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11. Administrative experience, if any : nil

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14. Membership of professional bodies : nil

15. Upgradation courses : nil

16. Soft skill/Life skill development Programs : nil

17. Technical training : nil

18. Paper publication : Total 18 publications

1. Highly efficient synthesis of amides from ketoximes using trifluoromethane sulphonic anhydride Authors: Rajesh G. Kalkhambkar,* **Hemantkumar M. Savanur**. RSC Advance, 2015, 74, 60106-60113. **IF: 3.070**

2. $Pd(OAc)_2$ Catalyzed Homocoupling of Arenediazonium Salts in Ionic Liquids: Synthesis of ymmetrical Biaryls. Authors: **Hemantkumar M. Savanur**, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Tetrahedron Lett. 2016, 57, 663-667. **IF: 2.275**

3. [bmim(SO_3H)][OTf]/ [bmim][X] and $Zn(NTf_2)_2$/[bmim][X] (X = PF_6 and BF_4); Efficient Catalytic Systems for the Synthesis of Tetrahydro- pyrimidin-ones (-thiones) via the Biginelli Reaction. Authors: **Hemantkumar M. Savanur**, Rajesh G. Kalkhambkar,* Gopalakrishnan Aridoss, Kenneth K. Laali* Tetrahedron Lett. 2016, 57, 3029-3035. **IF: 2.275**

4. Piperidine-appended Imidazolium Ionic Liquid as Task Specific Basic-IL for Suzuki and Heck Reactions and for Tandem Wittig-Suzuki, Wittig-Heck, Horner-Emmons-Suzuki, and Horner-Emmons-Heck Protocols. Authors: **Hemantkumar M. Savanur**, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Appl. Cat. A: General. 2017, 543, 150-161. **IF: 5.006**

5. Libraries of C-5 Substituted Imidazoles and Oxazoles by Sequential Van Leusen (VL)–Suzuki, VL–Heck and VL–Sonogashira in Imidazolium-ILs with Piperidine-Appended-IL as Base. Authors: **Hemantkumar M. Savanur**, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Eur. J. Org. Chem. 2018, 38, 5285-5288. **IF: 2.889**

6. Synthesis and molecular modeling studies of coumarin-and 1-aza-coumarin-linked miconazole analogues and their antifungal activity. Authors: **Hemantkumar M.**

Savanur, Geeta M. Pawashe, Kang Min Kim, Rajesh G. Kalkhambkar,* ChemistrySelect. 2018, 33, 9648-9653. **IF: 1.980**

7. Click Chemistry Inspired Design, Synthesis and Molecular Docking Studies of Coumarin, Quinolinone Linked 1,2,3-Triazoles as Promising Anti-microbial Agents. Authors: **Hemantkumar M. Savanur**, Krishna N. Naik, Shailaja M. Ganapathi, Kang Min Kim, Rajesh G. Kalkhambkar,* ChemistrySelect, 2018, 19, 5296-5303. **IF: 1.980**

8. Facile Access to Diverse Libraries of Internal Alkynes via Sequential iododediazoniation/Decarboxylative Sonogashira Reaction in Imidazolium ILs without Ligand or Additive Authors: Pavankumar Prabhala, **Hemantkumar M. Savanur**, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Eur. J. Org. Chem. 2019, 33, 2061-2064. **IF: 2.889**

9. Synthesis of Diverse Libraries of Carboxamides via Chemoselective N-Acylation of Amines by Carboxylic acids Employing Brønsted Acidic IL [bmim(SO_3H)][OTf] Authors: **Hemantkumar M. Savanur**, Pavankumar Prabhala, Shruti S. Malunavar, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Tetrahedron Lett. 2019, (60)42, 151-159. **IF: 2.275**

10. 1-Aryltriazenes in the Suzuki, Heck, and Sonogashira Reactions in Imidazolium-ILs, with [BMIM(SO_3H][OTf] or $Sc(OTf)_3$ as Promoter, and $Pd(OAc)_2$ or $NiCl_2$. glyme as Catalyst. Authors:Suraj Sutar, **Hemantkumar M. Savanur**, Shruti S. Malunavar, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Eur. J. Org. Chem. 2019, 35, 6088-6093. **IF: 2.889**

11. Facile access to libraries of diversely substituted 2-aryl-benzoxazoles/ benzothiazoles from readily accessible aldimines via cyclization/cross coupling in imidazolium-ILs with $Pd(OAc)_2$ or $NiCl_2$(dppp) as catalyst. Authors: Shruti S. Malunavar, Suraj Sutar, **Hemantkumar M. Savanur**, Rajesh G. Kalkhambkar,* Kenneth K. Laali* Tetrahedron Lett. 2020, 61, 151509. **IF: 2.275**

12. Synthesis and Molecular Modelling Studies of Coumarin and 1-Aza-Coumarin Linked Miconazole Analogues and Their Antimicrobial Properties. Authors: Suraj M. Sutar, **Hemantkumar M. Savanur**, Shruti S. Malunavar,Geeta M. Pawashe, Gopalakrishnan Aridoss,Kang Min Kim,* Jin Young Lee, Rajesh G. Kalkhambkar,* ChemistrySelect. 2019, 31, 1322-1330. **IF: 1.980**

13. Design of new imidazole-derivative dye having donor-Π-acceptor moieties for highly efficient organic-dye-sensitized solar cells Authors: Shashikant walki, Lohit Naik,* **Hemantkumar M Savanur,** Yoganand K. C, Soniya Naik, Ravindra M. K, G. H Malimath and K. M. Mahadevana, Optik. 2019, 208, 164074. **IF: 2.187**

14. Facile one pot synthesis of 3-aryl Coumarins using Phenyl acetic acids and Salicylaldehydes in Ionic liquids & Conventional solvents: Alkyne formation using Sonogashira approach. Authors: Pavankumar Prabhala, **Hemantkumar M. Savanur**, Suraj M Suar, Shrui S. Malunavar, Rajesh G. Kalkhambkar,* Kenneth K. Laali*

15. Synthesis, molecular modelling studies and antimicrobial activity of Coumarin and 1-Azacoumarin linked 1,2,3- Triazole Authors: Suraj Sutar, **Hemantkumar M. Savanur**, Chidanand Patil, Gopalkrishna Aridoss, Kang Min Kim, Rajesh G. Kalkhambkar,* Chem. Data Coll. 2020, 28, 100480. **IF: 0.215**

16. Palladium catalyzed electrophilic C2-arylation of azoles by aryltriazenes in ionic liquid promoted by acidic IL Authors: Suraj M. Sutar, **Hemantkumar M. Savanur**,Shruti S. Malunavar, Geeta M. Pawashe, Gopalakrishnan Aridoss, Rajesh G. Kalkhambkar, * ChemistrySelect. 2020 . **IF: 1.980**

17. Ionic liquid catalyzed Ritter reaction/Pd-catalyzed directed Ortho-arylation; facile access to diverse libraries of biaryl-amides from Aryl-nitries Authors: Suraj M. Sutar, **Hemantkumar M. Savanur**, Shruti S. Malunavar, Geeta M. Pawashe, Gopalakrishnan Aridoss,Rajesh G. Kalkhambkar, * Tetrahedron Lett. 2020, 152553. **IF: 2.275**

