</sup>Department of Chemical Sciences, I. K. Gujral Punjab Technical University, Kapurthala, India; <sup>b</sup>School of Chemistry and Physics, University of KwaZulu Natal, Durban, South Africa

### ABSTRACT

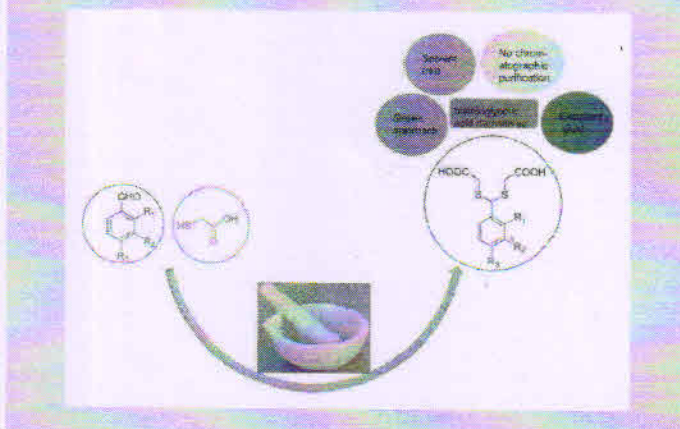
An eco-friendly, easily achievable and efficient strategy has been explored to synthesize functionalized bisthioglycolic acids using a variety of aldehydes and thioglycolic acid. The employed protocol is solvent free and provides the desirable products in excellent yields (90–99%) with atom economy. Besides, cost effectiveness, short reaction times and milder reaction conditions are among other captivating benefits of the reported methodology.

### ARTICLE HISTORY

Received 8 June 2021  
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### KEYWORDS

bisthioglycolic acid;  
mechanochemical synthesis;  
carbon–sulfur bond;  
formation; solvent-free  
synthesis; Green synthesis





### Introduction

The exploration of atom economical greener protocols with easily accessible final products without any additional extraction or chromatographic procedures is among the significant aims in organic chemistry. Solvent-free mechanochemical strategies for synthetic transformations have created a niche at the forefront of sustainable green chemistry. These strategic

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 Supplemental data for this article can be accessed here. <https://doi.org/10.1080/17415993.2021.1983574>

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## RESEARCH ARTICLE

## Oxa-Michael Addition Reactions of 3-hydroxy-2-azetidinones: Synthesis of 1, 3, 4-Trisubstituted-2-Azetidinones

Priyanka Sharma<sup>1</sup>, Maninderjeet Kaur Mann<sup>1</sup>, and Gaurav Bhargava<sup>\*1</sup><sup>1</sup>Department of Chemical Sciences, I. K. Gujral Punjab Technical University, Kapurthala, Punjab, 144 603, India

## ARTICLE HISTORY

Received: June 28, 2020  
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10.2174/1570178619666210610153744**Abstract:** The manuscript describes a facile and an efficient methodology for the synthesis of 1, 3, 4 trisubstituted- $\beta$ -lactams by base mediated oxa-Michael addition reactions of 3-hydroxy-2-azetidinones with acetylenic esters under different reaction conditions. These functionalized 1, 3, 4-trisubstituted-azetidin-2-ones are useful organic synthons for the synthesis of various heterocyclic compounds having diverse pharmacological applications.**Keywords:** Lactams, Oxa-Michael reaction, 3-Hydroxy lactams, Acetylenic ester.

## 1. INTRODUCTION

The reactions of Michael addition and its modified forms are versatile methods in organic synthesis [1-3]. Michael addition reactions offer tremendous synthetic potential since the products available are valuable intermediates in organic synthesis [4-10]. Extensive progress has been made in this field over the last decades. However, hetero-Michael addition, such as aza-Michael [11, 12], sulfa-Michael [13, 14], phospho-Michael [15] and oxa-Michael reactions, have gained considerably less attention [16, 17]. Oxa-Michael reactions are efficient tools, which afford a variety of pharmacologically important molecules, such as tetrahydropyrans, chromenes, xanthenes, etc. [18]. Functionalized 1, 3, 4-trisubstituted-azetidin-2-ones have been evaluated for their antibacterial, anti-tubercular, anti-hyperglycemic, anticancer, anti-HIV, anti-parkinson [19-21], antidepressant and anti-elastase activity and cholesterol absorption inhibitors, etc. [22, 23]. As a part of our ongoing interest in heterocyclic synthesis, we have earlier reported the synthesis of functionalized 1, 3, 4-trisubstituted azetidinones and their transformations to a variety of heterocyclic systems [24-26], such as proline esters [27, 28], benzodiazepinones and thiazolidinones [29], and pyrrolidines [30]. In continuation of this interest, we have recently studied aza-Michael addition reactions of 3-amino-2-azetidinones with different acetylenic esters for the formation of 4-oxo-dihydro-1H-pyrroles via tandem aza-Michael additions and intramolecular amidic ring-opening reactions (Fig. 1) [31]. Since Michael additions of functionalized azetidin-2-ones, such as *cis*-3-hydroxy-

azetidin-2-ones [32] with different Michael acceptors, can provide easy access to 1, 3, 4-trisubstituted-2-azetidinones, hence, it was thought worthwhile to explore the oxa-Michael addition reactions of *cis*-3-hydroxy-1-aryl-4-styrylazetidin-2-ones with a variety of acetylenic esters. The present manuscript describes a simple methodology for the preparation of functionalized 1, 3, 4 trisubstituted azetidin-2-ones via oxa-Michael addition reactions of functionalized 3-hydroxy-azetidin-2-ones with acetylenic esters.

## 2. RESULTS AND DISCUSSION

The starting *cis*-3-hydroxy-2-azetidinones were synthesized by [2+2] cycloaddition reactions of functionalized 1-azadienes with acetoxyacetic acid in the presence of triethylamine and *p*-TsCl (Scheme 1) according to the

Reported procedure [33-35], followed by the hydrolysis of *cis*-3-acetoxy-2-azetidinones using lithium hydroxide in THF/water (Scheme 1) [35]. Then, oxa-Michael addition reactions of the *cis*-3-hydroxy-2-azetidinones (**1a-c**) were explored for the synthesis of functionalized 1, 3, 4-trisubstituted-2-azetidinones. Initially, oxa-Michael addition reactions with acetylenic esters, such as DMAD and methyl propiolate, were optimized for best yields and selectivity. The results are presented in Table 1.

The reactions of **1a-c** with acetylenic esters **2** resulted in the formation of oxa-Michael adducts **3**, and the corresponding 4-oxo-5-(3-aryl-1-arylaminoallyl)-4, 5-dihydro-1H-furan-2, 3-dicarboxylate esters (**4**) were not observed (Scheme 2). The reaction of **1b** with **2a** gave better yields of oxa-Michael adducts using NaH as a base. The reaction did not occur in the absence of any base or by using weak bases, such as  $K_2CO_3$ ,  $Na_2CO_3$ , etc. (Table 1, Entries 5-14). The

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# Regioselective Copper(I)-Catalyzed Ullmann Amination of Halopyridyl Carboxylates using Sodium Azide: A Route for Aminopyridyl Carboxylates and their Transformation to Pyrido[2,3-d]pyrimidin-4(1H)-ones

Nisha,<sup>a,†</sup> Mr. Chetan Sharma,<sup>b,†</sup> Rupesh Kumar,<sup>b,†</sup> and Yogesh Kumar<sup>a,†,‡</sup>

Dedicated to Dr. Gaurav Bhargava on the occasion of his 40<sup>th</sup> birthday

We report herein an efficient, straightforward and ligand free synthesis of aminopyridyl carboxylates, an important building block used in pharmaceuticals and agrochemicals. The C(sp<sup>2</sup>)-N bond formation utilize a readily available Cu catalyst, NaN<sub>3</sub> as the amino source in ethanol and the corresponding ortho-functionalized aromatic amines were synthesized in good to excellent yields. This ligand free one-pot domino methodology proceeds through Ullmann-type coupling of halopyridyl carboxylates with sodium azide followed by reduction with ethanol. These functionalized aminopyridyl carboxylates provides an easy access to biologically potent pyrido[2,3-d]pyrimidin-4(1H)-one hybrids.

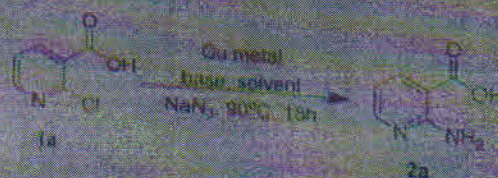
Occurrence of nitrogen containing heterocyclic compounds in synthetic intermediates, natural products, pharmaceutical and agrochemical agents and functional materials has provoked synthetic chemists to develop expedient and mild amination reactions. Over the last decades, transition metal catalysts provides versatile strategies to construct C(sp<sup>2</sup>)-NH<sub>2</sub> bond and presents a great opening to derivatize uncommon chemicals with modest functionality to synthetically novel compounds.<sup>[1-5]</sup> In this context, several catalytic methods have been used, particularly, the palladium- and copper-catalyzed amination of aryl halides has gained increasing interest.<sup>[6]</sup> Since all these methods involve the use of prefunctionalized arene starting materials, recent efforts are focused on the count of new methods by the use of parent arenes as the starting materials. Although the existing methods are quite useful,<sup>[6]</sup> however,

developing a direct route to achieve amination of o-functionalized haloheteroarenes with structural diversity from the readily accessible simple substrates would be enthralling while exigent at the same time.

On the other hand, aminopyridyl carboxylates are highly useful and valuable compounds that have numerous applications.<sup>[7-9]</sup> 2-aminonicotinic acid (vitamin B3) and 2-aminonicotinamide moieties appear frequently in medicinal chemistry programs and are valuable intermediates for the grounding of compounds with prospective as chemotherapeutic agents.<sup>[10-11]</sup> In view of the advances made in the formation of CC, CO, CN and C-halogen bonds by modern ortho-CH functionalizations, a similar approach would be interesting also for the regioselective synthesis of aminoheteroarenes.

Based on our previous efforts on developing the synthetic methods for heterocycles,<sup>[10-11]</sup> herein we report a novel ligand free one-pot copper-catalyzed direct amination of halopyridyl carboxylates using sodium azide in the presence of ethanol at moderate temperature. This newly exposed reaction is simple, straightforward, utilizing inexpensive copper catalyst and converts the readily available substrates i.e. 2-halonicotinic acid, 2-halonicotinamide into important aminoheteroarenes via a ligand free one-pot-Ullmann-type coupling with sodium azide followed by reduction. These aminoheteroarenes are novel synthons for the synthesis of highly functionalized pyrido[2,3-d]pyrimidin-4(1H)-ones.

Initially, to find an optimized reaction condition for the synthesis of 2-aminonicotinic acid **2a**, 2-chloronicotinic acid was chosen as the model substrate including the catalysts, bases, and solvents under nitrogen atmosphere as shown in Table 1. We started our experiment with 2-chloronicotinic acid **1a** and NaN<sub>3</sub> (4 mmol) in the presence of CuBr (10 mol %) and



Scheme 1. Copper Catalyzed Amination of 2-Chloronicotinic acid with NaN<sub>3</sub> (Gram Scale Synthesis)

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## Concentrated solar radiation promoted unconventional greener approach: solvent-free benign synthesis of functionalized benzimidazoles

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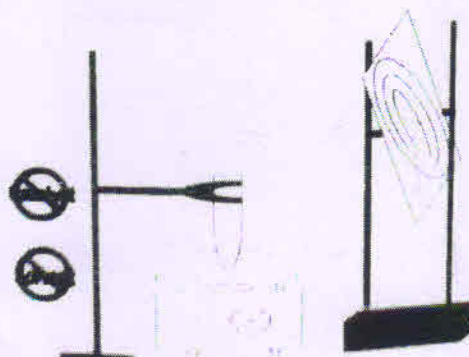
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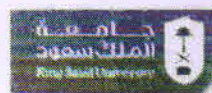
### Abstract

Renewable concentrated solar-radiation (CSR) offered a promising en route for the development of practically efficient, scalable, catalyst free and solvent-free clean process leading to the synthesis of functionalized benzimidazoles. Developed protocol has a very good substrate scope, involves mild reaction conditions and products obtained in good to excellent yields. Method presented the observations in which light alone could effect the remarkable changes with more than 85% energy saving and 75% less reaction time in listed organic transformations.



