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На правах рукописи

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ТРАНСФОРМАЦИИ МОНО- И ДИКАРБОНИЛЬНЫХ СОЕДИНЕНИЙ В РЕАКЦИЯХ С *C*-,*N*-,*O*-НУКЛЕОФИЛАМИ В УСЛОВИЯХ МЕХАНОАКТИВАЦИИ И В ИОННЫХ ЖИДКОСТЯХ

1.4.3. Органическая химия

ДИССЕРТАЦИЯ

на соискание учёной степени кандидата химических наук

ЕКАТЕРИНБУРГ – 2023

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Mukherjee Anindita

TRANSFORMATIONS OF MONO- AND DICARBONYL COMPOUNDS IN REACTIONS WITH C-, N-, O-NUCLEOPHILES UNDER MECHANOACTIVATION CONDITIONS AND IN IONIC LIQUIDS

1.4.3. Organic chemistry

THESIS
for the degree of candidate of chemical sciences

EKATERINBURG – 2023

CONTENTS

GENERAL DESCRIPTION OF WORK

Scientific relevance and degree of development of the research topic. The modern development of organic chemistry requires the use of more rational synthetic methods for the creation of promising molecules and materials based on them. Examples of such approaches are the so-called. "green" methods, including PASE (PASE - pot, atom, step economic) - methods, reactions in the absence of a solvent, including multicomponent ones, as well as mechanochemical methods. Mono- and dicarbonyl compounds are the most convenient partners in such transformations, primarily due to the high reactivity of the carbonyl group in reactions with a wide range of nucleophilic reagents (usually *C*-, *N*- and *O*-nucleophiles), with the most common side product this kind of reactions are water or alcohols. In addition, in most cases, the interaction proceeds effectively in the absence of catalysis by heavy metals (for example, Pd), which makes it possible to successfully use reactions involving carbonyl compounds to obtain drug candidates.

Speaking of multicomponent reactions involving carbonyl compounds, it is necessary to note the extremely high synthetic potential of such processes, since in a one-pot manner it is possible to simultaneously carry out a whole cascade of sequential or parallel chemical transformations, which as a result selectively leads to the production of target products that are inaccessible by traditional methods. However, to date, a relatively small array of publications has presented examples of transformations of carbonyl compounds in di- and multicomponent reactions in the absence of a solvent. Only a few examples present mechanochemical processes involving carbonyl compounds, including those for the production of bioactive compounds/drug candidates. Therefore, based on the above, the transformations of mono- and dicarbonyl compounds studied in this work in reactions with C- and N-centered synthons are relevant both for fundamental science (new transformations involving carbonyl compounds) and for applied purposes (obtaining drug candidates, fluorophores, chemosensors, etc.).

The aim of this work is to study the applicability of synthetic transformations of mono- and 1,2- and 1,3-dicarbonyl compounds in reactions with *C*- and *N*-centered synthons in the absence of a solvent as a tool for creating some promising molecules: potential drug candidates and fluorophores.

The implementation of this goal is achieved by solving the following tasks:

• analysis of the literature on examples of the interaction of mono- and dicarbonyl compounds with *C*-, *N*-, *O*-centered nucleophiles.

• selection of optimal reaction conditions based on the availability of synthons, catalysts and the E-factor of the reaction.

• study of the influence of the nature of the reagent and synthon, as well as reaction conditions on the direction of transformation.

• establishing the structure of key compounds, including using X-ray diffraction analysis.

• establishment of "structure-property" patterns both in relation to the initial synthons and in relation to the final products.

• study of photophysical properties of the resulting products.

Scientific novelty and theoretical significance.

Effective methods have been found for the synthesis of 4-substituted coumarins by condensation of 1,3-dicarbonyl derivatives with phenols as 1,3-C,O-dinucleophiles under mechanical activation conditions or in ionic liquids.

For the first time, C3-functionalization of 4-hydroxycoumarins was carried out in reactions with styrene in the absence of a solvent or in an environment of ionic liquids.

For the first time, new quinoxaline derivatives were synthesized by the reaction of 1,2-dicarbonyl compounds with 1,2-diamines under mechanochemical conditions or in ionic liquids.

New blue fluorophores based on tetrasubstituted pyrrole derivatives were synthesized by a multicomponent reaction under mechanochemical conditions.

New derivatives of 1-amidoalkyl-2-naphthols were synthesized for the first time.

An unusually high reactivity of acrylic acid derivatives with amines was discovered under conditions of catalysis with ionic liquids, tea extract, as well as under mechanical activation conditions, resulting in the selective formation of *β*-aminopropionic acid derivatives.

The practical value of the work lies in developments based on the transformations of mono- and dicarbonyl compounds in the absence of a solvent, effective methods for the synthesis of coumarins, pyrroles, phenazines and quinoxalines, as promising fluorophores and potential drug candidates. In a number of cases, it was possible to successfully carry out further post-functionalization of the resulting products.

The possibility of effectively obtaining multisubstituted pyrroles, 1-amidoalkyl-2-naphthols, coumarins, and β-aminopropionic acid derivatives using "green" methods has been demonstrated.

Promising photophysical properties of the resulting products were demonstrated: multisubstituted pyrroles, as well as aryl-substituted phenazines.

The applicability of some multisubstituted pyrroles for the visual detection of nitroaromatic (explosives) substances in solutions has been demonstrated.

The author's personal contribution consisted of searching, analyzing and systematizing literature data related to the purpose and objectives of the study; forming on their basis an analytical review of the literature; planning, carrying out and describing experimental syntheses; processing and discussing their results; preparing publications based on them, as well as presenting these results at conferences.

The methodology and methods of the dissertation research consist of studying the interaction of functionalized mono-/dicarbonyl compounds with nucleophiles, selecting interaction conditions and the nature of catalysts. All obtained compounds were isolated and characterized using the necessary set of instrumental methods, including X-ray diffraction analysis. The starting reagents/synthons are commercially available or have been prepared using previously described procedures that have been reproduced in full or optimized.

The degree of reliability of the results obtained is ensured by the use of the necessary set of instrumental methods for proving the structure of organic compounds (^{1}H and ^{13}C NMR spectroscopy, mass spectrometry, UV spectroscopy, elemental analysis, absorption and fluorescence spectroscopy). The studies were carried out using the equipment of the Center for Collective Use "SAOS" of the Institute of Organic Synthesis named after I.Ya. Postovsky Ural Branch of the Russian Academy of Sciences, as well as at the Department of Organic and Bimolecular Chemistry of the Chemical-Technological Institute of the Ural Federal University named after the first President of Russia B.N. Yeltsin.

The following provisions are submitted for defense:

1. Results of studies of transformations of mono- and dicarbonyl compounds in reactions with *C-, N-, O*-centered nucleophiles, proposed reaction mechanisms and study of the limits of their applicability.

2. Patterns of interaction of carbonyl compounds with the above-mentioned nucleophiles under conditions of mechanical activation or in an environment of ionic liquids.