18. A highly selective and sensitive thiophene substituted 1,3,4-oxadiazole based turn-off fluorescence chemosensor for Fe^{2}+and turn on fluorescence chemosensor for Ni^{2+} and Cu^{2+} detection Lohit Naik,[a] C.V.Maridevarmath,[b] M.S.Thippeswamy,[c] **Hemantkumar M.Savanur,[d]** Imtiyaz Ahamed M.Khazi,[e], G.H.Malimath,[a] Materials Chemistry and Physics, 2021. **IF: 3.408**

19. Paper Presentation : 02

i. National seminar on "Recent trends in chemical and material science" (12/2017 to 14/2017) Presented research paper poster in the conference on "Libraries of C-5 Substituted Imidazoles and Oxazoles by Sequential Van Leusen (VL)–Suzuki, VL–Heck and VL–Sonogashira in Imidazolium-ILs with Piperidine-Appended-IL as Base" Department of Chemistry, Kuvempu University, Kadur.

ii. Indian council of Chemist 37th annual national conference (2018) Presented research paper poster in the conference on "Synthesis and Molecular Modeling Studies of Coumarin-and1-Aza-Coumarin-Linked Miconazole Analogues and Their Antifungal Actiity" Department of Chemistry, NITK, Surathkal, Mangalore.

20. Research Guidance : nil

21. Other Publications **:** nil

22. Book Publication **:** nil

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27. Curriculum Design : nil

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29. Committee membership : nil

30. Conference participation **: 02**

i. National seminar on "Recent trends in chemical and material science" (12/2017 to 14/2017) Presented research paper poster in the conference on "Libraries of C-5 Substituted Imidazoles and Oxazoles by Sequential Van Leusen (VL)–Suzuki, VL–Heck and VL–Sonogashira in Imidazolium-ILs with Piperidine-Appended-IL as Base" Department of Chemistry, Kuvempu University, Kadur.

ii. Indian council of Chemist 37 th annual national conference (2018) Presented research paper poster in the conference on "Synthesis and Molecular Modeling Studies of Coumarin-and1-Aza-Coumarin-Linked Miconazole Analogues and Their Antifungal Actiity" Department of Chemistry, NITK, Surathkal, Mangalore.

I, Dr. Hemantkumar M Savanur, working as an Assistant Professor in P. G. Department and Research in Chemistry, KLE's P.C. Jabin Science College, Hubballi. As a leader in learning and teaching, I have an opportunity to build and share new knowledge and application with others to advance the overall sector of higher education of students. Hence, I strive to make an outstanding contribution to student learning, engagement and the overall student academics. In addition, I will build set of activities and events that communicate the influence and impact of student's career, especially in research and development to strengthen the basic research atmosphere at P C Jabin Science College, Hubballi.

(Dr H M Savanur)

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Highly efficient synthesis of amides from ketoximes using trifluoromethanesulphonic anhydride†

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Trifluoromethanesulphonic anhydride (triflic anhydride: TA) has been successfully used as a reagent for Beckmann rearrangement in the conversion of a variety of ketoximes into amides without any additive or base. This reagent works well for the synthesis of a library of amides with excellent yields.

Introduction

Amides are highly significant precursors for the synthesis of various natural products and intermediates for a large number of medicinally important compounds.[1] Of a number of methods reported for the synthesis of amides, Beckmann rearrangement is quite effective since it avoids the use of corrosive acid chlorides and has been employed in the industrial production of ω-caprolactam and laurolactam.[2] In many cases, this reaction requires strong Bronsted acids (which act as dehydrating agents),[3] thereby restricting its application to acid sensitive substrates.

A survey of literature reveals application of various techniques and reagents for the synthesis of amides. Methods involving vapour phase,[4] solvent free conditions,[5] supercritical water,[6] ionic liquids,[7–9] liquid phase conditions,[10–12] and microwave irradiation on silica support have been reported.[13] Heterogeneous reaction conditions that are facilitated by supported reagents on solid surfaces have also been developed to bring about Beckmann rearrangement with certain limitations.[14]

Metal salts like $Ga(OTf)_3$,[15] $Sc(OTf)_3$,[16] $Cu(OAc)_2$,[17] $TiCl_4$,[18] and In/Zn couple[19] have also been found to be effective in this reaction. Organic acids or reagents capable of acting as better leaving groups constitute a major group which includes sulfamic acid,[20] chlorosulfonic acid,[21] anhydrous oxalic acids,[22] *O*-alkyl DMF salt,[23] CF_3COOH,[24] trifluoromethanesulfonic acid,[25] and pivaloyl chloride-DMF complex.[26] However, some of these variants suffer from drawbacks such as toxicity, expensive reagents, and production of considerable amounts of by-products. In addition, these reactions also require longer reaction times, high temperature and produce low yields. Though, enzymatic methods are also available, their isolation costs and application to limited substrates can present challenges for their general applicability.[27] In spite of all these still there is a need for simpler and widely applicable method for the synthesis of amides.

Trifluoromethanesulfonic anhydride has been an effective reagent in a number of reactions.[28–31] We have demonstrated the applications of this reagent for the conversion of aldoximes into nitriles[32] and formation of amides from nitriles by Ritter reaction.[33] In continuation of our work, the present paper illustrate the utility of triflic anhydride in Beckmann transformations.

Results and discussion

For optimization of reaction conditions benzophenone oxime was selected as the model substrate to study the effect of solvent, temperature and reaction time on the overall yield of the reaction (Table 1). Reaction of equimolar quantities of benzophenone oxime **12a** and TA was attempted in methanol under reflux conditions. The yield of the product was very low in this case (Table 1, entry 1). Solvents such as ethanol, acetonitrile and acetone, were suitable for this reagent but to our disappointment only 39–65% of product was isolated even after 8 h under reflux conditions (Table 1, entries 2–4). Further, when we used CCl_4, reaction did not proceed even after 12 h under reflux conditions (Table 1, entry 5) and very poor conversion of the product was observed in THF and in dioxane (Table 2, entries 6 and 7). Reaction in dipolar aprotic solvents and high boiling aromatic solvents were not effective which are reflected in low percentage of the transformation (Table 1, entries 8–10). Serendipitously, excellent isolated yield (96%, Table 1, entry 11) at a shorter reaction time (2.5 h) was realized when the reaction was carried out at room temperature in DCM. On the other hand, the same reaction was completed in 2 h at reflux mode with 98% of isolated yield. In order to evaluate the influence of other chlorinated solvent in this reaction, ethylene dichloride (EDC) was tried. With EDC, 93% conversion and 81% isolated yield are achieved in 3 h at rt while at reflux mode, conversion and isolated yield noticed are 98% and 87% respectively in 2.4 h (Table 1, entry 12). On the grounds of obtained results and carcinogenic nature (class 2) with EDC, we have demonstrated

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$Pd(OAc)_2$ catalyzed homocoupling of arenediazonium salts in ionic liquids: synthesis of symmetrical biaryls

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ABSTRACT

A facile, high yielding, and simple method for the synthesis of a library of symmetrical biaryls by homocoupling of arenediazonium salts is reported, employing catalytic amounts of $Pd(OAc)_2$ and the readily available imidazolium ionic liquids (ILs), without oxidants, ligands, additives, or volatile solvents. Simple product isolation and recycling/reuse of the IL represent additional advantages of this method.