**Keywords:** Concentrated solar radiation, photocatalysis, solar synthesis, C-N bond formation, benzimidazole





# Chlorophyll triggered one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones via photo induced electron transfer reaction

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## KEYWORDS

Chlorophyll;  
3,4-dihydropyrimidin-2(1H)-ones;  
Photochemical reaction;  
Biginelli reaction;  
Concentrated solar radiation;  
Photo-induced electron transfer (PET)

**Abstract** The photocatalytic potential of chlorophyll has been investigated for the facile synthesis of dihydropyrimidinones utilizing concentrated solar irradiation towards sustainable energy solutions. This, one-pot, multicomponent Biginelli reaction, which involves a photoinduced electron transfer (PET) mechanism, affords a green and efficient approach for the transformation of the commercial aldehydes,  $\beta$ -keto ester and urea into valuable 3,4-dihydropyrimidin-2(1H)-ones with wide substrate scope and diversity. These improved reaction conditions allow the formation of a variety of substituted dihydropyrimidinones with high yields and purity in a short duration of time and mild reaction conditions.

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## 1. Introduction

Chlorophyll is a complex, natural and abundant organic pigment that acts as photocatalyst in green plants. It behaves as the principal photoreceptor in the green plants that transfers

energy to the reaction centres to form bigger sugar molecules from simple carbon dioxide and water through the initiation of photoinduced electron transfer (PET) (Bassham et al., 1950). Illuminating photochemical synthesis is greatly motivated by photosynthesis, one of the most captivating natural phenomena (Gust et al., 2009; Kim et al., 2015). The perfect harvesting of the solar light and photoelectron transfer through a series of steps to the redox centres is the theme of the photosynthesis (Denshoelter and Michel, 1989; Fleming et al., 1983). Imitating of the photosynthesis in the simulating environment is the key idea behind the use of solar energy for chemical research in the photocatalysis (Shaw et al., 2016; Xu and Sathulucki, 2018; Patel et al., 2018). Some of the organic chemists used photoredox catalysis in visible light for organic

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## REVIEW

# Recent development in the synthesis of pyrrolin-4-ones/ pyrrolin-3-ones

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**Abstract**

Pyrrolin-4-ones/pyrrolin-3-ones and its derivatives are important heterocyclic systems which are observed in vast variety of natural products, pharmaceuticals, and biologically important compounds. Different researchers all across the world have developed different synthetic methodologies for the construction of functionalized pyrrolin-4-ones/pyrrolin-3-one scaffolds such as the transition-metal catalyzed/mediated cycloisomerizations of 1-aminoynones and dimerization of enaminones or  $\alpha$ -diazo- $\beta$ -oxoamides etc. The present review article summarizes various reports on the synthesis of various simple and functionalized pyrrolin-4-ones/pyrrolin-3-ones from 2000 onward.

## 1 | INTRODUCTION

Pyrrolin-4-ones/pyrrolin-3-ones are prevalent in a vast variety of pharmaceutical active molecules, biologically important natural products, and a variety of vital materials having immense applications.<sup>1–3</sup> Functionalized pyrrolin-3/4-ones have received incredible attention, as privileged N-heterocycles, in the development of various molecules having anticancer, antithrombotic, and anti-malarial activities.<sup>4,5</sup> The pyrrolin-4-ones are also valuable intermediates in the development of functionalized pyrrolidines and other natural products. Pyrrol-3/4-ones occur extensively in natural products as fundamental units with useful biological activities (Figure 1).<sup>6–8</sup>

Different methods are reported in the literature (Figure 2) for the convenient synthesis of functionalized pyrrolin-4-ones/pyrrolin-3-ones such as condensation of functionalized amidines and 1,4-diazabutadienes with acetylenic esters and diazo compounds, cyclization reactions of readily available enaminones, and metal-catalyzed intramolecular cyclization of  $\alpha$ -aminoynones which are discussed later in the different sections of this review. Other diverse methods for the synthesis of substituted pyrrolin-4-ones are also discussed thoroughly in the present review which involves dimerization of enamides, oxidative C–H/N–H cross-coupling of  $\alpha$ -alkenoyl ketene

N,S-acetals, reactions involving formyl-2H-azirines and 3-amino-2-azetidinones highlighting their various important aspects of these reported protocols. As a whole, the present review summarizes all such reports associated with the developments pertaining to the synthesis of functionalized pyrrolin-4-ones/pyrrolin-3-ones, since 2000.

## 2 | CONDENSATION OF $\alpha$ -AMINO ACID ESTERS WITH ALDEHYDES

Smith III et al have disclosed an effective, three-step iterative solid support-based synthesis of polypyrrolinones for the formation of a wide variety of pyrrolinone scaffolds such as monopyrrolinone (–)6 and bispyrrolinone (–)10 (Scheme 1).<sup>8d</sup> The above methodology involves the initial synthesis of Wang resin-bound amino ester 3 using Teoc-protected amino acid (+)-2 via Mitsunobu reaction. Removal of the Teoc-protecting group (TBAF) followed by condensation of amino ester obtained 4 with hydrocinnamaldehyde ( $\text{PhCH}_2\text{CH}_2\text{CHO}$ ) providing functionalized imines. Imines 5 undergo cyclization to yield functionalized pyrrolinones (Scheme 1). The above synthetic methodology is further extended for the synthesis of bispyrrolinone (–)10 and tetrapyrrolinone (–)17 using modified resin-bound amino esters. The ozonolysis





ARTICLE



# Development of a sustainable ternary magnetic nanocomposite GCNI for efficient and synergistic photodegradation of Rhodamine B under solar irradiation: kinetic and mechanistic studies

Monika Thakur<sup>a</sup>, Harminder Singh<sup>b</sup>, Jaspreet Kaur Rajput<sup>c</sup> and Rupesh Kumar<sup>a</sup>

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## ABSTRACT

In this study, a novel sunlight-active ternary magnetic nanophotocatalyst GCNI (Nanozero valent Iron @ Graphene oxide and Chitosan support) was fabricated. This easily retrievable magnetic nanocomposite was prepared by depositing NZVI (Nano Zero Valent Iron, Fe<sup>0</sup>) over binary GO-CS in seven different compositions for its best optimisation in the solar-light-promoted degradation of RhB. NC (Nano Composite) was characterised by SEM demonstrating their surface morphology. Further characterisation and properties of NC were also studied using XRD, FT-IR, VSM and BET and EDS techniques. The efficacy of the NC was investigated for the removal of RhB in comparison to binary GO-CS and bare NZVI. GCNI 1:1:3 was found to be the best suitable photocatalyst showing synergistic effect in the photodegradation of RhB under given conditions of pH, concentration and time. The mechanism of dye removal and degradation was further discovered by UV-VIS and mass spectroscopy techniques. FT-IR and XRD results of fresh and treated GCNI successively corroborated the mechanism. The sorption kinetics of RhB on to GCNI was found to be described by the pseudo-second-order kinetic equation. The parameters such as dye concentration, pH and the reaction time are varied to understand the effective removal of RhB in wastewater. The outcomes exhibited the highly efficient; up to 99.4% of dye removal, easy magnetic separation of photocatalyst, excellent reusability up-to 87.5% till six consecutive cycles, synergistic effect in adsorption and photo-degradation of dye.

## ARTICLE HISTORY

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## KEYWORDS

Magnetic nanocomposite; photodegradation; ternary nanocomposite; Rhodamine B; water remediation

## 1. Introduction

Organic synthetic dyes are well-known water pollutants, as these dyes are used in textile, plastic, leather tanning and food processing industry. Discharge of huge amount of effluents from such industries causes water pollution [1,2]. These dyes are mutagenic and carcinogenic in nature which also prove to be toxic to both human and aquatic life. Also undesirable change in the colour of water causes aesthetic problem [3,4]. Various



# 7-Endo-trig Pictet–Spengler type cyclization of 5-alkylidene/arylidene-amino-3H-pyrimidin-4-ones: An efficient and diastereoselective synthesis of pyrimido[4,5-b][1,4]benzodiazepines

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## ABSTRACT

The manuscript describes an efficient, atom economical synthesis of pyrimido[4,5-b][1,4]benzodiazepin-4-ones by relatively unexplored 7-endo-trig Pictet–Spengler type cyclisations. The synthetic methodology involves the synthesis of different variants of 5-arylidene-amino-3H-pyrimidines and their *p*-toluene sulfonic acid mediated 7-endo-trig Pictet–Spengler type cyclisations to afford biologically relevant functionalized benzodiazepine condensed pyrimidinones such as pyrimido[4,5-b][1,4]benzodiazepines in good to excellent yields (82–94%).

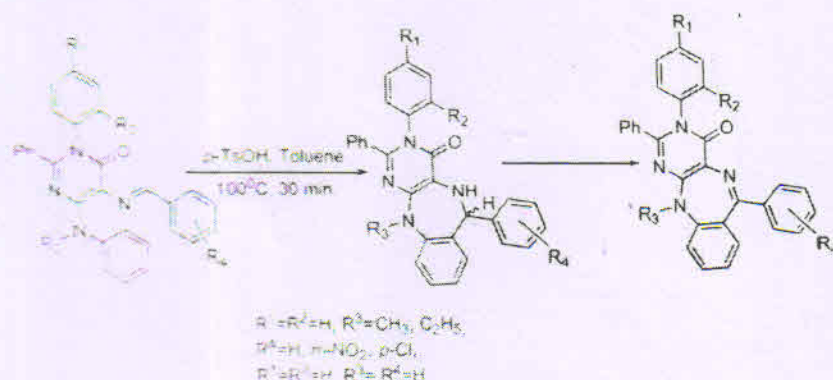
## ARTICLE HISTORY

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## KEYWORDS



Pictet–Spengler; 7-endo-trig cyclization; benzodiazepine; pyrimidinones; benzodiazepines condensed pyrimidinones


## GRAPHICAL ABSTRACT



## Introduction

Pictet–Spengler cyclizations are among the useful synthetic methodologies for the synthesis of a variety of heterocycles.<sup>[1]</sup> There are ample reports on the synthesis of biologically relevant heterocycles using 5/6-endo-dig Pictet–Spengler cyclisations.<sup>[1]</sup> However, the reports on the synthesis of corresponding seven-membered heterocycles via 7-endo-trig Pictet–Spengler cyclizations are still scarce in the literature.<sup>[2]</sup> Hence, exploration on atom economical Pictet–Spengler cyclizations using appropriately

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SYNTHETIC COMMUNICATIONS REVIEWS



# Recent developments in the synthesis of tricyclic condensed pyrimidinones

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## ABSTRACT

Functionalized tricyclicpyrimidinones, a class of condensed heterocyclic systems, are found in numerouspotentially active molecules having both innate as well as synthetic origin. Different researchers across the world have explored different synthetic methods for the construction of appropriately functionalized tricyclicpyrimidinones. The present review article recapitulates various reports pertaining to substituted and functionalized tricyclic pyrimidinones reported since 2000.