3. Results of studying the photophysical properties of the obtained compounds, including as sensors/tests for the presence of (nitro)analytes.

Approbation of work. The main results of this dissertation research were presented and discussed at conferences at various levels, such as: Chemical Science Symposium on Functional Organic Materials (London, UK, 2019); The XX Mendeleev Congress on General and Applied Chemistry (Yekaterinburg, 2016), the XXI Mendeleev Congress on General and Applied Chemistry took place (St. Petersburg, 2019); 4th Russian Conference on Medicinal Chemistry with international participation “MedChem-Russia 2019” (Yekaterinburg, 2019); I-VI All-Russian conferences with international participation “Modern synthetic methodologies for the creation of drugs and functional materials (MOSM2017-2022 (Ekaterinburg, 2017-2020, 2022, Yekaterinburg-Perm, 2021).

Publications. The main content of the work is presented in 10 scientific papers, of which 7 articles were published in peer-reviewed scientific journals and

publications determined by the Higher Attestation Commission of the Russian Federation and the Certification Council of the UrFU, including 6 articles in journals indexed in the international citation databases Scopus and WoS.

An application for a Russian patent entitled “Dimethyl 4-phenyl-5-(2-phenyl-1*H*-indolyl-3-yl)-1-(1*H*-pyrrolyl)-2,3-dicarboxylate – an optical chemical sensor for the detection of nitroaromatic explosives” has been submitted (Application No. 2023107957 dated 03/31/2023).

Structure and scope of work. The dissertation is written in English on 129 pages and consists of an introduction, a literature review, a discussion of the results obtained by the dissertation, an experimental part, a conclusion and a list of references, which contains 146 references to Russian and foreign sources.

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CHAPTER 1. SYNTHETIC TRANSFORMATIONS OF CARBONYL COMPOUNDS: LITERATURE REVIEW.

Mono-, 1,2- and 1,3-dicarbonyl compounds are considered as versitle building blocks for the synthesis of various heterocylic scaffolds as well as acyclic compopunds. The most common way for that is the reactions of carbonyl compounds with *C*-, *N*- and *O*-nucleophiles. In the frame of current literature reviews the most representative examples of the reactions of mono- and dicarbonyl compounds will be highlighted.

1.1. 1,3-DICARBONYL COMPOUNDS IN THE SYNTHESIS OF COUMARIN DERIVATIVES

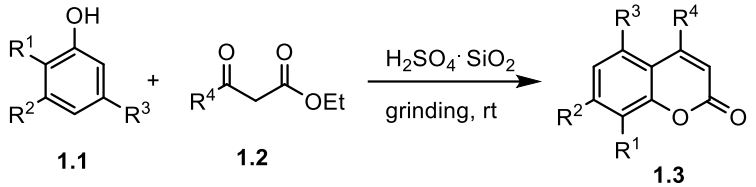
Coumarins (2*H*-chromone-2-one) are considered a significant class of heterocyclic compounds due to their versatile biological and medicinal properties such as antihelmintic, antioxidant [1], anticonvulsant [2], antitumor and anti-inflammatory activities [3]. Broad range antimicrobial properties are also attributed to this core due to its distinct structural properties. Coumarins have important applications in cosmetics, fragrances, pharmaceuticals and food additives [4]. It is recognized to introduce resistance in plant tissues against microbial attack, which is evident by the presence of coumarin derivatives in commercially available pesticides [5].

Owing to their importance in various fields several methods used for the synthesis of coumarins include Knoevenagel [6], Perkin [7], Pechmann [8], Wittig [9], Claisen [10] and Reformatsky reactions [11]. Pechmann condensation is a widely used method in which phenols are reacted with b-ketoester to give 4-substituted coumarins in the presence of acid catalyst [12]. We have discussed here some important recent works which have been published in last decade.

In 2013, Sharma and coworker reported a simple and highly efficient procedure for the synthesis of coumarins (**1.3**) via Pechmann condensation,

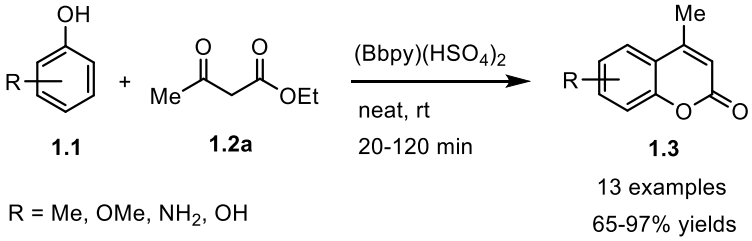
involving the grinding of different phenols (**1.1**) and β-ketoesters (**1.2**) in the presence of silica supported sulfuric acid at room temperature, under solvent free conditions (Scheme 1.1) [13]. The scope of the method was further studied by reacting differently substituted phenols with ethyl acetoacetate (**1.2a**), 1-chloroethylacetoacetate (**1.2b**) and benzoyl acetoacetate (**1.2c**), to give corresponding coumarins (**1.3**) in good yields under solvent free conditions at room temperature.

Scheme 1.1



In 2016, an efficient and environmentally friendly procedure was reported for the synthesis of coumarin derivatives (**1.3**) by the Pechmann condensation reaction between ethyl acetoacetate (**1.2a**) with various phenols (**1.1**) under solvent-free conditions and at ambient temperature using $(Bbpy)(HSO_4)_2$ as catalyst (Scheme 1.2) [14]. The results revealed that the rate of reactions increased in the presence resorciniol, pyrogallol, phloroglucinol, orcinol, 2,6-dihydroxy toluene, 4-nitrophenol and hydroquinone and produced coumarin derivatives in excellent yields. Also, 3-aminophenol reacted to provide the amino coumarin derivatives in good yield with slightly longer reaction times. 1-Naphtol reacted with longer reaction time and low yield due to having another phenyl group. Similarly, phenol reacted with longer reaction time and very low yield, but on the other hand, formation of 4-methylcoumarin in acceptable yield from the reaction of unsubstituted phenol. Mild reaction conditions, short reaction times, good to excellent yield independent of temperature, simple experimental and product isolation procedures are the significant advantages of the present method.