The biaryl moiety is an important structural motif and building block that is widely present in natural products, pharmaceuticals, advanced materials, conducting polymers and liquid crystals.[1] Consequently, a plethora of synthetic methods for aryl–aryl bond formation have been developed over the years.[1a] Among various metal-mediated protocols for the synthesis of biaryls, the palladium-catalyzed Suzuki coupling utilizing aryl halides, sulfonates, or triflates, and aryl-boronic acids have been widely employed.[1]

The discovery of aryl-diazonium salts as highly efficient coupling partners in Pd-catalyzed reactions,[2] opened up a new chapter in diazonium ion chemistry, and prompted the development of improved methods for arylation via Suzuki–Miyaura,[3–7] Sonogashira,[8–10] and Heck reactions.[11,12]

Imidazolium ILs represent ideal media for metal-mediated coupling reactions with arenediazonium salts because both ArN_2^+ salts and $Pd(OAc)_2$ can be dissolved in the ionic liquid. The method also offers the added advantage to recycle and reuse the IL.

We previously reported on Heck–Matsuda coupling reactions with $[ArN_2][X]$ in IL solvents to synthesize a wide range of olefins,[13] and on the synthesis of novel SF_5-bearing alkenes, alkynes, and biaryls via Heck, Sonogashira, and Suzuki couplings by employing the pentafluorosulfanyl-diazonium salt $[SF_5\text{-}PhN_2][BF_4]$ as coupling partner.[14]

Here we report our study of $Pd(OAc)_2$-catalyzed homocoupling of benzenediazonium terafluoroborates in readily available imidazolium ILs, exploring the scope of the reaction for access to a library of symmetrical biaryls (Scheme 1).

To our knowledge previous studies on the synthesis of symmetrical biaryls via Pd-catalyzed homocoupling of arenediazonium salts have not been extensive,[15] and use of methanol as solvent for this reaction in an earlier study resulted in competing formation of ArH due to hydro-dediazoniation.

Result and discussion

At the onset feasibility studies were performed for metal-catalyzed homocoupling of parent benzenediazonium-BF_4 to form biphenyl in $(bmim)BF_4$ and $(bmim)PF_6$ as solvents, and optimization of the reaction conditions namely type of catalyst, the IL, reaction time, and temperature were carried out (Table 1).

Optimizations were initially performed in $(bmim)PF_6$ with 10 mol % of $PdCl_2$ at 50 °C for 3 h under air, leading to a 36% yield of biphenyl (entry 1), and with a slight improvement in conversion (41%) when the reaction was carried out in $(bmim)BF_4$ at 50 °C for 4 h (entry 2). Poor conversions were noted (TLC monitoring) when $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ were used as catalysts in $(bmim)PF_6$ or in $(bmim)BF_4$ as solvent (entries 3–6; therefore not isolated). Slight improvement was observed by employing Pd-catalysts along with phosphine ligands (entries 7–10), and by using 10% Pd/C (entries 11–12). No significant improvement in the homocoupling yields was achieved in the Pd-I_2 catalyzed reaction (entries 13–14), and

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[bmim(SO$_3$H)][OTf]/[bmim][X] and Zn(NTf$_2$)$_2$/[bmim][X] (X = PF$_6$ and BF$_4$); efficient catalytic systems for the synthesis of tetrahydropyrimidin-ones (-thiones) via the Biginelli reaction

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ABSTRACT

A facile, high yielding, and simple method for the synthesis of a library of dihydropyrimidinones (and -thiones) via the one-pot Biginelli reaction of aldehydes is reported. The method employs the Brønsted acidic IL [bmim(SO$_3$H)][OTf] or Zn(NTf$_2$)$_2$ as catalyst along with the readily available imidazolium-ILs as solvent, and exhibits good potential for the recycling and reuse of the IL solvent.

Due to their wide spectrum of biological activity and unique properties dihydropyrimidinones (DHPMs) have been the subject of intense research activity. These bioactive compounds can be synthesized via a multicomponent reaction (MCR)[1–3] by reacting β-ketoesters with aldehydes and urea or thiourea (for the corresponding thiones).[4,5] Over the years this classical method known as the Biginelli reaction has undergone many modifications and tweaking, employing numerous catalysts and conditions. The mechanism of this transformation (iminium, enamine, or Knoevenagel) has been debated, and can vary depending on the reaction conditions and substrate ratios. The keto-enol tautomerization equilibrium of the 1,3-dicarbonyl compound has been recognized as an important factor for the success of this reaction.[6]

In the past several years a large number of studies have utilized ionic liquids (ILs) in the Biginelli reaction. These included the use of Brønsted acid ILs bearing various counterions, under homogeneous, heterogeneous, solvent-free, and catalyst-free conditions, in some cases assisted by sonication or microwave irradiation.[7–18] Among various classes of Brønsted acidic ILs that have been used, triazolium, benzimidazolium, 1-sulfopyridinium, pyridinium, and *N*, *N*-diethyl-*N*-sulfoethanaminium ILs are not readily available, and their synthesis in many instances require harsh and corrosive reagents.[7–11] Most other classes of ILs that were employed, such as [Hbim], [Hmim], and [Et$_3$NH],[12–14] are prepared by protonation of the cationic core. Tethered sulfonic acid ILs were also utilized.[15] Other workers focused on designing heterogeneous systems in which the IL was embedded in mesoporous silica or in some other support material,[16,17] or by combinatorial protocol in which one of the Biginelli reaction components is bound to the IL.[18] The Lewis acid-catalyzed version of Biginelli reaction (using conventional solvents) have also been extensively studied over the years, with B(C$_6$F$_5$)$_3$ and Li(glycine)(OTf) as notable recent examples.[19,20]

Whereas these and other studies have led to many publications and demonstrated the versatility of this MCR process, it is unclear if they brought about major developments or a paradigm shift. These issues have been critically examined by Neto and associates[21–23] who extensively studied this transformation under a variety of condition using different ILs, and performed kinetic, mechanistic, and computational studies to clarify the facts, myths, and presumptions about this important reaction, focusing specially on solvent–free and catalyst-free studies. Their computational studies underscored the interaction of the cationic intermediates with the IL anion, and pointed to spontaneous formation of supramolecular aggregates. They also examined the Lewis-acid catalyzed version of this reaction in ILs and identified several metal-complexed

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Feature Article

Piperidine-appended imidazolium ionic liquid as task-specific basic-IL for Suzuki and Heck reactions and for tandem Wittig-Suzuki, Wittig-Heck, Horner-Emmons-Suzuki, and Horner-Emmons-Heck protocols

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[BMIM][X] as solvent
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Wittig and Horner-Emmons
Tandem protocols
Bis-olefination

ABSTRACT

Facile, high yielding, one-pot methods for the synthesis of a library of diversely substituted bi-aryls, diarylethenes, and aryl-enoates, via Suzuki and Heck reactions, and by sequential Wittig-Suzuki, Wittig-Heck, Horner-Emmons-Suzuki, and Horner-Emmons-Heck reactions are reported. The reactions employ piperidine-appended imidazolium ionic liquid [PAIM][NTf_2] as a task-specific basic-IL, butyl-methyl-imidazolium ionic liquid [BMIM][X] (X = PF_6, BF_4) as solvent, and catalytic amounts of $Pd(OAc)_2$, with no other additives. Wittig and Horner-Emmons reactions are effected by reacting substituted benzaldehydes with 4-bromobenzyl-PPh_3 (or bromomethyl-PPh_3) phosphonium salts, or diethylphosphonate with bromobenzaldehydes respectively, to form the corresponding ethenes. Subsequent cross-coupling reactions are accomplished by addition of aryl-boronic acid or phenyl-ethenes along with $Pd(OAc)_2$ to bring about the aforementioned hyphenated transformations. The feasibility to perform double-olefination via Wittig and Horner-Emmons reactions with dialdehydes to form highly conjugated bis-styryl and bis-enoate compounds is also shown. The [BMIM][X] solvent is recycled and reused.