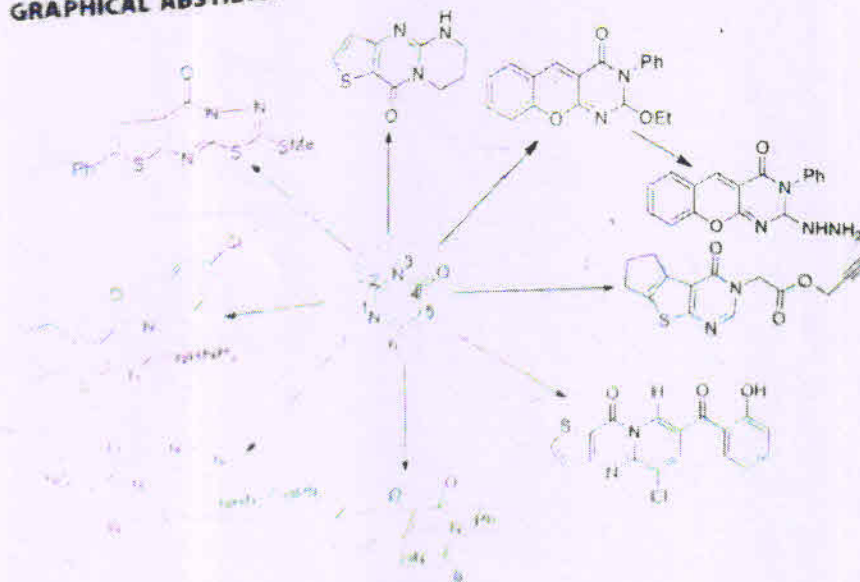
## ARTICLE HISTORY

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## KEYWORDS

Condensed pyrimidinones;  
fused pyrimidinones;  
tricyclic pyrimidinones

## GRAPHICAL ABSTRACT



## Introduction

Pyrimidinones are important heterocyclic compounds which are predominant innumerable biologically active molecules. Functionalized pyrimidinones have been employed as a useful template in the exploration of therapeutically active molecules.<sup>(1)</sup> The synthetic exploration for devising new routes for the formation of condensed pyrimidinones has been made comprehensively due to their wide spectrum of biological activity.<sup>(2)</sup> Pyrimidinones and its derivatives are prevalent in DNA, RNA, vitamins, coenzymes and



## Characterization of minerals present in the agricultural Soil

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**ABSTRACT :** Clay samples separated from agricultural soil of Ahmadgarh, Faridkot and Zira of Punjab, India were selected for systematic study. In this paper three samples of clay which were separated from soil of Punjab, India. Clay samples were characterized by XRD to know different minerals present in them. Kaolinite, smectite, montmorillonite, illite were analyzed by XRD which were further substantiated by FTIR and TG/DTA/TGA analysis.

**Key words:** Clay, FTIR, illite, Kaolinite, montmorillonite, texture, TG/DTA/TGA, smectite, XRD, whole soil

Clay is an important component of soil system. The formation of clay minerals in the soil involves slow processes which depend upon the weathering environment and that is mainly controlled by climate and drainage conditions of the landscape (konta 2005; Emadadul, 2013). Depending upon the structure developed in the course of soil formation different clay minerals will exhibit different physical, chemical and mechanical behaviors. Study of the clay minerals present in soils is very important to know the role of clay minerals in various soil processes. Due to their physical and chemical properties like abundance, high specific surface area, high layer charge, laminar morphology and chemical reactivity with both neutral and charge species, these are of great importance to industry, agriculture and the environment (Murray 1999; Hoidy *et al.*, 2009; Njoka *et al.*, 2015). They are hydrated aluminum silicates with very fine particle size, usually <2 mm (Moore and Reynolds, 1989). Structurally, clay minerals consists of two basic units, an octahedral sheet and a tetrahedral sheet which is joined by sharing the apical oxygens or hydroxyls to form the 1:1 clay mineral layer e.g., kaolinite or the 2:1 clay mineral layer e.g. illite, smectite, chlorite, vermiculite, gibbsite. The structure and composition of the major clays, i.e. kaolins, smectites and palygorskite-sepolite, are very different even though they are each comprised of octahedral and tetrahedral sheets as their basic building blocks. In this study, three regions of Punjab namely Ahmadgarh, Faridkot and Zira which are situated in different region of Punjab were selected. Samples of soil from these three regions were

collected from agricultural fields. In the present communication the clays have been separated from soil collected from agriculture fields which has both organic and inorganic components. These have been studied by XRD, FTIR and TG/DTA/TGA. Clay samples used were not commercial and were separated from soil of agricultural fields of Punjab, India. Analytical studies of clays of soil of Punjab have not been done earlier. The objective of the present study is to identify the mineralogy in samples of clay separated from agricultural soils of different texture. This study will help in identification of clays and understanding of their interaction behaviour with different chemicals used in agriculture.

### MATERIALS AND METHODS

Three samples of whole soil were collected from different agricultural fields of Ahmadgarh, Faridkot and Zira. The soil samples were taken from the upper horizons 0-20 cm, air dried, crushed and passed through 2 mm sieve and stored in plastic bags for analysis and further treatment. The soil samples collected from Ahmadgarh, Faridkot and Zira were designated code as AHM-S, FDK-S and ZRA-S respectively. Texture analyses of the two soil samples were done by Bouyoucos hydrometer method (Bouyoucos, 1962). Clay was separated from these three samples of whole soil by centrifugation method (Tan, 1996) and was designated as AHM-C, FDK-C and ZRA-C respectively. In order to identify the minerals from clays after separation, different samples of clay were analyzed by X-ray diffraction (X-ray





## Spectroscopic Characterization of Humic Acids Extracted From Different Type of Soils of Punjab

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The humic acids isolated from soils of different places of Punjab have been characterized by ultraviolet visible (UV-VIS) and Fourier transforms infrared (FTIR) spectrophotometers. The texture and chemical analyses of the whole soils were also carried out by X-ray fluorescence (XRF) spectroscopy. The molecular weight of extracted humic acids was determined by colour ratio ( $E_{265}/E_{465}$ ) from absorbance values recorded in UV-VIS region. The FTIR spectra revealed the presence of different functional groups of -COOH, -OH, C-O, C=N, C-OH, etc. The texture and the chemical characteristics of the whole soils have been correlated with their humic acids. It was observed that humic acids and soils of similar textures have almost identical characteristics and molecular weights.

**Key words:** Humic acid, FTIR, UV-VIS, soil texture

Soil consists of inorganic components, organic matter and living organisms. The inorganic components consist of the minerals and clay. The organic matter (OM) present in soils is a mixture of products formed at decomposition stages, resulting from chemical and biological degradation of plant and animal residues and synthetic activity of microorganisms. The soil organic matter has two components, humified (humic acid, fulvic acid and humin) and non-humified (carbohydrates, lipids, amino acids, nucleic acids and lignin). Humic substances are the major constituents of soils, and generally known as biologically refractory degradation components (Chefetz *et al.* 2002). The humic substances are dark-coloured amorphous polymers. They are formed in the environment with biomass constituents (Stevenson 1982). It is considered that humic substances initially lose those components which are easily decomposed, and thereafter condensation-polymerisation and oxidative reactions take place which results in a more stable structure (Kumada 1987). This process corresponds to the progression of humification, and it is identified on the basis of the degree of darkening of colour of humic acids, alkali-soluble and acid-

insoluble fraction (Watanabe and Takada 2006). These substances are usually fractionated on the basis of their solubility characteristics and the pH value of solvents as well. The humic substances are non-crystalline organic elements. They are composed with 40-60% carbon, 30-50% oxygen, 3-7% hydrogen, and 1-5% nitrogen. They consist of a very complex series of carbon chains and ring structures, with numerous chemically active functional groups like phenolic, carboxylic and alcoholic hydroxyl. Martin *et al.* (1998) characterized the humic substances extracted from soils of varying climate and altitude. They found the chemical and structural composition of humic acids (HAs) and fulvic acids (FAs) are influenced by climate and altitude of the region. The dominant effect of annual rainfall and vegetation on the composition of HAs and FAs has also been reported by Arshad and Schnitzer (1989). They found that humic substances of higher, wetter and cooler altitudes were lesser humified than those extracted from lower, warm and drier sites. At highest altitude, the nitrogen contents in HAs from both cultivated and natural forest soils were lowest perhaps due to accelerated leaching during the rainy period (1417 cm annual rainfall). Studies revealed that the characteristics of humic substances like functional group, molecular weights (Mukhopadhyay and Banerjee 1985) are too influenced by cultivation and vegetation type.

Clay and sand sediments have many differing physical and chemical characteristics, and

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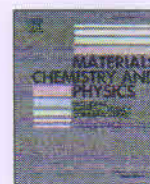
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## Influence of microwave processing and sintering temperature on the structure and properties of Sr/Zr doped hydroxyapatite

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## HIGHLIGHTS

- Sr-Zr hydroxyapatite has been sintered by microwave and conventional methods.
- The lattice parameters increase with temperature during conventional sintering.
- Reverse trend for lattice parameters is observed during microwave sintering.
- Microwave sintered products have higher density and hardness.
- Microwave sintered product at 1100 °C has a less percentage of secondary phase.

## ARTICLE INFO

## Keywords:

Calcium hydroxyapatite  
Microwave sintering  
Conventional sintering  
X-ray diffraction

## ABSTRACT

Among the different cations that are substituted to modify the properties of calcium hydroxyapatite, Sr and Zr have gained interest because of their effect on bone formation and mechanical properties, respectively. In the present work, Sr and Zr substituted hydroxyapatite,  $\text{Ca}_{9.39}\text{Zr}_{0.11}\text{Sr}_{0.5}(\text{PO}_4)_6(\text{OH})_2$  are synthesized by conventional and microwave sintering at different temperatures. The effect of different sintering techniques and temperatures are investigated on the structural and morphological properties of as-synthesized samples. The X-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FT-IR) is used to study the variation in structural properties and scanning electron microscopy (SEM) is used to investigate the morphology with the variation in sintering conditions. The changes in lattice parameters clearly show that Sr and Zr are incorporated into hydroxyapatite lattice. Microwave sintered samples retain the higher amount of hydroxyapatite and experience higher density levels as compared to conventional sintering. As compared to conventional sintering, the grain size is more uniform and low percentage of secondary phase is observed in microwave sintered sample.

## 1. Introduction

Increasing number of accidents, trauma, arthritis, and tumors have increased the interest of the scientific community to find new biomaterials [1–3]. Many research groups are working for the development and evaluation of new synthetic biomaterials for bone grafting. The main challenge in biomaterial engineering is the quest to find a material which has good biocompatibility, resorbability and mechanical strength [4–6]. Many materials are tried and tested, but they are found inappropriate regarding the above-mentioned properties. The most appropriate material to date is calcium hydroxyapatite (HA) [7–9]. HA is considered as a better option as compared to other calcium phosphates

due to its biocompatibility and osteoconductive properties. It also exhibits excellent chemical and biological affinity with the bone tissue [10]. HA is basically calcium hydroxyapatite which makes most of the mineral part of bone and tooth enamel. But its stability *in vivo* and low mechanical strength as compared to bone has limited its use in load-bearing applications [11,12]. To improve its mechanical properties, many approaches like the addition of dopants and different synthesizing routes have been investigated [13]. The best structural aspect of HA is its ability to accommodate a great variety of cations and anions while retaining its hexagonal structure. These substitutions can alter the thermal stability, surface reactivity and biological properties of HA [14–16].

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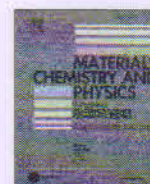
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## Comparison of microwave and conventionally sintered manganese and niobium doped lanthanum germanate based apatites by micro Raman Spectroscopy

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### HIGHLIGHTS

- Sintering of apatites have been done by conventional and microwave processing.
- The XRD revealed that the sintered products had single Phase hexagonal oxy apatite.
- Raman Spectroscopy revealed that monoclinic phase was also present in the apatites.
- Microwave sintered products had uniform grain growth and higher density.
- Microwave sintered products had higher hardness and conductivity value.

### ARTICLE INFO

#### Keywords:

Micro Raman spectroscopy  
XRD  
SEM and hardness

### ABSTRACT

In this paper, the effect of microwave and conventional sintering on doping behaviour of  $Mn^{2+}$  and  $Nb^{5+}$  in lanthanum germanate based apatite have been compared. The precursor of apatite has been prepared by mixed oxide method and conventionally calcined at 1100 °C for 6 h. The resulting powders have been sintered by microwave energy at 1400 °C for 30 min and by conventional heating 1400 °C for 4 h. The products prepared have been characterized by X-ray diffraction, scanning electron microscope, Micro Raman spectroscopy, and Vicker's hardness and the results are compared. The apatites of similar compositions sintered by microwave energy have higher density and hardness than the apatites sintered by electric heating.