Scheme 1.2

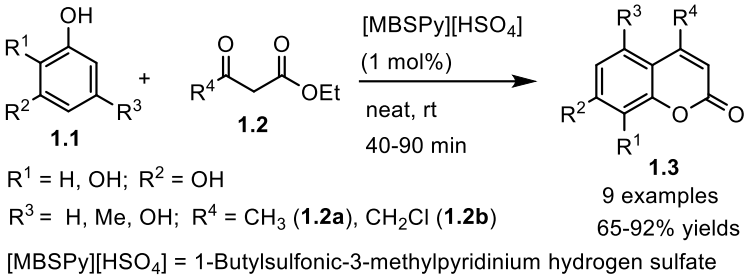


(Bbpy)$(HSO_4)_2$ = 1,1'-Butylenebispyridinium hydrogen sulfate

A series of new recyclable Bronsted acidic ionic liquids with perchlorate anion (BAILs-ClO_4) catalysts were reported to be green and efficient catalysts for the synthesis of coumarins via Pechmann condensation under solvent-free conditions [15]. These conditions are compatible with some acid sensitive functional groups, such as ether, homoallylic hydroxyl and benzyl. This catalyst furnished facile synthesis of coumarins from less activated phenols including hindered ones bearing ortho substituents or phenols with weak electron donating substituents. Moreover, this method was successfully extended to a wide variety of phenols and *β*-ketoesters including ethyl acetoacetate, ethyl benzoyl acetate, 3-acetyldihydrofuran-2(3*H*)-one, simple phenols and aminophenols as well as estradiol.

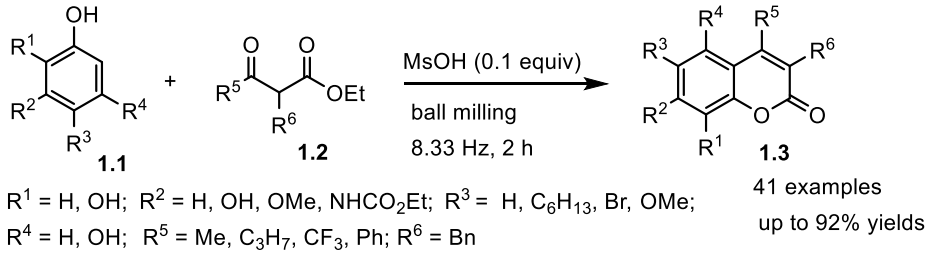
In 2022, Brønsted acidic task specific ionic liquid (TSIL) was utilized as an effective catalyst for the production of potential fungicidal coumarin derivatives for sustainable agriculture (Scheme 1.3) [16]. Nine different compounds were prepared using substituted phenols (**1.1**) and ethyl acetoacetate (**1.2a**) or its chloro-derivative (**1.2b**) under ambient, solvent-free conditions in significantly high yields. The synthesis is highly green and benign due to recoverable and recyclable TSIL catalyst, ambient conditions like room temperature and short reaction times. 93% Yield was obtained at room temperature in just one hour with only 1 mol% catalyst. Of all the tested compounds, two compounds showed excellent antifungal activity comparable to reference fungicide mancozeb.

Scheme 1.3



In the same year, we have introduced an efficient, scalable, ecofriendly protocol for the synthesis of coumarin derivatives (**1.3**) under solvent-free ball milling conditions at ambient temperature by the Pechmann condensation of phenols (**1.1**) and β-ketoesters (**1.2**) (Scheme 1.4) [17]. This procedure provides an easy access to a wide range of coumarins, including those substituted with aromatic, aliphatic and fluorine-containing substituents, coumarins fused with aromatic and cycloalkane moieties, as well as annulated pyrano[2,3-*f*]indole and pyrano[3,2-*f*]indole. In addition, this protocol is associated with a low E-factor and high EcoScale metrics, which are consistent with the principles of atom economy.

Scheme 1.4



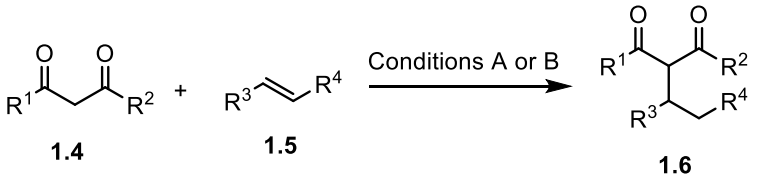
Very recently, in this year, Kouznetsov et al. developed an efficient method for the preparation of coumarin derivatives, including Coumarin 120 (7-amino-4-methylcoumarin) from phenols (or naphthols) and ethyl acetoacetate in the presence of 3 mol% $InCl_3$ [18]. Coumarins were obtained in good yields (52–92%) through Pechmann condensation, under a rapid and environmentally friendly protocol using a highspeed ball mill mixer at room temperature, with short reaction times, under solvent-free conditions.

1.2. 1,3-DICARBONYL COMPOUNDS IN REACTIONS WITH ALKENES OR ALKYNES

The addition of 1,3-dicarbonyl compounds to alkenes or alkynes, which yields alkylated dicarbonyls, is considered to be a highly atom economical process. This hydroalkylation of alkenes or alkynes by 1,3-dicarbonyl compounds is one of the most common methods for C–C bond formation. In this part we have compiled some important works which described intermolecular hydroalkylation of alkenes or alkynes in presence of different catalytic systems.

In 2004, Li and co-worker first reported an efficient addition of activated methylene compounds (**1.4**) to alkenes (**1.5**) in presence of gold and silver catalyst. The reaction was examined on various substrates (Scheme 5) [19]. Various diketones were effectively added to styrene and styrene derivatives in presence of $AuCl_3$ (5 mol%) and AgOTf (10 mol%) in DCM solvent at room temperature. Note that the addition of 1,3-diketones to indene is also highly effective. The use of β-ketone esters was also effective; however, it gave a complicated mixture. Additionally, simple terminal alkenes were also reactive under the current conditions; however, only very low conversion was observed. The use of norbornene provided 81% yield of the corresponding product under the same reaction conditions. The use of cyclic 1,3-diketones led to low conversions under the present conditions. In the next year, the same research group reported this reaction in presence of AgOTf (10 mol%) catalyst in nitromethane or 1,2-DCE solvent at 100 ºC under N_2 atmosphere (Scheme 1.5) [20]. The reaction is reversible through the cleavage of the carbon-carbon bond catalyzed by silver at an elevated temperature.

Scheme 1.5

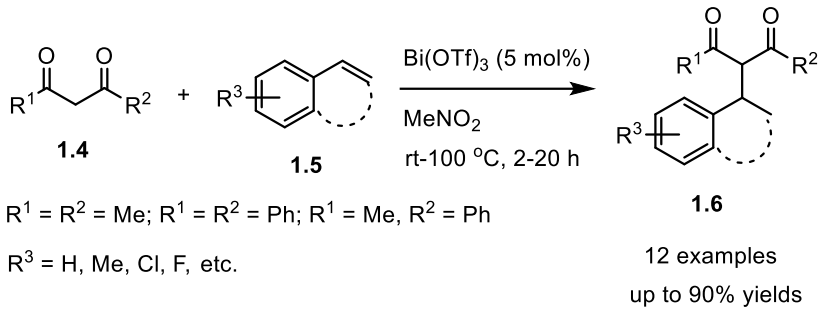


Conditions A: $AuCl_3$ (5 mol%), AgOTf (15 mol%), DCM, N_2 atm, rt , 2 h
$R^1 = R^2 = Me$; $R^1 = R^2 = Ph$; $R^1 = Ph$, $R^2 = Me$