1. Introduction

The Suzuki-Miyaura and Mizoroki-Heck reactions are two of the most important C–C bond forming protocols that have had a tremendous impact on the practice of synthetic/preparative chemistry, not only in academia but also in industry [1–4]. Their wide application stems from broad scope, flexibility and tolerance toward functional groups, and availability of the coupling components.

The essential ingredients of the Suzuki coupling reaction are Pd (or Ni) catalyst, along with a base, and ligand (depending on the substrates), and solvents such as THF, DMF and dioxane. The Heck reaction uses a Pd catalyst, with or without phosphine ligand, along with a base, and requires high temperature. In some cases, bases such as Et_3N also serve as solvent, but otherwise high boiling solvents such as DMF and THF are employed [3,4].

Ionic liquids (ILs) offer numerous advantages in Pd-catalyzed cross-coupling reactions, namely by lowering the energy of the polar transition state or intermediates in the catalytic cycle, by increasing the reactivity of the reactants, and by virtue of their ability to solubilize the Pd catalyst. They replace hazardous organic solvents and also offer good prospects for recycling and reuse. Various classes of ILs and Pd catalysts have been employed in the Suzuki and Heck reactions. Task-specific ILs (TSILs) that are base-appended, and/or ligand tethered, and supported-ILs with immobilized-Pd catalysts, have opened up new vistas in cross-coupling reactions. Progress in the Pd-catalyzed cross-coupling reactions in ILs is summarized in a comprehensive recent survey [5].

In continuation of our previous studies on the utility of ILs and TSILs as solvent and catalyst in metal-mediated transformations [6–8], and their utility in the Sonogashira coupling [9], we report here on high yielding one-pot methods for the synthesis of a library of diversely substituted biaryls, diarylethenes, and aryl-enoates via Suzuki and Heck reactions, and by sequential Wittig-Suzuki, Wittig-Heck, Horner-Emmons-Suzuki, and Horner-Emmons-Heck transformations, employing the piperidine-appended imidazolium-IL [PAIM][NTf_2] (Fig. 1) as a task-specific basic-IL, [BMIM][X] (X = PF_6, BF_4) as solvent and catalytic amounts of $Pd(OAc)_2$, with no other additives. Wittig and Horner-Emmons reactions were effected in [PAIM][NTf_2]/[BMIM][X] by using phosphonium salts or phosphonates respectively. Subsequent addition of the Pd-catalyst along with boronic acids or styrenes brings about the indicated hyphenated transformations, leading to a host of high value small molecules. The [BMIM][X] is used as solvent and is recycled and reused.

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Sequential Reactions | *Very Important Paper* |

VIP Libraries of C-5 Substituted Imidazoles and Oxazoles by Sequential Van Leusen (VL)–Suzuki, VL–Heck and VL–Sonogashira in Imidazolium-ILs with Piperidine-Appended-IL as Base

Hemantkumar M. Savanur,[a] Rajesh G. Kalkhambkar,*[a] and Kenneth K. Laali*[b]

Abstract: Facile access to diverse C5-substituted imidazoles and oxazoles via sequential Van Leusen–Suzuki, Van Leusen–Heck, and Van Leusen–Sonogashira protocols, employing imidazolium-ILs as solvents along with piperidine-appended imidazolium [PAIM][NTf_2] as task-specific basic IL has been demonstrated, in a high-yielding one-pot method, starting with readily available aldimines (for imidazole) or aldehydes (for oxazole) and tosylmethylisocyanide (Tos-MIC), under mild conditions with potential for recycling and reuse of the IL solvent. The scope of the method is supported 49 examples.

Introduction

Imidazoles and oxazoles are highly important classes of heterocyclic compounds that are present in numerous bioactive natural products and are widely utilized as building blocks in medicinal chemistry and drug discovery.[1,2] Imidazolium salts in particular are widely employed as ionic liquids and have found wide application as solvents and catalysts.[3] It is therefore highly desirable to develop synthetic methods that provide facile access to diversely functionalized imidazoles and oxazoles that can serve as small molecule building blocks for further elaboration.

The Van Leusen tricomponent imidazole and oxazole syntheses are practical one-pot protocols that utilize the unique reactivity of tosylmethylisocyanide (Tos-MIC) to prepare imidazoles from aldimines and oxazoles from aldehydes.[4] Continuing developments in multi-component (MC) sequential reactions have created a new life for the van Leusen reaction, by combining this key reaction with other transformations such as cycloaddition,[5] C–H bond activation,[6] ring closing metathesis,[7] and other C–C bond forming reactions sequential reactions.[8–10]

We are aware of only one previous report in which [BMIM][Br] was used as solvent to prepare oxazoles by Van Leusen reaction using mono-substituted Tos-MICs along with base.[11] To the best of our knowledge IL-mediated MC-sequential methods involving the van Leusen reaction have not been reported.

In continuation of our work on developing synthetic methods in ILs as catalysts and solvents,[12] and in relation our recent study on sequential reactions in ILs employing task-specific ILs as base,[13] we wish to report here a facile entry into diversely C-5 substituted imidazoles and oxazoles via sequential van Leusen–Suzuki, van Leusen–Heck, and van Leusen–Sonogashira protocols, employing imidazolium-ILs as solvent along with the piperidine-appended imidazolium-NTf_2[13] as task-specific basic IL, in one-pot high yielding reactions starting from readily available aldimines (for imidazole) or aldehydes (for oxazole) and tosylmethylisocyanide (Tos-MIC), under mild conditions. The potential for recycling and reuse of the IL solvent is also demonstrated, and scope of the method is highlighted by providing 49 examples.

Results and Discussion

At the onset, the potential to efficiently perform the van Leusen imidazole and oxazole reactions in [BMIM][X] with X = PF_6 and BF_4 as solvent with piperidine-appended imidazolium IL [PAIM][NTf_2] as base was examined, by using *p*-bromo-benzaldimines and benzaldehyde respectively, in one-pot reactions using Tos-MIC, and the reactions were monitored by TLC. The reactions went to completion at 60–70 °C typically after 5–6 hours (see exp. in SI file). The method also proved applicable when using *p*-bromo-furan-aldimine and *p*-bromo-furan-carboxaldehyde.

In the next phase, the feasibility to perform multi-component (MC) van Leusen imidazole–Suzuki and oxazole–Suzuki sequential reactions were examined by introducing $Pd(OAc)_2$ and [PAIM][NTf_2] along with various aryl/heteroaryl boronic acids into the same reaction tube with mild heating and TLC monitoring. The results are summarized in Table 1–Table 2 with 23 examples provided, and with isolated yields in the 70–80 % range

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Biological Chemistry & Chemical Biology

Synthesis and Molecular Modeling Studies of Coumarin- and 1-Aza-Coumarin-Linked Miconazole Analogues and Their Antifungal Activity

Hemantkumar M. Savanur,[a] Geeta M. Pawashe,[a] Kang Min Kim,*[b] and Rajesh G. Kalkhambkar*[a]

A series of new coumarin and 1-aza coumarin analogues of miconazole (**6 a-j**) were synthesized from 3-bromoacetyl coumarins. Further diversification was achieved by synthesizing coumarin-benzimidazole hybrids of miconazole (**7 a-j**) and evaluated for *in-vitro* anti-microbial activities. Amongst the tested compounds, **7 d** was found to be particularly effective as anti-fungal agents against *C. albicans* and *C. krusei*, with activity comparable to that of the standard. Comparative Docking studies with mevalonate-5-diphosphatedecarboxylase shows better binding affinity than imidazole counterparts which is primarily attributed to extended π-alkyl interactions facilitated by benzimidazole.