### 1. Introduction

The ideal general formula of apatite is  $A_{10}M_6O_{24}X_2$  (A = alkaline earth, rare earth; M = P, Si, Ge) and (X = OH, O and halide). Its applications ranging from biomaterial to electrolytes have been of interest and therefore highly researched [1]. Hassan et al. have written a review on microwave-assisted techniques for the synthesis of nano hydroxyl apatite but they did not cover the sintering of hydroxyapatite [2]. Transparent hydroxyapatite was prepared first time in the Microwave Processing & Engineering Center of Material Research Institute, Penn State by the group of Agrawal. They had used fine crystalline material prepared by hydrothermal process and microwave sintering of the fine powder at 1150 °C within 5 min of soaking time [2–5]. In another work,

the group used microwave processing in the preparation of HAP/ZrO<sub>2</sub> composites to avoid loss of calcium phosphate. They could prepare HAP/ZrO<sub>2</sub> by microwave processing at the temperature as low as 1200 °C within 20 min of sintering time. Conventionally HAP/ZrO<sub>2</sub> was prepared at 1200 °C in 240 min which led to the loss of calcium phosphate [6]. The sintering of hydroxyapatite to be used as a biomaterial has been reported by the group of Singh [7].

In the year 1995, Nakayama et al. investigated lanthanum silicate-based apatites  $La_{10}(SiO_4)_6O_3$ , (Ln = La, Nd, Sm, Gd, Dy, Y, Ho, Er and Yb) for its applications as an ionic conductor [8] and later lanthanum germanates was also studied for the applications as ionic conductors [9] to be used at intermediate temperature in the solid oxide fuel cells (SOFC). Since the  $La_{9.33+2x/3}(Si/Ge)_6O_{26-x}$  apatites have a conductivity

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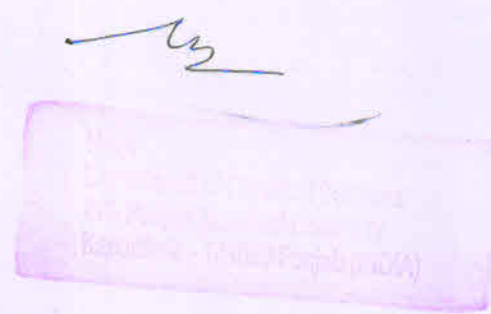
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## **Phytoremediation of Pulp and Paper Mill Effluents by *Salvinia molesta* and its comparison with Nanoparticles Inclusive Phytoremediation**

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### **Abstract**

Due to industrialization, there is increased disposal of pollutants such as heavy metals, various types of organic and inorganic compounds into the environment. These toxic pollutants affect soil, surface water, and ground water which can cause serious risks to health of human beings. Many physico-chemical processes such as screening, coagulation, activated carbon treatment, ion-exchange, electrodialysis, trickling filtration, reverse osmosis and activated sludge digestion have been used for the treatment of polluted water. But all these methods involve high energy and large capital investments. Therefore, phytoremediation has been employed successfully to clean up pollution which is emerging technology. In this paper, the Phytoremediation of Pulp and Paper Mill Effluent using *Salvinia molesta* has been assessed in terms of reduction in pH, EC, BOD, COD, TS, TSS and TDS and compared the results with nanoparticles inclusive phytoremediation. The effluent has been treated for 45 days. All parameters exhibited exponential decrease from the start up to 45 days and thereafter showed negligible decrease till the termination of the experiment. The proposed nanoparticles inclusive phytoremediation method can be profitably employed for the abatement of pollution from industrial waste water.

**Keywords:** Phytoremediation, Pulp And Paper Mill Effluent, *Salvinia molesta*, Silver Nanoparticles.

### **Introduction**

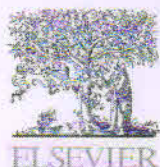
Pulp and paper industry is the major industry of our country. It consumes a large amount of water [1]. The ministry of environment and forest, Government of India has categorized the pulp and paper industry as one of the twenty most polluting industries [2]. Approximately 75 to 95% of total pollution load is contributed by small paper mills. The discharged effluents contain organic, inorganic pollutants and colouring materials. These chemicals may affect soil and in turn the growth and development of plants [3]. Marwaha et al reported that the pulp and paper industry waste water might cause oxygen deficiency, acute toxicity, eutrophication in recipient waste water bodies [4]. Various investigators had studied the effect of paper mill effluent on various crops [5-9]. There is decline in germination of rice seeds and seedling growth with paper mill effluent treatment in comparison to control [10]. Rajannan and Oblismai [11] reported that the germination of rice, black gram and tomato seeds was effected by paper mill effluent. However, the diluted form of effluent (25 and 50%) enhance the growth.

Pulp and paper mill effluents contain heavy metals and other organic toxicants which are hazardous to the environment [12]. Studies on assessment of Phytoremediation potential of water hyacinth and *Trapa bispinosk* of pulp and paper mill waste water have been carried

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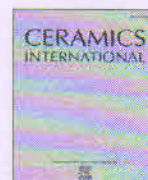






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## Effect of microwave and conventional processing techniques on mechanical properties of Strontium substituted hydroxyapatite

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### ARTICLE INFO

#### Keywords:

Microwave and conventional sintering  
XRD  
Micro Raman spectroscopy  
Microhardness

### ABSTRACT

The effect of different sintering routes: conventional and microwave sintering along with different sintering temperatures has been studied on Sr-doped hydroxyapatite bioceramics. The physical and mechanical properties of different samples synthesized at different sintering temperatures and sintering techniques have been evaluated by X-ray diffraction (XRD), Raman spectroscopy, Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy and microhardness. X-ray diffraction studies showed that microwave sintering suppresses the formation of secondary phases. The density, grain size along with microhardness was higher for samples sintered by microwave processing as compared to samples sintered by conventional technique. The results from different characterization techniques show that microwave sintering technique is not only efficient in terms of energy-saving and time reduction but also improves the formation of phases and mechanical properties.

### 1. Introduction

Biomaterials are those materials which are meant to interact with biological systems and are used in medical devices [1]. Advancements in biomaterials have significantly increased the lifetime of patients suffering from trauma, injuries, large bone defects, and osteoporosis. But, still, enhancements are required to improve the physicochemical and biological properties of biomaterials to mimic the natural bone [2,3].

For implantation and other orthopedic issues, Bioceramics are widely accepted due to their useful properties like non-toxicity and excellent biocompatibility [4]. Among different bioceramics, calcium phosphate-based bioceramics constitute a great promise for bone tissue engineering as they resemble the mammalian bone and teeth [5]. Single-phase hydroxyapatite (HA) or biphasic calcium phosphate (BCP) comprising  $\beta$ -tricalcium phosphate (TCP) is an interesting candidate for synthetic bone substitution applications [6,7]. Hydroxyapatite provides a scaffold for osteoconduction and  $\beta$ -TCP oversaturates the local environment with  $\text{Ca}^{2+}$  and  $\text{PO}_4^{3-}$  ions to speed up the new bone formation [8]. HA/ $\beta$ -TCP ratio predicts the extent and rate in vivo resorption of biphasic calcium phosphate, higher  $\beta$ -TCP content allows rapid and substantial resorption [9]. However, the solubility of HAp is

poor as compared to other bioceramics which affect the rate of biodegradation in vivo and increases patient's rehabilitation time [10]. The solubility of bioceramics is affected by chemical composition, crystallinity, particle size, surface area, pore size, density/porosity and extent of ionic substitution in HAp lattice [11–13]. To improve the mentioned properties, several methods like variation of sintering techniques and temperature, granule size, and electrical polarity have been proposed [14]. Besides these methods, ionic substitution is also considered to improve the solubility of HAp and hence osteoconductivity [15].

The biological apatite contains trace ions like  $\text{Na}^+$ ,  $\text{Sr}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{SiO}_4^{4-}$ ,  $\text{SO}_4^{2-}$ ,  $\text{F}^-$  etc. and is non-stoichiometric [16]. These ions play a vital role in bone metabolism. But, synthetic hydroxyapatite is stoichiometric and deficient of these ions which make it a poor bone repair material [17]. But, the properties of synthetic hydroxyapatite can be improved by ionic substitution. After ionic substitution, HAp more closely mimics the biological HAp [18]. From the above-mentioned ions,  $\text{Sr}^{2+}$  ion helps to maintain the balance between the bone formation and resorption process in vivo and low dosage of  $\text{Sr}^{2+}$  helps in increasing bone mass and volume. It also accelerates the osteogenic differentiation of mesenchymal stem cells and enhances the functionality of osteoblasts [19].

Synthesis of hydroxyapatite has been reported by several different

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## Estimation of Genetic Variability in *Jatropha Curcas* L. Genotypes for Vegetative Traits and Seed yield

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### Abstract

Twenty five *Jatropha curcas* genotypes collected from the foothills of the Shivalik range of the Himalayas in a narrow belt called Tarai were grown in Randomized Block Design with three replications at Medicinal Plant Research and Development Centre, G. B. Pant University of Agriculture and Technology, Pantnagar, Uttarakhand and evaluated for 8 characters. The genotypes showed significant differences in most of traits. The phenotypic coefficient of variation was the highest for seed yield/ plant, followed by 100 seed weight (gm) and collar diameter (cm). Similarly, the genotypic coefficient of variation was the highest for seed yield/plant, followed by 100 seed weight (gm) and collar diameter (cm). Very high level of broad sense heritability was observed for seed yield /plant, 100 seed weight, Number of Secondary branches/plant, Collar diameter, Flower initiation (days) after 31<sup>st</sup> July, Number of Primary branches/plant, Plant Height, Oil content. High estimates of genetic gain as per cent mean were recorded for Flower initiation (days) after 31<sup>st</sup> July, Oil content, while low estimates of genetic gain as per cent were recorded for plant Height.

Selection for Number of Primary branches/plant, Number of Secondary branches/plant, collar diameter, seeds/fruit and 100 seed weight would result in some improvement in yield. Thus, the ideotype to achieve high yield in *Jatropha* should have more number of flowering bunches/plant and fruits per plant and moderate to high value for seeds/fruit and 100 seed weight.

**Keywords:** Genetic Variability, Vegetative Traits, *Jatropha curcas*, Seed yield

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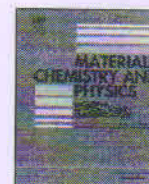
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### Introduction

*Jatropha curcas* Linn. (Physic nut or Ratanjot) is a crop tree-borne oil seed crop. It is native to Tropical America and belongs to family Euphorbiaceae. Global increase in demand for renewable energy to combat the greenhouse effect and rapid depletion of ozone layer as a result of discharge of harmful gases into the environment, couple with the depletion of reserved fossil fuel has mandated the use of biomass energy feedstock for sustainable production of biofuel. Biofuel has been known to be a good alternative to fossil fuel due to its cheap, sustainable and environmental friendly properties [1]. This newly introduced crop which grows abundantly in wild and abandoned land has its seed and oil yield unpredictable especially in tropical climate. Favorable environmental conditions that affect its production has yet to be known [2] and [3]. In spite of the great potentials and attributes of *Jatropha* as a biodiesel crop, the full potentials of *Jatropha* have not been realized. One of the reasons for this, apart from the agronomic, social economic and institutional constraints is the facts that there is presently no planned rational conventional breeding and genetic programs. [4] reported that, for the fact that *Jatropha* has adapted itself to wide range of environmental and ecological conditions suggests that, there exists considerable amount of genetic diversity yet to be detected for potential realization. [5] reported variability observed in *J. curcas* in Central India which was mainly limited to seed source variation in morphology, germination and seedling growth. [6] have reported divergence in seed oil traits of *J. curcas* from a limited number of locally collected accessions. Since heritability estimate in perennial plants decrease with age because of compounded environmental effects masking genotypic differences, there is an urgent need for the knowledge of these estimates in the progenies.

However, one of the limitations to this conventional breeding programme work is the wide genetic diversity, which has to be evaluated before selection of suitable accessions could be possible. Also breeding of high yielding variety is not possible without knowing the extent of variation that exists among the available germplasm in India, the growth, yield and extent of environmental influence on these factors, heritability and genetic gain of the material.





## Microwave and conventional processing of niobium and manganese doped lanthanum germanate based apatites

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### HIGHLIGHTS

- In this paper, apatites have been prepared by microwave heating as well as conventional heating.
- The single phase of the apatite could be prepared at 1100 °C within 1 h by microwave heating.
- By the conventional heating, the single phase of the apatite could not be prepared at 1100 °C within 1 h.
- The grain growth in the microwave sintered products was more uniform than the conventionally sintered products.
- The density of the sintered products was as high as 96% of the theoretical density.