Conditions B: AgOTf (10 mol%), $MeNO_2$, N_2 atm, 100 ^oC, overnight
$R^1 = R^2 = Me$; $R^1 = R^2 = Ph$; $R^1 = Ph$, $R^2 = Me$

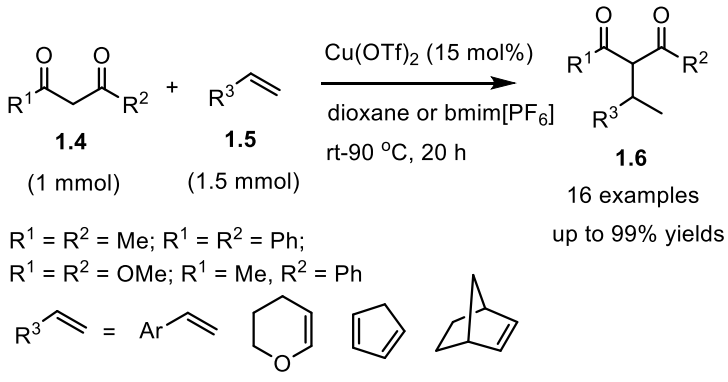
In 2007, Rueping et al. developed an efficient bismuth-catalyzed hydroalkylation of various styrenes, norbornene, and cyclohexadiene derivatives with different diketones (Scheme 1.6) [21]. The short reaction times, simplicity and practicability as well as the use of small amounts of reactive, cheap, non-moisture-sensitive, and nontoxic $Bi(OTf)_3$ catalyst renders this hydroalkylation procedure an interesting alternative to previous methods. Generally different styrene derivatives (**1.5**) and diketones (**1.4**) were employed and the corresponding products (**1.6**) were isolated in good yields after short reaction times. With regard to the styrene derivatives electron-donating, as well as electron withdrawing substituents were tolerated and even indene resulted in the cyclic 3-substituted dihydroindene, though only in moderate yield. Furthermore, the authors were able to extend the scope of this transformation to other substrates, including norbornene and cyclohexadiene. For instance, bismuth-catalyzed hydroalkylation of norbornene with the more reactive dibenzoylmethane gave the corresponding alkylated norbornene in 90% yield after 90 minutes. Surprisingly, cyclohexadiene was also successfully transformed to the alkylated cyclohexene, although the reaction was performed at ambient temperature.

Scheme 1.6



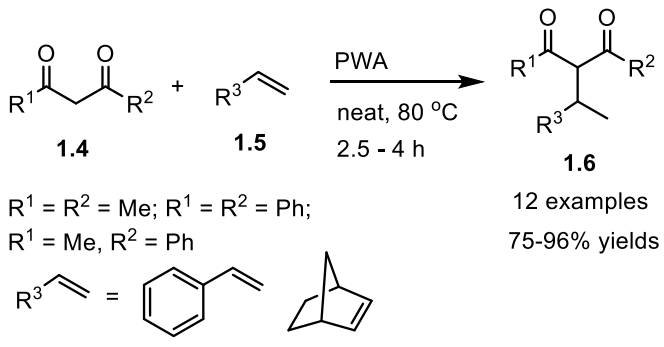
In the next year efficient regioselective addition of *β*-diketones to styrenes, norbornene, cyclic enol ether, and diene was reported by means of copper(II) triflate as the catalyst (Scheme 1.7) [22]. The solvent effect is prominent on the reactions, and the desired addition products were obtained in good to excellent yields only in dioxane or ionic liquid [bmim]PF_6. The mechanism suggested that copper(II) triflate activated the enolic O-H bond of a *β*-diketone substrate to initiate the addition reaction. The reactions were carried out using variety of β-diketones (**1.4**) reacting with alkenes (**1.5**). Most of the 1,3-dicarbonyl compounds were effectively added to styrenes, norbornene, cyclic enol ether, and diene, but no desired product was detected from the reactions of dimethyl malonate with alkenes, which might be attributed to the incapability of dimethyl malonate to be enolized during the reaction. The addition of 2,4-pentanedione to styrenes and norbornene in dioxane formed the desired products in 42-69% yields.

Scheme 1.7



Wang et al. demonstrated an efficient methodology for the solvent-free direct hydroalkylation reactions of styrene and norbornene with 1,3-dicarbonyl compounds catalyzed by 12-phosphotungstic acid (PWA) (Scheme 1.8) [23]. The reactions proceeded in excellent yields, performed in air, and avoided the usage of toxic organic solvent. The authors investigated the scope of 1,3-diketone substrates in the hydroalkylation reaction of styrene and norbornene. The reaction of symmetric 1,3-diarylpropane-1,3-diones with para-substituents on the phenyl moiety with styrene at 80 ºC was investigated, furnishing the final adducts in slightly decreased yields compared with 1,3-diphenylpropane-1,3-dione. The electronic factor of the substituents exhibited an insignificant influence on the reactivity of 1,3-diketones. When acetylacetone was heated with styrene at 80 ºC, the corresponding product was isolated in low yield. Elevating the temperature to 120 ºC proved helpful, the reaction completed in 2 h, affording the corresponding product in 75% yield. Two asymmetric 1,3-diketones were employed, both of them gave the corresponding adducts in high yields as mixtures of inseparable diastereoisomers. Norbornene was usually employed as an active alkene in the Lewis acid-promoted hydroalkylation reactions. Its feasibility of hydroalkylation with 1,3-dicarbonyl compounds under the present reaction conditions was investigated subsequently.

Scheme 1.8



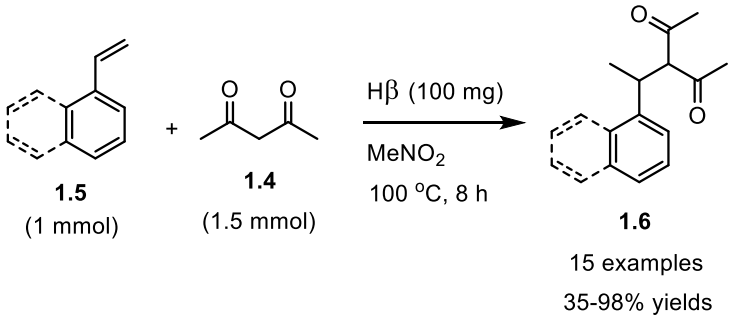
$HClO_4$ was used as an effective catalyst for the direct addition of various β-dicarbonyl compounds to a series of alkenes [24]. The metal-free reactions gave out moderate to excellent yields with water as the only byproduct. Moreover, silica-gel-supported $HClO_4$ was also successfully applied to give a solvent-free catalytic

addition as an environmentally benign protocol. The supported catalyst could be readily recovered and reused for 4 runs. The catalytic abilities of different Brønsted acids were investigated through DFT calculations and HClO4 was found to be the stronger promoter for the generation of the carbocation intermediate than TfOH and H_2SO_4.