1. Introduction

Miconazole (Monistat, M-Stat, Micatin) is an azole-based anti-fungal agent forming largest class of synthetic antimycotics which work primarily by reducing the availability of ergosterol (fungal equivalent of cholesterol)[1] by inhibiting lanosterol 14-α-demethylase, a cytochrome P-450 dependent enzyme leading to increased permeability.[2] Use of azoles as anti-fungal agents has been widely studied and scrutinized which is evident from the fact that a bulk of anti-fungal drugs in the market today are variants of imidazole, benzimidazoles and triazoles.[3] Micanozole and their analogues have attracted much more considerable attention due to their extensive biological activities such as antibacterial therapy especially in the management of superficial bacterial skin infections and super infected, which are mainly caused by gram-positive bacteria.[4a] Interestingly, azole based anti-fungals are also equally efficacious as antibacterial agents.[4b] For instance, the broad-spectrum imidazole anti-fungal miconozole was found to be potent against skin infections caused by gram-positive bacteria both in vitro and in vivo.[4a] Minimum inhibitory effect of miconazole was found against the gram-negative bacteria.[5] Miconazole exerts its antibacterial efficacy through binding to flavohemoglobin, which in turn results in oxidative stress leading to cell death.[6] Although various classes of anti-fungal drugs are available in clinical use such as polyenes, azole derivatives, allylamines, thiocarbamates, and fluoropyrimidines class of compounds have acquired more attention for the researchers. Even though there is an expansion of anti-fungal agents list the results are unsatisfactory in healing the diseases.[7] In current decades, however, resistance to fungal infections has lead to a lot of studies is being carried out in designing viable miconazole analogues.[8]

Coumarin and its nitrogen counterpart (1-aza coumarin) also known as quinolinone and carbostyril are a family of naturally-occurring lactones and lactams respectively, which are widely found in nature and routinely used as herbal remedies since early days. A comparative study of these two systems have been reviewed for their varies biological properties from our laboratory.[9] In the development of newer anti-microbials, coumarin hybrids have been identified as a specific platform for anti-bacterial agents and selective growth inhibitory potential particularly against Gram-positive species.[10] The increase in the number of coumarin moiety within the molecule has displayed greater potency in the treatment of diseases[9a] and with over 1300 coumarins identified principally as secondary metabolites in green plants, fungi, and bacteria.[9a,11] In addition, synthetic coumarins with a wide variety of pharmacophoric groups at C-3, C-4 and C-7 positions have been extensively screened for their biological properties. Over the last two decades there has been a considerable amount of work with coumarins being tested for anti-HIV,[12] anti-cancer,[13] anti-tumor,[14] anti-oxidant,[15] anti-retroviral,[14] anti-tuberculosis,[16] acetylcholine inhibitors,[17] anti-inflammatory[11] and DNA Gyrase inhibitors.[18] Further, chemistry and biological profiles of various pharmacophores of 1-aza coumarin derivatives, which ultimately metabolize as the corresponding 8-hydroxy coumarins in the biological system and therefore found to be very good anti-inflammatory agent.[19] Both coumarin and 1-aza coumarin have been widely reported to exhibit anti-microbial activity [20] owing to its unique structural features.[21]

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Biological Chemistry & Chemical Biology

Click Chemistry Inspired Design, Synthesis and Molecular Docking Studies of Coumarin, Quinolinone Linked 1,2,3-Triazoles as Promising Anti-Microbial Agents

Hemantkumar M. Savanur,[a] Krishna N. Naik,[a] Shailaja M. Ganapathi,[b] Kang Min Kim,[c] and Rajesh G. Kalkhambkar*[a]

A series of new coumarin, quinolinone and benzyl linked 1,2,3-triazole derivatives have been synthesized and screened for their anti-bacterial and anti-fungal activities. Results of bioassay indicate that, compounds containing chloro and methoxy substituents in coumarin (**6j**), chloro substitution in quinolinone (**7g**) and 3-chloro benzyl analogue (**8f**) exhibit excellent anti-bacterial activities. The results of anti-fungal activities also reveal that methoxy and chloro substituted coumarins (**6e** and **6j**) were highly active against yeast strains. In addition, chloro and methyl substituted coumarins (**6h** and **6i**) were also exhibited excellent activity. Further, methyl substituted quinolinone with chloro substituted coumarin (**7f**) was found to highly active against yeast fungi and filamentous strain *A.niger*. It is evident from the results obtained and SAR studies that electron withdrawing or donating character of the substituents do not seem to be a major factor in increasing or decreasing anti-microbial activity.

1. Introduction

With the dawn of organic chemistry, libraries of molecules have been synthesized which are having their own importance in pharmaceuticals worldwide. Coumarin and its nitrogen analogue quinolinone (also known as carbostyril or 1-aza coumarin) still remain as one of the most versatile class of compounds against microbes and therefore, are useful substructures for further molecular exploration.[1,2] A comparative review of these two systems has been reported for their natural occurrence, anti-microbial, anti-inflammatory, anti-cancer and other miscellaneous properties from our laboratory.[3] In the development of newer anti-microbials, coumarins have been identified as target specific plant anti-bacterial agents with growth inhibitory potential particularly against Gram-positive species.[4] Further, chemistry and biological profiles of various pharmacophores of quinolinone derivatives, which ultimately metabolize as the corresponding 8-hydroxy coumarins in the biological system and therefore found to be very good anti-inflammatory agent.[5,6] The literature survey revealed interest in coumarins and quinolinone as antibiotics is due to the observations that these are potent inhibitors of bacterial DNA gyrase, which is involved in cell growth.[7,8] Many coumarin and quinolinone derivatives, with variety of substituents at C-4 position, with very good anti-bacterial activity have been reported from our laboratory (**Figure 1, A**).[9–11] 4-substituted 1,2,3-triazole with C-4 position of coumarin hybrid displayed promising activity against *E. faecalis* and *E. faecium* (**Figure 1, B**).[12] Recent SAR and docking studies of various 3-substituted coumrins also reavels that they are novel selective ligands for the CB2 receptor and fluorogenic probes to generate fluorescent DNA probes used in the molecular biology.[13] Bis-coumarin with C-3 position analogue displayed potent activity against different microbes than its mono-coumarin (**Figure 1, C**).[14] In addition, various 3-substituted coumarins linked with imidazole, thiazole[15] and thiadiazole[16] has been reported as good anti-microbials and as a new class of anti-tumor agent against liver carcinoma recently. A long aliphatic chain of bis-triazoles bridged with C-5 and C-7 coumarin moiety showed greater activity against bacterial and fungal strains and gave the best anti-MRSA than mono-triazole (**Figure 1, D**).[17]