### ARTICLE INFO

#### Keywords:

Apatite  
Electrolyte  
Microwave processing  
XRD  
SEM

### ABSTRACT

The paper reported calcination and sintering of apatites of compositions  $\text{La}_{9.5}\text{Ge}_{5.5}\text{Nb}_{0.5}\text{O}_{26.5}$  and  $\text{La}_{9.5}\text{Ge}_{5.5}\text{Mn}_{0.5}\text{O}_{26}$  using microwave energy for the first time from the precursor prepared by the mixed oxide method. The calcination was done conventionally under an identical condition to compare the results. The single phase of  $\text{La}_{9.5}\text{Ge}_{5.5}\text{Nb}_{0.5}\text{O}_{26.5}$  and  $\text{La}_{9.5}\text{Ge}_{5.5}\text{Mn}_{0.5}\text{O}_{26}$  could be obtained by microwave processing at temperature 1100 °C within 1 h. But the single phase of apatites could not be prepared by conventional heating under the identical conditions. The calcined powder obtained by microwave heating was sintered by microwave heating as well as conventional heating. The products obtained were characterized by XRD and SEM. It was observed that the microwave sintered products had higher density and uniform microstructure compared to the sintered products obtained by the conventional heating.

### 1. Introduction

Yttria-stabilized zirconia (YSZ) exhibits high oxygen ion conductivity at high temperatures in the range of 850–1000 °C. Therefore, YSZ is used as an electrolyte in SOFC. Since YSZ shows appreciable conductivity only at elevated temperature consequently, the operation of SOFC causes problems related to the degradation of materials and mechanical and chemical compatibility in oxidizing and reducing atmospheres [1]. Many other oxide electrolytes are being studied to lower the operating temperature of the SOFC. Some of the oxide ion conductors are fluorite, perovskite, pyrochlore, brownmillerite, and apatite [2–7]. Lanthanum oxide, due to its multivalent valence state, is used as a catalyst, photocatalyst [8,9], and in the fabrication of supercapacitor [10]. Lanthanum has also attracted attention because lanthanum doped

hydroxyapatite has improved performance as dental implants in osteoporotic cases [11]. Further, lanthanum-based apatite,  $\text{Ln}_{10-x}\text{Si}_6\text{O}_{26} \pm y$  ( $\text{Ln} = \text{La}$ ) (LSA), has found its application as an electrolyte in the intermediate temperature solid oxide fuel cell (IT-SOFC) because of its higher conductivity (of the order of  $10^{-3} \text{ Scm}^{-1}$ ) at 500 °C which is higher than that of YSZ at an intermediate temperature [12–16]. Lanthanum silicate based apatite requires higher sintering temperature which is usually higher than 1700 °C and a long soaking time of more than 4 h before they can be used as an electrolyte in SOFCs [17]. The substitution of Si ions by Ge ions has been found to decrease sintering temperature and improve electrical conductivity [18,19] at the intermediate temperature. But during the preparation of lanthanum germanate based electrolyte, the  $\text{GeO}_2$  gets evaporated at a higher temperature which changes the La/Ge stoichiometric ratio resulting in

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ORIGINAL RESEARCH

## Vermicompost and vermiwash as supplement to improve seedling, plant growth and yield in *Linum usitatissimum* L. for organic agriculture

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### Abstract

**Purpose** To study the organic production in two varieties of *Linum* (Linseed) crop using different proportions of vermicomposts and combination of vermiwash as an environment friendly substitute to chemical fertilizers for organic farming of Linseed.

**Method** Vermicompost prepared from cattle dung was mixed in different proportions, i.e. 0, 20, 40, 60, 80, and 100% vermicompost v/v with soil and commercial potting media (Perlite, Peat and Coconut coir). To study the germination, vegetative growth, reproductive growth and yield in two varieties of *Linum usitatissimum* L. LC-54 and LC-2063 were grown in a polyhouse for a 2 years trial. A total of 960 seedlings and 240 plants were studied for assessment of result in 24 treatments. Additional treatments with foliar application of 1:1 v/v vermiwash and recommended dose of inorganic fertilizer were done to determine and compare the role of vermicompost, vermiwash and inorganic treatment.

**Results** Substituting soil with 60% (v/v) vermicompost in LC-54 and with 40% (v/v) vermicompost in LC-2063 improved the performance of seeds, root morphology and stem growth. Life cycle of crop was shortened in two

varieties of Linseed raised under different treatments of vermicompost and vermiwash. Performance of LC-54 was better at 60% and that of LC-2063 was at 40%, which can be attributed to their genotypic differences. Vermicompost proportion above 60% was of no use at any stage of life cycle in both the varieties of *Linum*. Germination and yield were further improved when foliar application of vermiwash was integrated with vermicompost for nutrient management when compared with recommended chemical fertilizer treatment and control.

**Conclusion** Bio-efficacy of vermicompost and vermiwash for production of organic Linseed crop has been well established with enhanced yield.

**Keywords** Agriculture · Earthworm · Linseed · Organic farming · Plant growth · Vermicompost

### Introduction

Organic foods have recently gained importance in developed, as well as developing countries with the growing awareness about adverse effects of agricultural chemicals on human health. Demand for organic food has increased worldwide which has led to increased interest in organic agriculture (Folley et al. 1981; Sinha et al. 2009). Crops with a label of 'organically grown' fetch much higher value to farmers in domestic and international market (Lim et al. 2015; Crowder and Reganold 2015). Organic agriculture also promotes ecological conservation due to sustainable use of natural resources (Reganold et al. 1993; Letourneau and Goldstein 2001; Mäder et al. 2002). In cultivation of organically grown crops, chemical usage is excluded at all stages so organic agriculture broadly provides the dual benefit of soil quality improvement and chemical free

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# Modulatory role of vermicompost and vermiwash on growth, yield and nutritional profiling of *Linum usitatissimum* L. (Linseed): a field study

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## Abstract

Vermicompost, recommended inorganic fertiliser, vermiwash and their combinations were used in the present study to know their impact on the germination, growth, yield, oil content and nutritional status in seeds of two varieties of *Linum usitatissimum* L., LC-54 and LC-2063. Eight treatments, in 48 plots with three replicates, were studied and compared with control. Application of vermicompost enhanced growth and yield in both varieties of *Linum*. Vermicompost modulated the ratio of  $\omega$ -3 and  $\omega$ -6 fatty acids in seeds of Linseed. Growing degree days (GDD) indicated the significantly shortened of crop life cycle with vermiwash. Vermiwash particularly increased the yield indices. Fatty acid profile through GC-FID showed the increase in polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA) and saturated fatty acids (SFA) with Integrated Nutrient Management (INM). Different effects on nutritional status of LC-54 and LC-2063 seeds can be attributed to their unique genotypes. INM proved to be nutritionally balanced strategy with enhanced yield leading to better soil health. INM can be hypothesised as a transitional step to the organic agriculture after the green revolution, when compared with recommended inorganic fertiliser treatment and control. In terms of oil yield, highest oil content 34.85% and 33.67% was obtained with Integrated Nutrient Management in both the varieties, whereas treatments with vermicompost and vermiwash produced modulated and most suited ratio of omega-3 and omega-6 in Linseed seeds.

**Keywords** Agriculture · Earthworm · Organic farming · Omega-3 fatty acids

## Introduction

During green revolution, the land of Punjab (India) had been left hungrier due to excessive use of chemical fertilisers (Shiva 1991). Some regions of India had been affected by serious diseases like cancer due to excessive use of chemical fertilisers, insecticides, pesticides etc. (Halder 2009). People are now getting aware about the harmful effects of conventional inorganic produce since past few decades. Thus, the

demand of organic products at consumer outlets has drastically increased (Crowder and Reganold 2015). Organic agriculture promotes human health with ecological conservation and sustainable use of natural resources (Lefourneau and Goldstein 2001; Maeder et al. 2002). Land and water resources need to be restored by adopting traditional or other organic practices (Hardin 2011). In organic produce, no chemicals are used at any stage of agricultural practices; thus, soil health is improved in addition to providing organic foods (Thottathil 2014).

Use of vermicompost as an organic soil amendment is one such practice in current scenario. Studies are going on to establish the positive impact of vermicompost on plant growth under greenhouse conditions or field conditions (Joshi et al. 2013; Zuo et al. 2018). Studies establish that vermicompost has enhanced the morpho-physiological parameters and plant growth in pea (*Pisum sativum*) (Maji et al. 2017), chickpea (*Cicer arietinum*) (Yadav and Garg 2015) and lettuce (Khosravi et al. 2018). Vermicompost addition significantly increased the crop yield indices in groundnut (*Arachis*

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## Research Article

# Synthesis, Characterization and Evaluation of Anticancer Activity of Nanoresveratrol in B16 Melanoma Cell Line

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## ABSTRACT

Resveratrol, a member of the stilbene family, is a naturally occurring polyphenolic compound in grapes and other botanicals. It carries a potential to prevent or treat several chronic diseases, including cancers. Despite various promising health benefits, including chemopreventive and chemotherapeutic benefits against cancer, clinical translation of resveratrol is hampered due to its poor bioavailability, solubility and stability. Here we present the study to prepare nano-formulation of resveratrol for improving the resveratrol profile. Calcium phosphate loaded nanoresveratrol has been synthesized, characterized and its anti-proliferative effects were examined in a B16 murine melanoma cell line. The nanoresveratrol induced anti-cancer effects of nanoresveratrol were directly compared with free resveratrol and chemotherapy drug 5-FU. Nanoresveratrol induced apoptosis in B16 melanoma more efficiently as compared to resveratrol alone and 5-FU. A nuclear staining profile following Hoechst staining of B16 cells is indicative of apoptosis and shows that the anti-cancer effect of nanoresveratrol is due to apoptosis induction. Since antioxidant activity is a hallmark of resveratrol, we also measured the biochemical antioxidant activities of superoxide dismutase (SOD) and catalase, antioxidant enzymes. We found that, concurrent with the anti-cancer activity, the antioxidant activity of nanoresveratrol increased. Collectively, these findings clearly show that nanoresveratrol is superior to free resveratrol in suppressing cell growth in B16 murine melanoma cell line, and that the anti-cancer activity is primarily through apoptosis induction.

**Keywords:** Resveratrol, Nanoresveratrol, Formulation, B16 cell line, Cancer, Melanoma, Chemopreventive, Chemotherapeutic

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## 1. INTRODUCTION

Resveratrol (chemically: 3,5,4'-trihydroxystilbene) a member of stilbene family, is a naturally occurring polyphenolic compound present in grapes, berries, peanuts and red wine. It is a very well-known antioxidant and exhibits various biological effects including anticancer, antiangiogenic, immunomodulatory and cardioprotective activities [1,2,3]. Its beneficial potential in a variety of indications includes the chemoprotective & chemotherapeutic effects in several cancers [4]. Resveratrol has been reported to have a role in reducing the growth of human cancers originating from diverse organs/sites, including breast, cervix, ovary, uterine, kidney, liver, eye, bladder, thyroid, oesophagus, prostate, brain, lung, skin, gastric, colon, head and neck, bone and blood [5-13]. Several studies indicate that resveratrol shows multiple anticancer effects such as protection against tumour initiation and cancer progression, apoptosis, antioxidant, anti-angiogenesis, anti-inflammatory, and antitumor migration [6-13]. Evidence show that resveratrol exerts its effects through different signalling pathways and several molecular players. Various studies report that resveratrol has a range of cellular effects, including cell cycle, invasion/metastasis

angiogenesis, apoptosis and autophagy. Several molecular players such as BCL-2/BAX and AMPK, PI3K/AKT/mTOR, WNT, MEK, ERK pathways mediate resveratrol-induced cellular effects in different cancers [14]. However, the precise mechanisms remain to be delineated. There are several reports indicating the promising effects of resveratrol in treatment of skin cancer [15,16,17]. A recent report shows that resveratrol induces mitochondrial apoptosis in melanoma cell line through downregulating Bcl-2, activating BAX leading to apoptosis [18]. Additionally, this report also showed that pyruvate kinase PKM2 played a role in apoptosis through interacting with Bcl-2.