In the same year, in 2010, Jadav et al. observed that the vinyl arenes underwent smooth hydroalkylation with 1,3-diketones in the presence of 10 mol % of iodine to afford phenethyl diketones and ketoesters in good yields in short reaction times [25]. The authors studied the reaction of alkenes with different 1,3-diketones such as 3-methylacetylacetone, dibenzoyl methane and 1-phenylbutane-1,3-dione. Interestingly, 3-methylpentane-2,4-dione also underwent smooth addition onto styrenes under similar conditions. Furthermore, β-ketoesters, for example, methyl acetoacetate also reacted smoothly with styrene to produce methyl 2-acetyl-3-phenylbutanoate.

Very recently Nama et al. developed a direct addition reaction of 1,3-diketone (**1.4**) with alkenes (**1.5**) employing solid acid zeolites (Hβ) (Scheme 1.9) [26]. The presence of acidic sites and the porous structures exhibited and influenced the catalytic activity. These heterogeneous catalysts were used directly for the nucleophilic addition/substitution reactions. Hβ zeolite was used for the reaction of several substituted alkenes with acetyl acetone and afforded their corresponding products from 35 to 98% yields. The validation of large-scale experiments (10 mmol) adds additional dividend to this protocol. Moreover, these heterogeneous zeolites were readily separated from the reaction mixture by simple filtration process**.** The efficiency of these zeolites for recyclability was proved for five cycles.

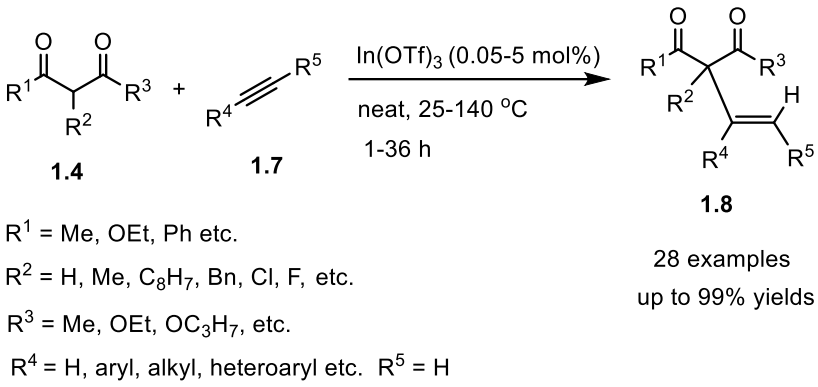
Scheme 1.9



In 2003, the Nakamura group found that heating of a neat mixture of nearly stoichiometric amounts of an active methylene compound and a terminal alkyne at 100-140 °C in the presence of a catalytic amount of $In(OTf)_3$ gave the desired α-alkenylated carbonyl compound in a high to excellent yield [27]. The reaction possessed several synthetically attractive features: (1) simple procedure allowing large-scale preparation, (2) high catalytic efficiency, (3) high yield, (4) perfect regioselectivity, (5) no requirement of solvent, and (6) the ability to create densely functionalized molecules in a single step without loss of any atoms in the starting materials.

Few years later the same group observed that 1,3-dicarbonyl compounds (**1.4**) added to unactivated alkynes (**1.7**) in the presence of a catalytic amount of indium(III) trifluoromethanesulfonate in high to excellent yield to give 2-alkenylated 1,3-dicarbonyl compounds (**1.8**) with exclusive regioselectivity as to the position of C-C bond formation on the acetylene moiety (Scheme 1.10) [28]. In most of the cases, the reaction required less than 1 mol % loading of the catalyst and did not require solvent. The reaction tolerated a wide variety of functional groups including ester, ether, allylic halide, furan, thiophene, and protected amine. Experimental and theoretical studies suggested that the reaction proceeded via a concerted carbometalation reaction of an indium(III) enolate with the acetylene, where indium-acetylene interaction is important.

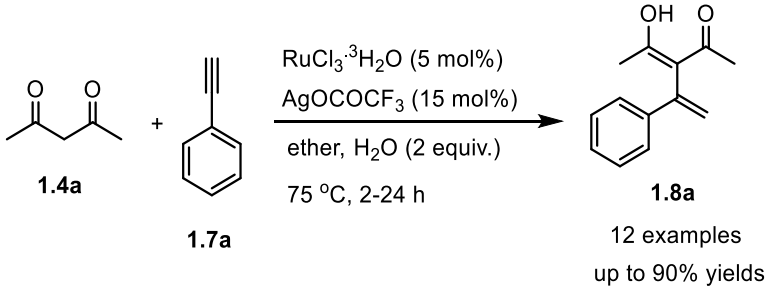
Scheme 1.10



In 2020, Bhattacharjee and co-worker reported this Nakamura reaction using a cationic cobalt(III) complex, $[Cp^*Co(CH_3CN)_3][SbF_6]_2$ as the catalyst under neutral and aerobic conditions at 110 ºC [29].

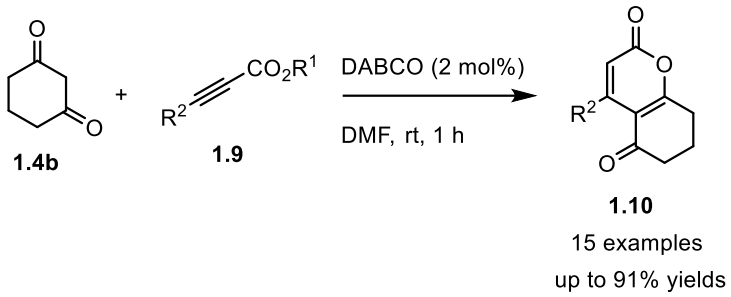
In 2012, the Williams group developed new catalytic conditions for the ene-type coupling reaction of alkynes with 1,3-diketones (Scheme 1.11) [30]. These reactions proceeded at mild temperature under air and in the presence of water with relatively low catalyst loading and minimal solvent waste. The rhenium catalyst involved significantly greater cost, and though the cost of both the indium and hydro(trispyrazolyl)boratoruthenium(II) catalysts were similar all three must be prepared and conducted under inert atmosphere with rigorously dried materials. This system was not limited by this need and was therefore more practically applicable. Additionally, all catalytic materials were commercially available, and the conditions were applicable to a diverse variety alkynes and diketones.

Scheme 1.11



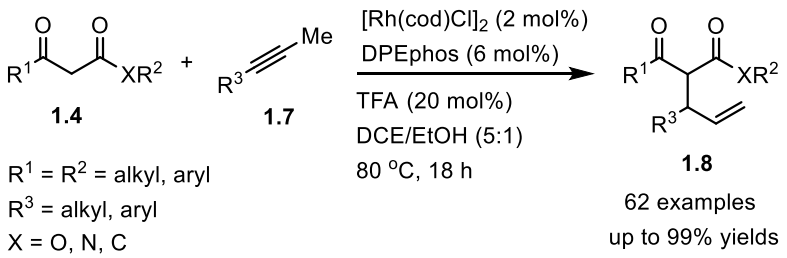
At the same time, Cao et al. developed a DABCO-catalyzed addition of 1,3-dicarbonyl compounds (**1.4b**) to alkynes (**1.9**) for the formation of C-C bonds (Scheme 1.12) [31]. The transformation provided a facile route for the synthesis of pyran derivatives (**1.10**). This reaction explored the new possibilities of *N*-catalysts for Michael addition of nucleophiles with alkynoates.