On the other side, medicinal chemists have considered synthesis of 1,2,3-triazole based heterocycles as the corner stone of medicinal chemistry due to their important biological activities.[18] Triazole nucleus is one of the most important and well known heterocycles which is a common and integral feature of a variety of natural products and medicinal agents.[19] The triazole ring system is a very well-recognized pharmacophore,[20] which is prominent among U.S. FDA approved pharmaceuticals.[21] Due to high dipole moment, 1,2,3-triazoles are able to participate actively in hydrogen bond formation as well as in dipole-dipole and π stacking interactions which helps them in binding easily with the biological targets and improves their solubility.[22] Recently literature survey reveals that 8-

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Accepted Article

Title: Facile Access to Diverse Libraries of Internal Alkynes via Sequential Iododediazoniation/Decarboxylative Sonogashira Reaction in Imidazolium ILs without Ligand or Additive

Authors: Pavankumar Prabhala, Hemantkumar Savanur, Rajesh Kalkhambkar, and Kenneth K. Laali

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Synthesis of diverse libraries of carboxamides via chemoselective *N*-acylation of amines by carboxylic acids employing Brønsted acidic IL [BMIM(SO_3H)][OTf]

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ABSTRACT

Chemoselective *N*-acylation of amines with carboxylic acids as acyl electrophiles and Brønsted acidic IL [BMIM(SO_3H)][OTf] as promoter is reported under both thermal and microwave irradiation to produce libraries of carboxamides in good to excellent yields after a simple workup. The protocol is compatible with structurally diverse 1° and 2° amines and works in the presence of sensitive functional groups such as thiols and phenols. The potential for recycling and reuse of the IL is also demonstrated.

Transformation of amines to carboxamides by *N*-acylation is fundamental to both chemistry and biology, and the ability to perform this important step in a selective manner in the presence of other functional groups such as thiols and phenols by using readily available reagents and catalysts is highly desirable.

There have been numerous literature reports on the use of acid chlorides and anhydrides as acyl electrophiles under basic or acidic conditions. Reactions are typically mediated by Lewis basic, Lewis acidic, or Brønsted acidic additives, or by metal catalysts such as copper sulfate, zinc oxide, and oxomolybdenum species, and in some cases carried out without additives [1–6]. In comparison, the readily available and easier to use carboxylic acids have less frequently been used as acyl electrophiles due to their lower reactivity. The *N*-acylation of anilines, especially those bearing electron-withdrawing substituents, is more challenging often requiring thermal or microwave activation. *N*-Acyl-benzotriazoles under neutral or in acid, and [*N*-acyl-DBN] [BPh_4] salts have been employed in several studies as alternatives to acyl halides for selective *N*-acylation of aromatic amines [7–9]. However, these *N*-acyl transfer reagents are not widely available and some have limited stability.

Continuing our interest in application of task-specific ILs as catalysts in synthetic method development [10], we report here on the efficacy of [BMIM(SO_3H)][OTf] as a Brønsted-acidic IL to prepare diverse libraries of carboxamides via chemoselective *N*-Acylation of aromatic, heterocyclic, alicyclic, and aliphatic amines using readily available carboxylic acids as acyl electrophiles (Scheme1).

Initial optimization studies (Table 1) with parent aniline using acetic acid and [BMIM(SO_3H)][OTf] (Table 1) showed that high conversations are achievable provided sufficient volume of the IL is employed. Similar conversions could be achieved under microwave heating at lower temperatures and with shorter reaction times (entries 6 and 7 versus 13 and 14).

These optimal conditions were then employed for a survey study (Table 2) with diversely substituted anilines bearing activating and deactivating substituents (entries 1–17), as well as representative examples of heterocyclic (entries 18–20), alicyclic (entries 25–26), aliphatic (entries 28–29), and benzylic (entry 27) amines, as well as *N*-methylaniline (entry 24), and *o*-phenylenediamine (entry 23). Entries 21 and 22 provide test examples to demonstrate chemoselectivity in the presence of OH and SH groups (entries 21–22). Microwave-assisted reactions were superior since similar conversions were reached at significantly lower temperatures and shorter reaction times.

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Cross-Coupling | *Very Important Paper* |

VIP

1-Aryltriazenes in the Suzuki, Heck, and Sonogashira Reactions in Imidazolium-ILs, with [BMIM(SO_3H)][OTf] or Sc($OTf)_3$ as Promoter, and Pd($OAc)_2$ or $NiCl_2$·glyme as Catalyst

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Abstract: 1-Aryltriazenes, the protected and more stable form of aryl-diazonium species, can be conveniently unmasked with Brønsted acidic-IL or Sc($OTf)_3$ and coupled with a host of aryl/heteroaryl boronic acids, styrenes, and aryl/alkyl acetylenes in the Suzuki, Heck and Sonogashira reactions in one-pot and in respectable isolated yields, by using palladium or nickel catalyst in readily available imidazolium ILs as solvent, under mild conditions. The scope of these reactions are explored, and the potential for recovery/reuse of the IL solvent is also addressed.

Introduction

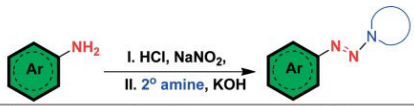
1-Aryltriazenes Ar–N=N–NR_2 are accessible by reaction of secondary amines with the in-situ generated ArN_2^+,[1] or directly from diazonium salts.[2] Compared to ArN_2^+ salts, 1-aryltriazenes have increased stability and longer shelf life, and can be readily purified.[3] Upon treatment with protic or Lewis acids, Ar–N=N–NR_2 is transformed back to ArN_2^+.[3,4] These attributes imply that Ar-triazenes may be ideal electrophilic partners for cross-coupling reactions as substitutes for ArN_2^+ salts. To that end, limited number of studies focusing on the Heck[3]and Suzuki reactions[4,5] have so far been reported employing Pd^0 catalysts along with phosphine ligands[4] or polymer-supported NHC,[5] with BF_3·Et_2O, TFA, or HBF_4 as typical promoters[3–5] to "unmask" the triazene. For the Suzuki reaction using BF_3·Et_2O, it was suggested that formation of an aryltriazenes-BF_3 complex promotes trans-metallation, possibly in a concerted fashion.[4] The reactions were performed in a variety of solvents (DME, DMF/H_2O, dioxane, DMAC, NMP, toluene, THF, and refluxing MeOH),[3,–5] and the yields varied significantly depending on the solvent.[4]

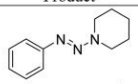
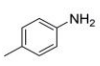
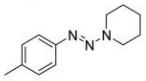
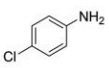
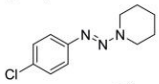
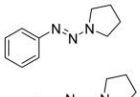
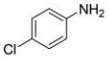
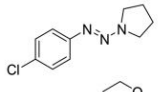
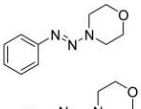
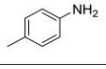
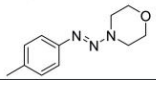
In continuation of our work on developing synthetic methods in ILs as catalysts and solvents,[6] and our recent studies of metal-mediated cross-coupling reactions,[7] we report here on the utility of 1-aryltriazenes as coupling partners in the Suzuki, Heck, and Sonogashira reactions, by employing Brønsted acidic IL and Sc($OTf)_3$ as promoters, and the piperidine-appended-IL [PAIM][NTf_2] as base for the Sonogashira reaction,[7e,7f] without the need for ligand. Considering the ongoing interest in the use of Ni-based catalysts in place of Pd, and the reports of successful application of Ni in the Suzuki reaction,[8–10] we also report on the efficacy of $NiCl_2$·glyme as substitute for Pd($OAc)_2$ in the present study.