Despite widely established promising health benefits of resveratrol and its potential as a chemopreventive and chemotherapeutic agent in cancer based on in vitro and preclinical studies against several human cancers, its clinical translation remains challenging. Key challenges associated with the therapeutic application of resveratrol include poor solubility, stability and limited bioavailability [19,20].

Nanotechnology offers a wide range of innovative strategies to address the challenges associated with resveratrol. Plant metabolites can be incorporated into nano structures so that

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# Probing interactions of neurotransmitters with twin tailed anionic surfactant: A detailed physicochemical study

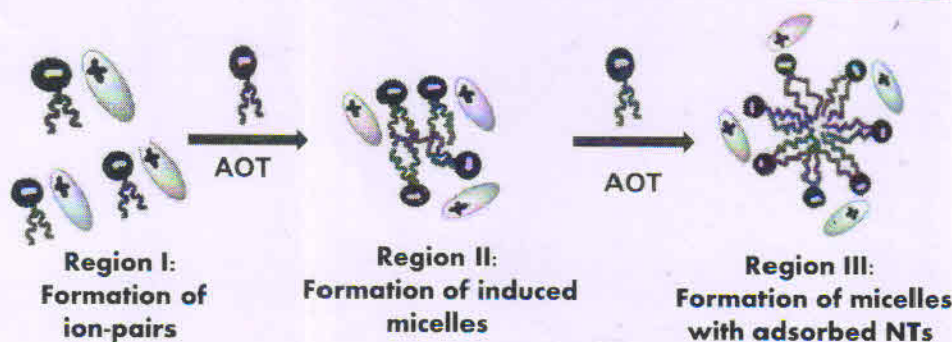


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## GRAPHICAL ABSTRACT



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## ABSTRACT

Keeping in view the role of neurotransmitters (NTs) in central nervous system diseases and in controlling various physiological processes, present study is aimed to study the binding of neurotransmitters (NTs) such as norepinephrine hydrochloride (NE) and serotonin hydrochloride (5-HT) with twin tailed surfactant sodium bis(2-ethylhexyl)sulfosuccinate (AOT). Spectroscopic and electrochemical measurements combined with microcalorimetric measurements were used to characterize the interactions between AOT and NTs. Meteoric modifications to emission profile and absorption spectra of NTs upon addition of AOT are indicative of the binding of NTs with AOT. Distinct interactional states such as formation of ion-pairs, induced and regular micelles with adsorbed NTs molecules have been observed in different concentration regimes of AOT. The formation of ion-pairs from oppositely charged NTs and AOT is confirmed by the reduced absorbance, quenched fluorescence intensity and decrease in peak current ( $i_{pa}$ ) as well as shifts in peak potential ( $E_{pa}$ ) values. The stoichiometry and formation of the NTs–AOT complexes has been judged and the extent of interactions is quantitatively discussed in terms of binding constant ( $K$ ) and free energy of binding ( $\Delta G^\circ$ ). The enthalpy ( $\Delta H^\circ_{mic}$ ) and free energy of micellization ( $\Delta G^\circ_{mic}$ ) for AOT in presence and absence of NTs are determined from the enthalpy curves.

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## 1. Introduction

Mental health issues are now more common in our society and is in the throes of a virtual epidemic of depression whose numbers are quite staggering. Major depressive disorder (MDD) is a



## Electro, Physical &amp; Theoretical Chemistry

## Biamphiphilic Ionic Liquids-Drug Mixtures: Interactional and Morphological Aspects

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The interactional and morphology behavior of mixed system embracing chlorpromazine hydrochloride (CPZ) drug and surface active biamphiphilic ionic liquids (BAILs); 1-hexyl-3-methylimidazolium dodecylsulfate ( $[\text{C}_6\text{mim}][\text{C}_{12}\text{OSO}_3]$ ) and 1-butyl-3-methylimidazolium octylsulfate ( $[\text{C}_4\text{mim}][\text{C}_8\text{OSO}_3]$ ) at pH 7 have been investigated to develop new strategies to use BAILs as carriers of pharmaceutical active compounds. UV-vis absorption spectroscopy and cyclic voltammetry (CV) methods are used to shed light on the foremost interactions governing CPZ + BAILs

mixtures. The higher value of binding constant ( $K_b$ ) and Gibbs free energy change ( $\Delta G$ ) for CPZ +  $[\text{C}_6\text{mim}][\text{C}_{12}\text{OSO}_3]$  mixture, determined from absorbance measurements depict the existence of more attractive interactions than CPZ +  $[\text{C}_4\text{mim}][\text{C}_8\text{OSO}_3]$ . The composition mediated self-assembly of CPZ + BAIL mixed aggregates in bulk has been investigated by small angle neutron scattering (SANS), dynamic light scattering (DLS) and zeta potential measurements.

## Introduction

Chlorpromazine hydrochloride (CPZ) the nitrogen-containing heterocyclic drug, belongs to phenothiazine family. The CPZ widely used as psychopharmacological agent, as a peripheral vasodilator, tranquilizer, to control aggression, anxiety, tension, excitement and psychomotor disturbances in patients suffering from schizophrenia.<sup>[1–3]</sup> However, CPZ has some minor side effects such as movement problems, sleepiness, and low blood pressure upon standing and dry mouth. Along with minor side effects, the major side effects of CPZ are, permanent movement disorder, neuroleptic malignant syndrome and low level of white blood cells.<sup>[4,5]</sup> The amphiphilicity of CPZ is essentially governed by hydrophobic tricyclic ring linked to hydrophilic portion propyl chain having charged amino group which make them good enough molecules to bind membrane systems causing disruption and solubilization, similar to surfactants.<sup>[6,7]</sup>

Due to its amphiphilicity, CPZ forms micelles in solution which would have an effect on the nature of its interactions in biological systems. A delicate balance lies between the stabilization of amphiphiles by micelle formation and the degree of steric repulsion that is encountered.<sup>[8,9]</sup> This balance manifests itself in the size and shape of the micelle. CPZ is often regarded as a model drug for the investigation of interactions between drugs and biological or model membranes. Phenothiazine drugs aggregate in a micelle-like manner with the value of  $N_{\text{agg}}$  (aggregation number) being of the order of 6 to 15.<sup>[10,11]</sup> The binding of CPZ with membranes is an issue of major concern because it depicts the mechanism of drug action. In organisms the pharmacodynamics mechanism involves the interactions of small amount of drug with large amount of biomacromolecules or biomembranes. Thus, the amphiphilic drugs are beneficial for understanding the association between molecular architecture and the physicochemical properties. The biological activity of CPZ is the consequence of its binding with biological molecules.<sup>[12,13]</sup>

In pharmacy, the interactions between drugs and surfactants are important as the undesirable side effects of drugs can be eliminated when the drugs are used along with surfactants as mixed micelles.<sup>[14]</sup> Surfactants molecules mimic the complex biomembrane environments due to their surface and structural properties. The importance of drug + surfactant interactions based on the fact that an extreme amount of medication causes excess stimulation and psychotic illness.<sup>[15,16]</sup> Consequently, targeted drug delivery in body organs is compulsory. Moreover the oppositely charged drug + surfactant mixed system possess great synergism and have been shown to form various molecular assemblies such as, spherical micelles, rods, worm like micelles, bilayer, vesicles, ribbons disks etc.<sup>[17,18]</sup>

There are number of reports published based on the interactions of drugs with surfactants.<sup>[19–24]</sup> Ghosh *et al.* have investigated the interactions of common nonsteroidal anti-

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### 3.4.5 Number of research papers per teacher in the Journals notified on UGC website during the last five years (20)

Title of paper	Name of the author/s	Department of the teacher	Name of journal	Year of publication	ISSN number	Link of the recognition in UGC enlistment of the Journal
Probing interactions of neurotransmitters with twin tailed anionic surfactant: A detailed physio chemical study	R. Kaur, <b>R. Sanan</b> and R. K. Mahajan	Chemical Sciences	J. Colloid Interface Sci.	2016	0021-9797	<a href="https://www.scopus.com/sourceid/26950">https://www.scopus.com/sourceid/26950</a>
[2+2] Cycloaddition Reactions of Butadienyl Ketene with 1,4-Diazabuta-1,3-dienes: Synthesis of Functionalized Butadienyl-4-iminomethyl-azetidin-2-ones and Butenylidene-butadienyl-[2,2'-biazetidine]-4,4'-diones	Deepak Bains, Yogesh Kumar, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	Journal of Heterocyclic Chemistry	2016	1943-5193	<a href="https://www.scopus.com/sourceid/25882">https://www.scopus.com/sourceid/25882</a>
Tandem Aza-Michael and Intramolecular Amidic Ring-Opening Reactions of $\beta$ -Lactams: A Facile Synthesis of 4-Oxo-4, 5-dihydro-1H-pyrroles from $\beta$ -Lactam Synthons, 2	Priyanka Sharma, Maninder Jeet Kaur Mann, Bilash Kuila, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	Synlett	2016	093-65214	<a href="https://www.scopus.com/sourceid/26491">https://www.scopus.com/sourceid/26491</a>
Self-assembled Nano rods of Bay functionalized perylenediimide: Cu <sup>2+</sup> based 'turn on' response for INH, complementary NOR/OR and TRANSFER logic functions and fluorosolvatochromism,	Prabhpreet Singh, Kapil Kumar, <b>Gaurav Bhargava</b> and Subodh Kumar	Chemical Sciences	Journal of Materials Chemistry C	2016	2050-7534	<a href="https://www.scopus.com/sourceid/21100229207">https://www.scopus.com/sourceid/21100229207</a>
Self-assembled vesicle and rod-like aggregates of functionalized perylene diimide: Reaction based near-IR intracellular fluorescent probe for selective detection of palladium,	Prabhpreet Singh, Lalit Singh Mittal, Vanita Vanita, Rahul Kumar, <b>Gaurav Bhargava</b> , Amandeep Walia, and Subodh Kumar	Chemical Sciences	J. Mater. Chem. B	2016	2050-7518	<a href="https://www.scopus.com/sourceid/21100199807">https://www.scopus.com/sourceid/21100199807</a>
A Facile and Chemoselective Synthesis of 1,4-Benzodiazepin-2-ones and Dienyl Thiazolidin-4-ones",	Bilash Kuila, Yogesh Kumar, Dinesh Mahajan, Kapil Kumar, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	RSC Advances	2016	2046-2069	<a href="https://www.scopus.com/sourceid/21100199840">https://www.scopus.com/sourceid/21100199840</a>


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Cu(I) mediated Kinugasa Reactions of $\alpha,\beta$ -unsaturated Nitrones: A Facile, Diastereoselective Route to 3-(Hydroxy/bromo)methyl-1-aryl-4-(styryl)azetidin-2-ones"	Yogesh Kumar, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	New Journal of Chemistry	2016	1144-0546	<a href="https://www.scopus.com/sourceid/24824">https://www.scopus.com/sourceid/24824</a>
, "Highly Chemo and Diastereoselective Synthesis of Diaza-bicyclo[3.2.0]heptan-7-ones, Pyrrolidines and Aziridinopyrrolidine"	Yogesh Kumar, Bilash Kuila Prabhpreet Singh and <b>Gaurav Bhargava</b>	Chemical Sciences	Arkivoc	2016	15517012	<a href="https://www.scopus.com/sourceid/22182">https://www.scopus.com/sourceid/22182</a>
*, Recent developments in the synthesis of condensed- $\beta$ -lactams",	Yogesh Kumar, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	RSC Advances	2016	2046-2069	<a href="https://www.scopus.com/sourceid/21100199840">https://www.scopus.com/sourceid/21100199840</a>
A facile and highly chemoselective synthesis of 1-thia-3a,6-diaza-benzo[e]azulen-3-ones by 7-exo-dig/trig halocyclizations,"	Bilash Kuila, Dinesh Mahajan, Prabhpreet Singh and <b>Gaurav Bhargava</b>	Chemical Sciences	RSC Advances	2016	2046-2069	<a href="https://www.scopus.com/sourceid/21100199840">https://www.scopus.com/sourceid/21100199840</a>
"Diphenylpyrimidinone-salicylideneamines – New ESIPT based AIEgens with applications in latent fingerprinting"	Prabhpreet Singh, Harminder Singh, Rashmi Sharma, <b>Gaurav Bhargava</b> , Subodh Kumar,	Chemical Sciences	Journal of Material Chemistry C	2016	2050-7534	<a href="https://www.scopus.com/sourceid/21100229207">https://www.scopus.com/sourceid/21100229207</a>
Nanomolar Cu <sup>2+</sup> Detection in Water Based on Disassembly of AIEgen: Applications in Blood Serum, Cell Imaging and Complex Logic Circuits,	Prabhpreet Singh, Harminder Singh, Vanita Vanita, Rashmi Sharma, <b>Gaurav Bhargava</b> , Subodh Kumar	Chemical Sciences	ChemistrySelect	2016	2365-6549	<a href="https://www.scopus.com/sourceid/21100850505">https://www.scopus.com/sourceid/21100850505</a>
"To kill many birds with one stone': Addressing half-adder, half-subtractor, demultiplexer, 2-to-4 decoder, comparator, keypad lock with unimolecular system"	Prabhpreet Singh, Harminder Singh, <b>Gaurav Bhargava</b> , Subodh Kumar,	Chemical Sciences	Sensors and Actuators B: Chemical	2017	0925-4005	<a href="https://www.scopus.com/sourceid/25236">https://www.scopus.com/sourceid/25236</a>
"Ionic Self-assembled Platform of Perylenediimide-Sodium dodecylsulfate for Detection of Spermine in Clinical Samples	Prabhpreet Singh, Lalit Singh Mittal, <b>Gaurav Bhargava</b> , Subodh Kumar	Chemical Sciences	Chemistry–An Asian Journal	2017	1861-471X	<a href="https://www.scopus.com/sourceid/4800156201">https://www.scopus.com/sourceid/4800156201</a>