Scheme 1.12



In 2016, Breit and co-worker reported the first rhodium-catalyzed regioselective addition of 1,3-dicarbonyl compounds (**1.4**), including β-keto esters, β-keto amides, and 1,3-diketones, to internal alkynes (**1.7**) affording branched allylic compounds (**1.8**) (Scheme 1.13) [32]. By applying RhI/DPEphos/TFA as the catalytic system, aliphatic as well as aromatic internal methyl-substituted alkynes acted as suitable substrates to yield valuable branched α-allylated 1,3-dicarbonyl compounds regioselectively in good to excellent yields. A simple basic saponification-decarboxylation procedure provided access to valuable γ,δ-unsaturated ketones. The reaction showed a broad functional-group tolerance, and numerous structural variations on both reaction partners highlight the synthetic potential and flexibility of this method.

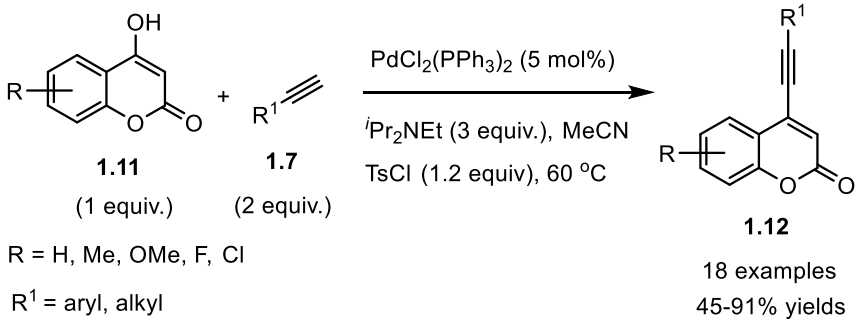
Scheme 1.13



In the next part, we have discussed about two works where 4-hydroxycoumarin has been used as 1,3-dicarbonyl compound reacting with alkenes or alkynes.

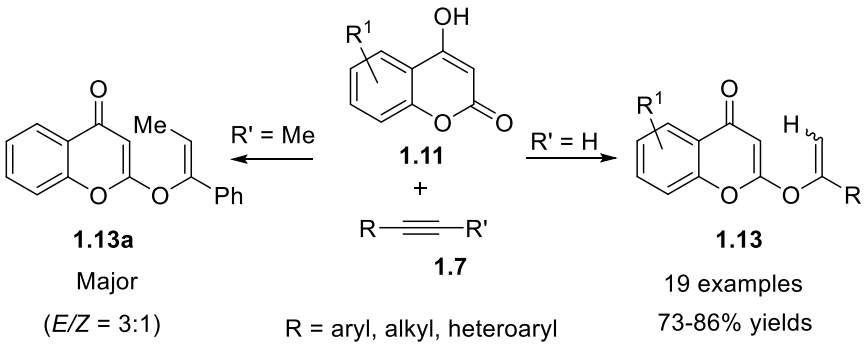
Wu and co-worker described an efficient method for the palladium-catalyzed direct cross-coupling reactions of 4-hydroxycoumarins (**1.11**) with alkynes (**1.7**) (Scheme 1.14) [33]. *p*-Toluenesulfonyl chloride was used as an activation reagent in the reaction process. In addition, this transformation was performed under copper-free conditions which generated the 4-alkynylcoumarins (**1.12**) in good yields.

Scheme 1.14



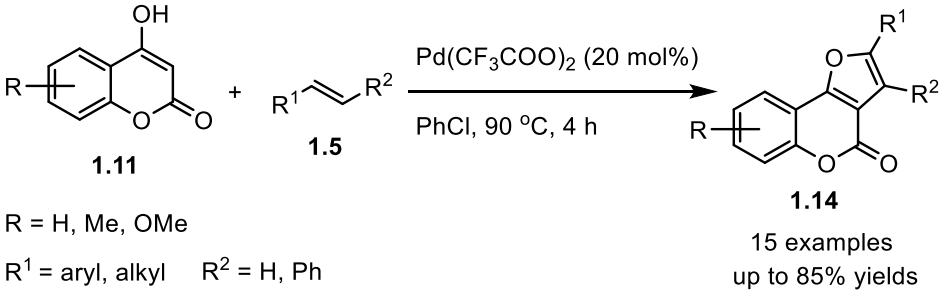
An unprecedented *O*-vinylation of 4-hydroxycoumarin has been achieved by our group from the reaction of 4-hydroxycoumarins (**1.11**) and alkynes (**1.7**) by employing $BF_3 \cdot OEt_2$ under mild reaction conditions (Scheme 1.15) [34]. This was the first report in which the carbonyl oxygen of an ester or lactone (here 4-hydroxycoumarin) reacted with an electrophile to give an O-alkylated product. A library of 2-(vinyloxy)-4*H* chromen-4-one derivatives (**1.13**) was synthesized by employing this atom-efficient methodology. During optimization, it was established that no external solvent was needed to carry out the reaction.

Scheme 1.15



In 2015, Pan and Chen et al. developed an efficient synthetic method to synthesis furo[3,2-c]coumarins (**1.14**) from readily available 4-hydroxycoumarins (**1.11**) and alkenes (**1.5**) (Scheme 1.16) [35]. This operationally simple method gives a rapid access to the furo[3,2-*c*]coumarins. Both aryl substituted internal alkenes and terminal alkenes produced high yields of furo[3,2-*c*]coumarins (**1.14**) in presence of $Pd(CF_3COO)_2$ as catalyst.

Scheme 1.16



1.3. CONDENSATION OF 1,2-DICARBONYL COMPOUNDS WITH DIAMINES FOR THE SYNTHESIS OF QUINOXALINE AND DIARYL PHENAZINE DERIVATIVES

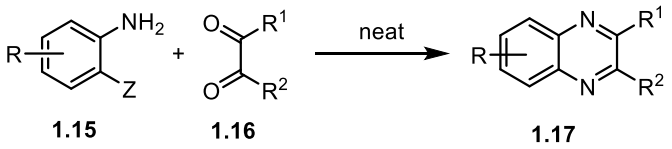
Chemically quinoxalines are fused ring system having benzopyrazine and pyrazine moiety. Diversely substituted quinoxaline derivatives with plethora of biological activities have been synthesized, tested and a unique set of libraries of novel quinoxaline scaffolds have been generated over the years [36]. Quinoxaline is one such heterocycles having plethora of biological activity [37,38] ranging from anti-cancer [39,40], anti-diabetic as PPARγ and SUR agonists [41], antibiotics/anti-microbial [42], anti-convulsant [43], anti-fungal [44], anti-tubercular [45], anti-malarial [46], anti-leishmanial [47], anti-amoebic [48], anti-HCV [49], anti-inflammatory [50], anti-viral [51], etc.