Results and Discussion

At the onset, a small library of 1-aryltriazenes was prepared in good isolated yields by in-situ diazotization of aniline and

Table 1. Synthesis of 1-aryltriazenes.



Entry	Ar-NH_2	2° amine	Product	Yield[a] (%)
1				88
2				81
3				79
4				79
6				88
7				77
8				80

[a] Isolated yields of pure products.

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Facile Access to Libraries of Diversely Substituted 2-Aryl-Benzoxazoles/Benzothiazoles from Readily Accessible Aldimines via Cyclization/Cross Coupling in Imidazolium-ILs with $Pd(OAc)_2$ or $NiCl_2$ (dppp) as Catalyst

Shruti S. Malunavar, Suraj M. Sutar, Hemantkumar M. Savanur, Rajesh G. Kalkhambkar, Kenneth K. Laali

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Chemistry SELECT Full Papers

Biological Chemistry & Chemical Biology

Synthesis and Molecular Modelling Studies of Coumarin and 1-Aza-Coumarin Linked Miconazole Analogues and Their Antimicrobial Properties

Suraj M. Sutar,[a] Hemantkumar M. Savanur,[a] Shruti S. Malunavar,[a] Geeta M. Pawashe,[a] Gopalakrishnan Aridoss,[b] Kang Min Kim,*[c] Jin Young Lee,[d] and Rajesh G. Kalkhambkar*[a]

A series of coumarin and 1-Aza coumarin analogues of miconazole(**5a-6e**) were synthesized from 2-bromo-1-(2,4-dichlorophenyl)ethanone and diversification was achieved by synthesizing coumarin-benzimidazole(**7a-7e**) and 1-aza coumarin-benzimidazole(**8a-8e**) hybrids of miconazole and evaluated for in-vitro anti-microbial activities. Among the tested compounds, **8b-8e** were found to be effective as anti-fungal against *C. albicans, C. utilis* and *C. krusei*, with activity compared to that of the standard. Comparative docking studies with mevalonate-5-diphosphatedecarboxylase shows better binding affinity than imidazole counterparts which is primarily attributed to extended π-alkyl interactions facilitated by benzimidazole.

1. Introduction

The mounting sales of antifungal agents that account for more than US$1 billion per year signify the extent of threatening by fungal disease to the society. The majority of these fungal diseases are rather benign, but it's become life-threatening in immune compromised or malnourished patients. Further, development of drug resistance to the first line antimicrobial therapies paved the way for new synthetic drugs containing the same active templates of marketed drugs. Azole based agents are the wide class of unnatural antimycotics and still epitomize a feasible lead framework in the pursuit of improved fungicides.[1–4] Among them, miconazole is widely used as an antifungal agent owing to the relatively low rate of resistance development. Their mechanism of action is presumed to be interfering with ergosterol biosynthesis thereby damage the fungal organism besides the formation of toxic side products (methyl sterol) that are fatal to the fungi.[5] Furthermore, Kobayashi et al gave another mechanism that accumulation of drug induced reactive oxygen species (ROS) within the fungal organism led to oxidative damage and cell death. These coupled mechanisms have drawn renewed attention to this drug candidate. Interestingly, miconazole has also shown to exert antibacterial efficacy, particularly against gram-positive bacteria.[6]

Over the years of active research by the scientific community, imidazole and benzimidazole have evolved as privileged structural motifs because of their omnipresence in a wide spectrum of antimicrobial agents[7] and in particular antifungal drugs.[8] Likewise, coumarin[9,10] and its aza-analogue (aza-coumarin) scaffolds are also frequently encountered in well-known clinical agents.[11]

In recent years, our lab focuses on the synthesis of biologically pertinent heterocycles, particularly azole based agents and explore their antimicrobial efficacies.[12a,b] In this trait, we also identified better lead drug candidates. In connection with our program towards the development of better and new broad-spectrum antimicrobials, we were interested in compounds obtained by the formal structural modification of potent drug: Miconazole, wherein azole and benzyloxy systems were modified. Since the activity of miconazole relies on 2,4-dichlorophenyl group, we kept this subunit intact in our newly designed target molecule whereas the imidazole and 2,4-dichlorobenzyloxy groups were replaced respectively by benzimidazole and coumarin/1-aza coumarin with the aim of finding a new lead that possesses improved antifungal/antibacterial effectiveness.

2. Results and Discussion

2.1. Chemistry

The sequence of the reactions employed for the construction of required target molecule is outlined in Scheme 1. 1-(2,4-dichlorophenyl)ethanone (**1**) was brominated to obtain the

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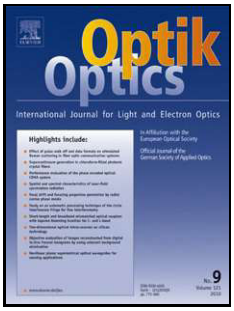

Design of new Imidazole-derivative dye having donor-Π-acceptor moieties for highly efficient organic-dye-sensitized solar cells

Shashikant Walki, Lohit Naik, Hemantkumar M. Savanur, Yogananda K.C, Soniya Naik, Ravindra M K, G.H. Malimat, K.M. Mahadevan

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Facile one-pot synthetic access to libraries of diversely substituted 3-aryl (Alkyl)-coumarins using ionic liquid (IL) or conventional base/solvent, and an IL-mediated approach to novel coumarin-bearing diaryl-ethynes

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ABSTRACT

The *in-situ* formed carbonylimidazole derivatives of Ar(alkyl)-CH_2COOH react at r.t. with substituted salicylaldehydes in [BMIM][PF_6] or [BMIM][BF_4] as solvent, and [PAIM][NTf_2] as basic-IL, to produce libraries of 3-aryl(alkyl)coumarins. Whereas these reactions can also be performed with similar efficiency in THF by employing DBU, the IL approach offers easier work-up and recycling of the IL solvent. An IL-mediated approach to the synthesis of novel coumarin-bearing diaryl-ethynes by the Sonogshira reaction is also reported, and the potential for recycling/reuse of the IL solvent is shown.

Coumarins are important constituents of biologically active natural products and valuable building blocks in synthetic and medicinal chemistry [1–4], that have also found application in materials chemistry [5]. Substituted 3-arylcoumarins are of particular interest due to their diverse biological activity notably as anti-Alzheimer agents [6,7].

Drawbacks and limitations associated with the classical methods such as Pechman and Perkin reactions, have prompted the development of newer strategies for the synthesis of 3-arylcoumarins. These methods include oxidative ($KMnO_4$/AcOH) arylation of coumarins using arylboronic acids [8], Pd-catalyzed Suzuki coupling starting with 3-chlorocoumarins in DMF/H_2O/reflux [9], decarboxylative coupling using N-hydroxyphthalimide esters with Ir(ppy)$_3$/DMSO/TFA [10], and condensation of allenes with phenols and anisoles employing TfOH/DCE [11]. Among the methods that employ salicylaldehydes as reaction partner are condensation of salicylaldehydes with ynamides employing $ZnBr_2$ [12], reaction of N-acylbenzotriazoles with salicylaldehydes via acylation/cyclization [13], reaction of salicylaldehydes with phenylacetic acid using $POCl_3$/pyridine to form the benzyl ester followed by a base-catalyzed cyclization (KOH/pyridine) [14a], reaction of salicylaldehydes with substituted phenylacetic acids using cyanuric chloride/N-methylmorpholine/DMF/reflux [14b], and condensation of salicylaldehydes with aryl-substituted 1,1-dibromo-1-alkene [15].