Vermicompost & Vermiwash as a supplement to improve seedlings, plant growth and yield in <i>Linum usitatissimum</i> L. for organic agriculture.	Cinny Makkar, Jaswinder Singh & <b>Chander Parkash</b>	Chemical Sciences	International Journal of Recycling of Organic Waste in Agriculture.	2017	2251-7715	Int J Recycl Org Waste Agricult (2017) 6:203-218 DOI 10.1007/s40093-017-0168-4 <a href="https://www.scopus.com/sourceid/21100395913">https://www.scopus.com/sourceid/21100395913</a>
"Perylene diimide-based organic $\pi$ -motif for differentiating $CN^-$ and $F^-$ ions by electron-transfer and desilylation mechanisms: applications to complex logic circuits,"	P Singh, LS Mittal, H Singh, <b>G Bhargava</b> , S Kumar	Chemical Sciences	New Journal of Chemistry	2017	1144-0546	<a href="https://www.scopus.com/sourceid/24824">https://www.scopus.com/sourceid/24824</a>
Spectroscopic Characterization of Humic acids extracted from different types of Soils of Punjab	<b>Naithani Vandana</b> ; Singh, Anirudh P; Nautiyal, M.K.	Chemical Sciences		2017	0019-638X	<a href="http://www.indian-soil-society.org/ugc_admin_journal_report.aspx.htm">Journal of the indian soil science society ugc admin journal report.aspx.htm</a>
Characterization of Minerals present in the Agricultural Soil	<b>Naithani Vandana</b> ; Singh, Anirudh P., Nautiyal, M.K.	Chemical Sciences	International Journal of Basic and Applied Agricultural Research	2017	0972-8813	<a href="http://www.indian-soil-society.org/ugc_admin_journal_report.aspx.htm">ugc admin journal report.aspx.htm</a>
Copper (I)-Catalyzed Regioselective C-H Amination of N-Pyridyl Imines Using Azidotrimethylsilane and TBHP: A One-Pot, Domino Approach to Substituted Imidazo [4, 5-b] pyridines	P Singh, LS Mittal, H Singh, <b>G Bhargava</b> , S Kumar	Chemical Sciences	Chemistryselect	2017	2365-6549	<a href="https://www.scopus.com/sourceid/21100850505">https://www.scopus.com/sourceid/21100850505</a>
"Fluorometric differential detection of $Zn^{2+}$ and $Cu^{2+}$ by picolylamine appended pyrimidinone-based receptor: Application in mimicking TRANSFER and INH logic gate"	Prabhpreet Singh, Sanjeev Dhawan, Parvesh Singh, Harminder Singh, Rashmi Sharma, <b>Gaurav Bhargava</b> , Subodh Kumar	Chemical Sciences	Journal of Photochemistry and Photobiology A: Chemistry	2018	1010-6030	<a href="https://www.scopus.com/sourceid/26966">https://www.scopus.com/sourceid/26966</a>
Self-assembled small molecule based fluorescent detection of serum albumin proteins: Clinical detection and cell imaging"	Prabhpreet Singh, Lalit Singh Mittal, S Kaur, S Kaur, <b>Gaurav Bhargava</b>	Chemical Sciences	Sensors and Actuators B: Chemical	2018	0925-4005	<a href="https://www.scopus.com/sourceid/25236">https://www.scopus.com/sourceid/25236</a>

  
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Controllable supramolecular self-assemblies (rods-wires-spheres) and ICT/PET based perylene probe for palladium detection in solution and solid state"	Prabhpreet Singh, Kapil Kumar, <b>Gaurav Bhargava</b> , Subodh Kumar	Chemical Sciences	New Journal of Chemistry	2018	1144-0546	<a href="https://www.scopus.com/sourceid/24824">https://www.scopus.com/sourceid/24824</a>
Modulatory role of vermicompost and vermiwash on growth, yield and nutritional profiling of Linum usitatissimum L. (Linseed): a field study	Cinny Makkar, Jaswinder Singh & Chander Parkash	Chemical Sciences	Environmental Science and Pollution Research	2018	0944-1344E-1614-7499	Environmental Science and Pollution Research (2018) <a href="https://doi.org/10.1007/s11356-018-3845-6">https://doi.org/10.1007/s11356-018-3845-6</a> <a href="https://www.scopus.com/sourceid/23918">https://www.scopus.com/sourceid/23918</a>
"Transition Metal Catalysed [3+2+2] Cycloaddition Reactions,	Bilash Kuila, Maninderjeet kaur, Prabhpreet Singh and <b>Gaurav Bhargava</b>	Chemical Sciences	European Journal of Organic Chemistry	2018	1099-0690	<a href="https://www.scopus.com/sourceid/25853">https://www.scopus.com/sourceid/25853</a>
Facile and Chemoselective Acetylenic Ester Promoted Tandem Ring opening and cyclizations of Dienyl Thiazolidin-4-ones: Synthesis of Functionalized Pyridine-2-Carboxylates,	Bilash Kuila, Kapil Kumar, Dinesh Mahajan, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	Synlett	2018	093-65214	<a href="https://www.scopus.com/sourceid/26491">https://www.scopus.com/sourceid/26491</a>
Quadruple-signaling (PET, ICT, ESIPT, -C=N-rotation) mechanism-based dual chemosensor for detection of Cu <sup>2+</sup> and Zn <sup>2+</sup> ions: TRANSFER, INH and complimentary OR/NOR logic circuits,	Harminder Singh, <b>Gaurav Bhargava</b> , Subodh Kumar, Prabhpreet Singh	Chemical Sciences	Journal of Photochemistry and Photobiology A: Chemistry	2018	1010-6030	<a href="https://www.scopus.com/sourceid/26966">https://www.scopus.com/sourceid/26966</a>
"Microstructural (self-assembly) and optical based discrimination of Hg <sup>2+</sup> , CN <sup>-</sup> and Hg(CN) <sub>2</sub> ion-pair; Hg <sup>2+</sup> promoted-ESIPT assisted guanylation of thiourea"	Prabhpreet Singh, Harminder Singh, <b>Gaurav Bhargava</b> , Subodh Kumar	Chemical Sciences	Sensors & Actuators: B. Chemical	2018	0925-4005	<a href="https://www.scopus.com/sourceid/25236">https://www.scopus.com/sourceid/25236</a>
"Dissymmetric Bay Functionalized Perylene diimides"	Prabhpreet Singh, <b>Gaurav Bhargava</b> , Subodh Kumar	Chemical Sciences	Synlett	2018	093-65214	<a href="https://www.scopus.com/sourceid/26491">https://www.scopus.com/sourceid/26491</a>
"AIE+ESIPT based red fluorescent aggregates for visualization of latent fingerprints" New	Harminder Singh, Rashmi Sharma, <b>Gaurav Bhargava</b> , Subodh Kumar, Prabhpreet Singh	Chemical Sciences	New Journal of Chemistry	2018	1369-9261	<a href="https://www.scopus.com/sourceid/24824">https://www.scopus.com/sourceid/24824</a>



Pyrimidinone-hydroxyquinoline conjugate for sequential recognition of $Zn^{2+}/Cd^{2+}, Cu^{2+}$ and its ensemble with $Cd^{2+}$ for secondary sensing of ATP in water: Application in OR, INH logic gate and 'Set-Reset' memorized device"	Prabhpreet Singh, Harminder Singh, Rashmi Sharma, <b>Gaurav Bhargava</b> , Subodh Kumar,	Chemical Sciences	chemistryselect	2018	2365-6549	<a href="https://www.scopus.com/sourceid/21100850505">https://www.scopus.com/sourceid/21100850505</a>
"Thermal [2+2] Cycloaddition of Butadienylketene with Imines/1-Azadienes: A One Pot, Domino Approach for $\alpha$ -Alkylidene- $\beta$ -lactams and their computational studies and Antimicrobial evaluation"	Yogesh Kumar, Preet Mohinder Singh Bedi, Prabhpreet Singh, Adebayo A. Adeniyi, Ashona Singh-Pillay, Parvesh Singh and <b>Gaurav Bhargava</b>	Chemical Sciences	Chemistryselect	2018	2365-6549	<a href="https://www.scopus.com/sourceid/21100850505">https://www.scopus.com/sourceid/21100850505</a>
Phytoremediation of Pulp and Paper Mill Effluents by <i>Salvinia molesta</i> and its comparison with Nanoparticles Inclusive Phytoremediation.	Punit Bhardwaj, Jyotsna Kaushal, <b>Vandana Naithani</b> , Anirudh P Singh	Chemical Sciences	International journal of basic and applied research	2018	22493352 E-ISSN: 22780505	Welcome to UGC, New Delhi, India
Microwave and conventional processing of niobium and manganese doped lanthanum germanate based apatites	Chetan sharma; kanchan L.Singh; Anirudh P.Singh; <b>vandana Naithani</b> ; Payal sharma; Sonia Mago and Ravinder Kumar chadha	Chemical Sciences	<i>Materials Chemistry and Physics</i>	2018	DOI: 10.1016/j.m	<a href="https://www.scopus.com/sourceid/17800">https://www.scopus.com/sourceid/17800</a>
Biamphiphilic Ionic Liquids-Drug Mixtures: Interactional and Morphological Aspects	R. Vashishat, <b>R. Sanan</b> , D. Ray, V. K. Aswal and R.K. Mahajan	Chemical Sciences	Chemistry Select	2018	2365-6549	<a href="https://www.scopus.com/sourceid/21100850505">https://www.scopus.com/sourceid/21100850505</a>
Regioselective Copper(I)-Catalyzed Ullmann Amination of Halopyridyl Carboxylates using Sodium Azide: A Route for Aminopyridyl Carboxylates and their Transformation to Pyrido[2, 3-d]pyrimidin-4(1H)-ones	Nisha, Chetan Sharma, <b>rupesh Kumar</b> and Yogesh Kumar	Chemical Sciences	ChemistrySelect	2018	2365-6549	<a href="https://www.scopus.com/sourceid/21100850505">https://www.scopus.com/sourceid/21100850505</a>