Owing to its diverse biological activity, the development of novel, greener and efficient synthetic methodology for accessing quinoxalines has long been a reverent subject of research for synthetic medicinal chemists. The most frequently utilized methodology for the synthesis of quinoxalines has been the simple condensation reaction of 1,2-diketones with 1,2-phenylenediamines. However, other approaches such as Schmidt reaction, oxidative condensation and oxidative dehydrogenation are also being utilized to access quinoxalines.

The specific conditions and catalysts required for the synthesis of quinoxalines avoiding the use of solvent via cyclocondensation involving 1,2-diones with 1,2-diamines has been presented in Table 1. A heterogeneous biocompatible organocatalysts, CN-Pr-VB1, generated by the covalent functionalization of graphitic car- bon nitride (g-C_3N_4) nanosheets (CN) with vitamin B1 (VB1) by using 1,3-dibromopropane (Pr) as a covalent linker, was reported for the synthesis of quinoxalines at 100 °C [52]. These catalysts gained the advantage of recyclability, which can be considered as important features for sustainable green catalysis. Rutile phase of TiO_2 NPs as green catalysts have been explored as the heterogeneous

catalyst for the synthesis of quinoxalines by the acid-catalyzed condensation of isatin and *o*-phenylene diamine avoiding the use of solvent at 100 °C in good to excellent yields [53]. Another way out through simple cyclocondensation for the synthesis of quinoxalines from 1,2-diamines with diversely substituted 1,2-diketones or α-bromoketones using an heterogeneous nano-Y-Fe_2O_3-SO_3H catalysts was reported under solvent-free conditions by Harsha *et al*. [54]. The catalysts protonated carbonyl oxygen of 1,2-diketones to promote the cyclocondensation with *o*-phenylene diamine to yield quinoxalines in excellent yields and could have been recycled under the influence of external magnet. Further, these quinoxaline derivatives were evaluated for cytotoxic activity against HCT 116 cell lines. The greener synthesis of quinoxaline from *o*-phenylene diamine with 1,2-diketones has been achieved by avoiding the use of catalysts and solvent at rt via their crystallization in aqueous ethanol [55]. Sulfonated rice husk ash (RHA-SO_3H) was explored as a reusable (up to five runs), inexpensive, green and efficient solid acid catalysts for the synthesis of quinoxalines by avoiding the use of solvent for the condensation of *o*-phenylene diamine with 1,2-diketones (Table 1 , Entry 5) [56]. Another efficient protocol for the synthesis of quinoxaline derivatives from *o*-phenylene diamine and isatins was reported by avoiding the catalyst, solvent along with workup via solid state melt reaction (SSMR) with excellent yields [57]. It was also extended for the synthetic construction of other benzoheterocycles such as benzothiazoles, benzimidazoles, and benzospirothiazoles. The straightforward and mild synthesis of quinoxalines catalyzed by recyclable graphene oxide/reduced (GO/rGO) have been reported by Basu *et al*. directly from 2-nitroaniline and 1,2-diketones under complete metal-free conditions via one-pot reduction-condensation using hydrazine as the reductant for 2-nitroaniline [58].

Table 1. Specific conditions and catalysts required for the solvent-free synthesis of quinoxalines (**1.17**) via cyclocondensation involving 1,2-diones (**1.16**) with 1,2-diamines (**1.15**)



1.15 **1.16** **1.17**

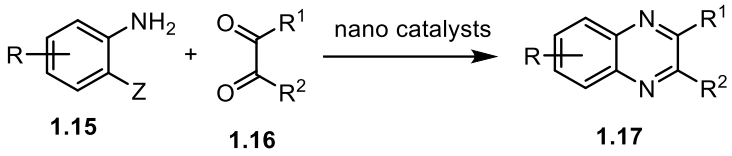
Z = NH_2, NO_2; R^2, R^3 = aryl, alkyl, heteroaryl

Entry	Catalysts	Conditions	Ref.
1	CN-Pr-VB1 (g-C_3N_4 nanosheets (CN) with vitamin B1 (VB1) by using 1,3-dibromopropane as a covalent linker)	neat, 100 °C, 3-40 min, 81–97%	[52]
2	nano TiO_2 (17 mol%)	solvent free condition, 100 °C, yield up to 95%	[53]
3	nano-Y-Fe_2O_3 -SO_3H (100 mg)	neat, 120 °C, 58-97% yields	[54]
4	-	neat, rt, excellent yield	[55]
5	sulfonated rice husk ash (RHA-SO_3H) (30 mg)	neat, 10-45 min, 90-98% yields	[56]
6	-	neat, 160 °C, 1 h,	[57]
7	Graphene oxide (GO) or reduced graphene oxide (rGO) (20 mg)	NH_2-NH_2·H_2O, 100 °C, 3 h, 48-95% yields,	[58]

The direct cyclocondensation involving 1,2-diones with 1,2-diamines has also been reported for the synthesis quinoxalines in the presence of catalytic amounts of nano-catalysts (NCs, Table 2). Among these catalysts, γ-Fe_2O_3@oxotriazolidinesultone [59], monoclinic zirconia NPs [60], and amorphous

FeNPs [61] were reported for the synthesis of quinoxalines. The NCs were easily separated from the reaction mixture by external magnet, recycled and reused for five runs without noticeable reduction in catalytic activity. The reusable and nanostructured ZrO_2 exhibited high efficiency in catalyzing condensation of various 1,2-diamines and 1,2-dicarbonyl compounds for the synthesis of quinoxaline derivatives using ethanol as ultimate green solvent [60]. It was also extended for the synthetic construction of heterocyclic compound like pyridopyrazines. The yields of quinoxalines were observed to be highly dependent on the substrates substituted with electronically demanding functional groups. The biosurfactant-stabilized iron nanoparticles (FeNPs) was reported by Salunkhe *et al*. as an amorphous, heterogeneous, nontoxic, inexpensive catalysts for the synthesis of quinoxaline via cyclocondensation of 1,2-diamines and 1,2-dicarbonyl compounds in aqueous medium at ambient conditions and they could be reused up to five runs with least alterations in catalytic performance [61]. Further, α-dicarbonyls and 1,2-diamines were used as precursor reagents to construct *N*-heterocyclic quinoxalines by Sharma *et al*. under mild reaction conditions with the characteristics of excellent functional group tolerance, high yields, and remarkable durability of catalysts (six consecutive runs). Here, simple and scalable Kirkendall effect were used to create Co_3O_4 nanocages, which involved thermal breakdown of $Co_3[Co(CN)_6]_2$ followed by loading nanocages with nickel nanoparticles to produce the final $Ni@Co_3O_4$ catalysts [62]. Under Ultrasonic/visible light irradiation, quinoxalines were synthesized from substituted benzil and 1,2-diamines in the presence of catalytic amount of $g\text{-}C_3N_4/Cu_3TiO_4$ by Arunachalapandi and Roopan in 83–98% yields under mild conditions [63]. Here, the simple thermal condensation method was used to make the reusable nanocomposites (six runs) from polymer of melamine ($g–C_3N_4$) and dual metal oxide (Cu_3TiO_4).