In continuation of our studies on synthetic and catalytic chemistry in ILs [16], we sought to develop a simple IL-based one-pot method using readily available low cost reagents that enables the assembly of a library of 3-arylcoumarins under very mild conditions. By using [PAIM][NTf_2] as the basic-IL,[16e-g] and [BMIM][PF_6] or [BMIM][BF_4] as solvent, the *in-situ* formed carbonylimidazole derivatives of Ar(alkyl)-CH_2COOH, formed by reaction with carbonyl-diimidazole (CDI), smoothly reacted with salicylaldehyde at r.t. to furnish 3-aryl(alkyl)coumarins (Fig. 1). Following an initial feasibility study, the scope of the reaction was examined by employing diversely substituted salicylaldehydes and substituted phenylacetic acids, and the results are gathered in Table 1. Fig 2.

Further feasibility studies showed that this transformation could also be achieved with similar efficiency at r.t. by using BDU in THF; therefore the scope of the reaction was reexamined in order to provide a broader side-by-side comparison (Table 2).

Whereas the IL-based method and the conventional base/solvent method appear to have similar efficiency, the IL method is advantageous from a practical point of view due to easier

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0040-4039/

"Synthesis, Molecular Modelling Studies and Antimicrobial Activity of Coumarin and 1-Azacoumarin Linked 1,2,3- Triazole"

Suraj M. Sutar , Hemantkumar M. Savanur , Chidanand Patil , Geeta M. Pawashe , Gopalakrishnan Aridoss , Kang Min Kim , Rajesh G. Kalkhambkar

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Organic & Supramolecular Chemistry

Palladium Catalyzed Electrophilic C2-Arylation of Azoles by Aryltriazenes in Ionic Liquid Promoted by Acidic Ionic Liquid

Suraj M. Sutar,[a] Hemantkumar M. Savanur,[b] Chidanand Patil,[c] Pavankumar Prabhala,[a] Gopalakrishnan Aridoss,*[d] and Rajesh G. Kalkhambkar*[a]

A green C–H bond activation of azole based bio-pertinent substrates such as benzoxazole, benzothiazole, benzimidazole are accomplished using readily prepared 1-aryltriazenes as arylating agent. Under an optimized condition employing Pd $(OAc)_2$ and CuI in either hydrophilic [Bmim][BF_4] or hydrophobic [Bmim][PF_6] IL medium with [BMIM(SO_3H)][OTf] as a promoter, these arylation reactions proceeded smoothly to afford 2-aryl substituted azoles in acceptable to better yields besides noticeable functional group tolerance. The prospective for recovery and re-use of ionic liquid solvent is demonstrated.

2-Aryl substituted azoles and their derivatives are frequently encountered scaffolds in diverse range of medicaments, natural products and synthetic materials[1] thereby claim the necessity for the development of novel synthetic methodology. Direct coupling protocols that unite the azole based heterocycles with diverse aryl counter parts remain mainstay transformation as it avoids the need for stoichiometric amount of aryl-metal reagents. Of the numerous methods developed over the decades to synthesize these compounds of interest,[2–4] the C(2)-H activation of the azole rings gains significance among the chemists[5–10] and in particular activation effected by transition metal catalyzed arylation at C(2) position in azole frameworks is of considerable importance.[11–13] This metal catalyzed direct arylation strategy employs aryl electrophiles such as aryl-halides,[14]-triflates,[15]-sulfinates[16–17] and organoboranes[18] etc. However, there were some reports claiming the formation of homo diarylated products that supersedes the desired heterodiarylation by the use of transition metal catalyst.[19–20]

Recent reports witness the use of aryl amines as electrophiles when converting them into more reactive aryltriazenes wherein the C–N bond is made so labile under a suitable metal based catalytic condition.[21–22] Thus, these readily accessible and shelf stable 1-aryltriazenes became more promising synthetic equivalent in place of arenediazonium salt[23–25] for the synthesis of unsymmetrical biaryls. Most of the existing methodologies, however require, noxious solvents, elevated temperatures, excess reagents, ligands and catalyst or other non-green conditions. A very recent report[26] claims C-2 arylation of azoles employing DMF, a class 2 carcinogenic solvent that is not appropriate in API process industry, at 130 °C in an airtight atmosphere (sealed reactor). Dai and Wang described[27] similar kind of transformation yet again in DMF in the presence of additives such as ligand (dppe) and strong base (Bu^tOLi) at 120 °C over a period of 24 h. Driven by these impediments, development of biocompatible, recyclable, and green chemistry methodologies[28] using eco-friendly and sustainable conditions with an objective of better yields and selectivity are highly desirable. Thus, in an endeavor to overcome these limitations, a greener synthetic protocol towards the access of the target molecule is conceived by the use of ionic liquids as a reaction medium/promoter mainly due to its environmental acceptability. In our long pursuit of developing sustainability and greener strategies,[29] we have established green synthetic methodologies employing ionic liquids as solvent or catalyst for the synthesis of benzoxazole and benzothiazoles[29f–h] and metal-mediated cross-coupling reactions[29a–i] exploiting 1-aryltriazenes as a coupling partner. With these previous knowledge, we report herein the base/ligand free and open-air Pd/Cu catalyzed arylation of azoles at C2 position with three different 1-aryltriazenes as coupling partner instead of a single triazene reagent that reported elsewhere.[26]

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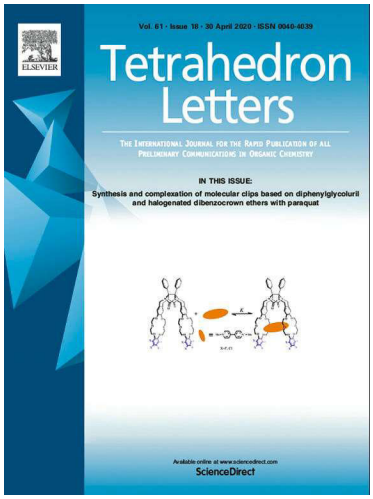

Ionic Liquid Catalyzed Ritter Reaction/Pd-Catalyzed Directed *Ortho*-Arylation; Facile Access to Diverse Libraries of Biaryl-amides from Aryl-nitriles

Suraj M. Sutar, Hemantkumar M. Savanur, Rajesh G. Kalkhambkar, Gabriela L. Borosky, Gopalakrishnan Aridoss, Kenneth K. Laali

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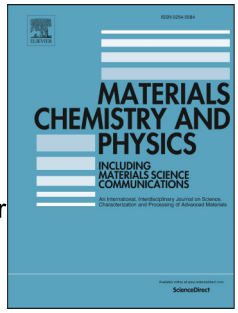

A Highly Selective and Sensitive Thiophene substituted 1,3,4-oxadiazole based Turn-Off Fluorescence Chemosensor for Fe^{2+} and Turn On Fluorescence Chemosensor for Ni^{2+} and Cu^{2+} Detection

Lohit Naik, C.V. Maridevarmath, M.S. Thippeswamy, Hemantkumar M. Savanur, Imtiyaz Ahamed M. Khazi, G.H. Malimath

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