Concentrated solar radiation promoted unconventional greener approach: solvent-free benign synthesis of functionalized benzimidazoles	Simran Harsh, Mohamad Yusuf, Rohit Sharma, Yogesh Kumar and <b>Rupesh Kumar</b>	Chemical Sciences	ARKIVOC, <b>2018</b> , VII, 119-130.	2018	1551-7012	<a href="https://www.scopus.com/sourceid/22182">https://www.scopus.com/sourceid/22182</a>
Influence of microwave processing and sintering temperature on the structure and properties of Sr/Zr doped hydroxyapatite	Ravinder Kumar Chadha, Anirudh P. Singh, Kanchan L. Singh, Chetan Sharma, <b>Vandana Naithani</b>	Chemical Sciences	<i>Materials Chemistry and Physics</i>	2019	0254-0584	<a href="https://www.scopus.com/sourceid/17800">https://www.scopus.com/sourceid/17800</a>
Design and Applications of Small Molecular Probes for Calcium Detection	<b>Roopa</b> , Naresh Kumar, Manoj Kumar and Vandana Bhalla	Chemical Sciences	Chemistry-An Asian Journal	2019	1861-471X	<a href="https://www.scopus.com/sourceid/4800156201">https://www.scopus.com/sourceid/4800156201</a>
Coronene diimide-based self-assembled (fibre-to-disc) fluorescent aggregates for visualization of latent fingerprint	Kapil Kumar, Harminder Singh, Vanita Vanita, Ramesh Singh, K.B. Joshi, <b>Gaurav Bhargava</b> , Subodh Kumar, Prabhpreet Singh,	Chemical Sciences	Sensors and Actuators B: Chemical	2019	9254005	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Direct Conversion of Carboxylic Acids to Various Nitrogen-Containing Compounds in the One-Pot Exploiting Curtius Rearrangement	Arun Kumar, Naveen Kumar, Ritika Sharma, <b>Gaurav Bhargava</b> , Dinesh Mahajan	Chemical Sciences	Journal of Organic Chemistry	2019	0022-3263 (print); 1520-6904 (web)	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Transition metal catalyzed [6 + 2] cycloadditions,	Amit Anand, Prabhpreet Singh, Vipin Kumar and <b>Gaurav Bhargava</b>	Chemical Sciences	RSC Advances	2019	2046-2069	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Synthesis, Characterization and Evaluation of Anticancer Activity of Nanoresveratrol in B16 Melanoma Cell Line	Reena Arora & <b>Chander Parkash</b>	Chemical Sciences	Journal of Drug Delivery and Therapeutics	2019	2250-1177	Journal of Drug Delivery & Therapeutics. 2019; 9(4-A):625-631 <a href="http://dx.doi.org/10.22270/jddt.v9i4-A.3521">http://dx.doi.org/10.22270/jddt.v9i4-A.3521</a> <a href="https://ugccare.unipune.ac.in/Apps1/User/WebA/SearchList">https://ugccare.unipune.ac.in/Apps1/User/WebA/SearchList</a>



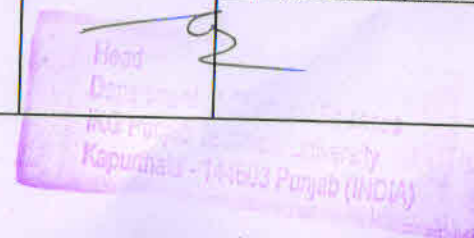


Perylene diimide-Cu <sup>2+</sup> based fluorescent nanoparticles for the detection of spermine in clinical and food samples: a step toward the development of a diagnostic kit as a POCT tool for spermine	Kapil Kumar, Sandeep Kaur, Satwinderjeet Kaur, <b>Gaurav Bhargava</b> , Subodh Kumar and Prabhpreet Singh	Chemical Sciences	J. Mater. Chem. B	2019	2050-7518	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Estimation of Genetic Variability in <i>Jatropha Curcas</i> L. Genotypes for Vegetative Traits and Seed yield	Bhawesh Joshi <sup>1</sup> , MK Nautiyal, Leela Bhatt, Vikas Mangal, <b>Vandana Naithani</b> ,	Chemical Sciences	<i>Chem Sci Rev Lett</i>	2019	2278-6783	UGC Approved Journal (No.45864, 2017-2018).
Influence of microwave processing and sintering temperature on the structure and properties of Sr/Zr doped hydroxyapatite	Ravinder Kumar Chadha, Anirudh P. Singh, Kanchan L. Singh, Chetan Sharma, <b>Vandana Naithani</b>	Chemical Sciences	<i>Materials Chemistry and Physics</i>	2019	0254-0584	<a href="https://www.scopus.com/sourceid/17800">https://www.scopus.com/sourceid/17800</a>
Chlorophyll triggered one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones via photo induced electron transfer reaction	Simran Harsh, Sanjay Kumar, Rohit Sharma, Yogesh Kumar and <b>Rupesh Kumar</b>	Chemical Sciences	Arabian Journal of Chemistry, <b>2020</b> , 13(3), 4720-4730.	2020	1878-5352	<a href="https://www.scopus.com/sourceid/19400158709">https://www.scopus.com/sourceid/19400158709</a>
Recent development in the synthesis of pyrrolin-4-ones/pyrrolin-3-ones	Priyanka Sharma, <b>Rupesh Kumar</b> , <b>Gaurav Bhargava</b>	Chemical Sciences	Journal of Heterocyclic Chemistry, 2020, 57(12), 4115-4135.	2020	1943-5193	<a href="https://www.scopus.com/sourceid/25882">https://www.scopus.com/sourceid/25882</a>
Near-IR discriminative detection of H <sub>2</sub> S and Cysteine with 7-nitro-2,1,3-benzoxadiazole- <i>perylene</i> diimide conjugate in water, live cells and solid state: Mimicking IMP, INH and NOR/OR complimentary logic	Poonam Sharma, Kapil Kumar, Sandeep Kaur, Satwinderjeet Kaur, <b>Gaurav Bhargava</b> , Subodh Kumar, Prabhpreet Singh	Chemical Sciences	Journal of Photochemistry and Photobiology A: Chemistry	2020	1010-6030	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
A multifunctional perylenediimide-based dual-analyte chemodosimeter for specific and rapid detection of H <sub>2</sub> S and Pd(0) in water, biofluids, live cells and solid state	Kapil Kumar, Sandeep Kaur, Satwinderjeet Kaur, <b>Gaurav Bhargava</b> , Subodh Kumar, Prabhpreet Singh	Chemical Sciences	Journal of Photochemistry and Photobiology A: Chemistry	2020	1010-6030	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Nickel (0) Catalyzed (3+2) Cycloadditions of Bis-alkylidenecyclopropanes with Diazenes: A Facile Synthesis of Functionalized Pyrrolidine-1,2-Dicarboxylates	Bilash Kuila, Rayees Ahmad, Dinesh Mahajan, Prabhpreet Singh, <b>Gaurav Bhargava</b>	Chemical Sciences	Synlett	2020	0936-5214 (print) 1437-2096 (web)	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>

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Self-assembled nanofibers of perylene diimide for detection of hypochlorite in water, bio-fluids and solid state: Exogenous and endogenous bioimaging of hypochlorite in cells	Kapil Kumar, Sandeep Kaur, Satwinderjeet Kaur, <b>Gaurav Bhargava</b> , Subodh Kumar and Prabhpreet Singh	Chemical Sciences	Journal of Materials Chemistry B	2020	2050-7518	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Rhodium-catalysed chemo- and regio-selective [3 + 2+2] cycloadditions of bis(methylenecyclopropanes) and alkynes: Synthesis of spirocyclic 5–7 condensed cycloheptenes,	Bilash Kuila, Priyanka Sharma, Dinesh Mahajan, Prabhpreet Singh and <b>Gaurav Bhargava</b>	Chemical Sciences	Synthetic Communications	2020	0039-7911 (print); 1532-2432 (web)	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
3-Butadienyl- $\beta$ -lactams: A useful synthon for functionalized heterocycles,	<b>Gaurav Bhargava</b> , Maninderjeet K. Mann and Rayees Ahmad Naikoo,	Chemical Sciences	Synthetic Communications	2020	0039-7911 (print); 1532-2432 (web)	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>
Comparison of microwave and conventionally sintered manganese and niobium doped lanthanum germanate based apatites by Micro Raman Spectroscopy.	Chetan Sharma, Anirudh P. Singh, Kanchan L Singh, Payal Sharma; Sonia mago; <b>Vandana Naithani</b> ; Ravinder Chadha	Chemical Sciences	<i>Materials Chemistry and Physics</i>	2020	0254-0584	<a href="https://www.scopus.com/sourceid/17800">https://www.scopus.com/sourceid/17800</a>
Effect of Microwave and Conventional processing techniques on mechanical properties of Strontium substituted hydroxyapatite	Ravinder Kumar Chadha, Anirudh P. Singh, Kanchan L. Singh, Chetan Sharma, <b>Vandana Naithani</b>	Chemical Sciences	<i>Ceramics International</i>	2020	0272-8842 (print)	<a href="https://www.scopus.com/sourceid/21522">https://www.scopus.com/sourceid/21522</a>
Bioactivity of microwave and conventionally synthesized 70Sr-HA.xZn (30-x)Si composites.	Chetan sharma; kanchan L.Singh; Anirudh P.Singh; Vandana Naithani	Chemical Sciences	<i>Material Chemistry and Physics</i>	2021	0254-0584	<a href="https://www.scopus.com/sourceid/17800">https://www.scopus.com/sourceid/17800</a>
Development of a sustainable ternary magnetic nanocomposite GCN/ for efficient and synergistic photodegradation of Rhodamine B under solar irradiation: kinetic and mechanistic studies	Monika Thakur, Harminder Singh, Jaspreet Kaur Rajput & <b>Rupesh Kumar</b>	Chemical Sciences	International Journal of Environmental Analytical Chemistry, 2021.	2021	0306-7319	<a href="https://www.scopus.com/sourceid/24012">https://www.scopus.com/sourceid/24012</a>
Recent developments in the synthesis of tricyclic condensed pyrimidinones	Rayees Ahmad Naikoo, <b>Rupesh Kumar</b> , Vipam Kumar & <b>Gaurav Bhargava</b>	Chemical Sciences	Synthetic Communications, 2021.	2021	0039-7911	<a href="https://www.scopus.com/sourceid/26509">https://www.scopus.com/sourceid/26509</a>





7-Endo-trig Pictet–Spengler type cyclization of 5-alkylidene/arylidene-amino-3H-pyrimidin-4-ones: An efficient and diastereoselective synthesis of pyrimido[4,5-b] [1,4]benzodiazepines	Rayees Ahmad Naikoo, <b>Rupesh Kumar</b> , Parvesh Singh & <b>Gaurav Bhargava</b>	Chemical Sciences	Synthetic Communications, 2021, 51(8), 1232-1241.	2021	0039-7911	<a href="https://www.scopus.com/sourceid/26509">https://www.scopus.com/sourceid/26509</a>
Assessment of heavy metal contamination and its effect on earthworms in different types of soils	F. Verma, S. Singh, J. Singh, S. Singh Dhaliwal, <b>C. Parkash</b> , V. Kumar and R. Kumar	Chemical Sciences	International Journal of Environmental Science and Technology	2021	1735-1472	International Journal of Environmental Science and Technology <a href="https://doi.org/10.1007/s13762-021-03297-z">https://doi.org/10.1007/s13762-021-03297-z</a> <a href="https://www.scopus.com/sourceid/4000148503">https://www.scopus.com/sourceid/4000148503</a>
Beyond zinc coordination: Bioimaging applications of Zn(II)-complexes Coordination Chemistry Reviews	Naresh Kumar, <b>Roopa</b> , Vandana Bhalla and Manoj Kumar	Chemical Sciences	Coordination Chemistry Reviews	2021	0010-8545	<a href="https://www.scopus.com/sourceid/23470">https://www.scopus.com/sourceid/23470</a>
Xanthene-based Fluorescence Turn-on Probe for Highly Acidic pH Range in Aqueous Solution	Bhanu Priya, Vibha Mahajan, Naresh Kumar and <b>Roopa</b>	Chemical Sciences	Journal of Fluorescence	2021	10530509	<a href="https://www.scopus.com/sourceid/25282">https://www.scopus.com/sourceid/25282</a>
Oxa-Michael addition reactions of 3-hydroxy-2-azetidinones: synthesis of 1,3,4-trisubstituted-2-azetidinones	Priyanka Sharma, Maninderjeet Kaur Mann, <b>Gaurav Bhargava</b>	Chemical Sciences	Letter in organic chemistry	2021	1570-1786 (print); 1875-6255 (web)	<a href="https://www.scopus.com/sources.uri">https://www.scopus.com/sources.uri</a>