Table 2. Cyclocondensation involving 1,2-diones (**1.15**) with 1,2-diamines (**1.16**) for the synthesis quinoxalines (**1.17**) in the presence of nano-catalysts



1.15 **1.16** **1.17**

Z = NH_2, NO_2; R^2, R^3 = aryl, alkyl, heteroaryl

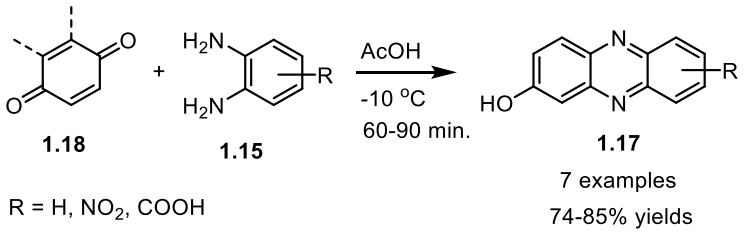
Entry	Catalysts	Conditions	Ref.
1	γ-Fe_2O_3@oxotriazolidinesultone	EtOH, 70 °C, 90-93% yields	[59]
2	Nano ZrO_2	EtOH, 60 °C, 70-96%	[60]
3	Amorphous FeNPs (5 mol%)	rt, water, 80–98% yields	[61]
4	Ni@Co_3O_4 nanocages	EtOH, 15-20 min, 30 °C, 85-100% conversion estimated by NMR	[62]
5	g-C_3N_4/Cu_3TiO_4	EtOH, ultrasonication/visible light, 3-5 min, 83-98% yields	[63]

Phenazine is a significant class of nitrogen-containing heterocycles supplying specific spine structure with electron- deficient π framework and lone pair electrons on N atoms [64-66]. It has been generally investigated in the fields of medication, pesticides, colors, and conductive materials [67,68]. From that point forward, plenteous phenazine subsidiaries have been combined and distinguished because of their alluring exhibition. As per the literature [69,70], it was firstly reported in the nineteenth century. Then, the systematically synthetic methodologies about the phenazine derivatives have been advanced in recent years.

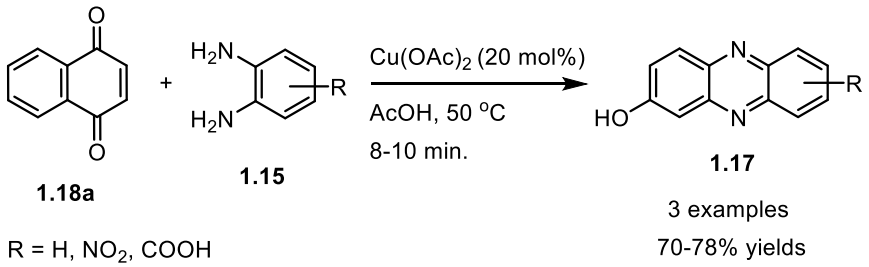
In 2013, Kour and co-workers have developed for the synthesis of phenazine and derivatives by a mild and simple method [71]. This method involved the synthesis of the expected products via cross-coupling of benzoquinones (**1.18**) with *o*-phenylenediamines (**1.15**). Substituted and unsubstituted quinones reacted smoothly with substituted or unsubstituted *o*-phenylenediamines to furnish the corresponding cross-coupled products in moderate yields. All reactions could be

carried out under air and the yields were excellent. More often than not, as shown in Scheme 1.17, this process took a long time (90 min) without catalyst. Moreover, as shown in Scheme 1.18, a remarkable effort of copper(II) acetate as a catalyst on the reaction time was discovered. Surprisingly, this reaction process only took short time (10 min) in the presence of copper(II) acetate as a catalyst, which demonstrated excellent catalytic activity to afford the expected products. This could provide an effective method for the preparation to obtain a variety of highly functionalized phenazine derivatives.

Scheme 1.17

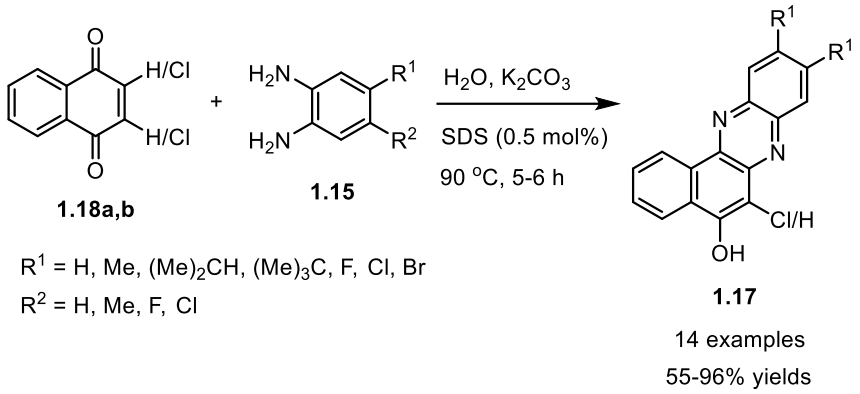


Scheme 1.18



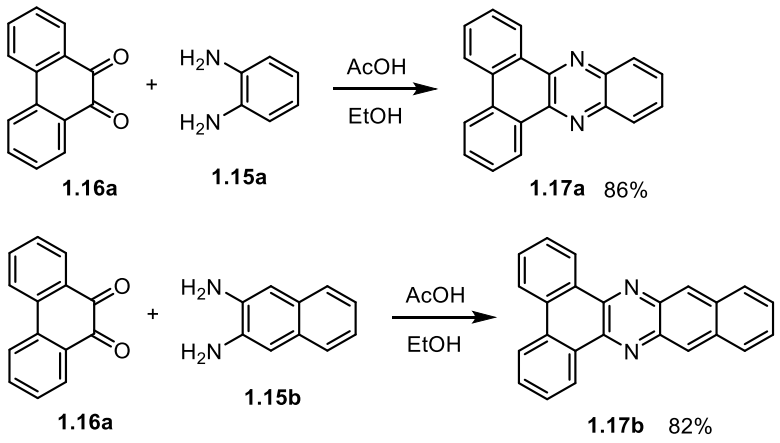
In 2014, Tandon and co-workers reported an efficient and concise one-pot regio- and chemo-selective synthesis of benzo[*a*]phenazine and derivatives [72]. As shown in Scheme 1.19, this method was employed for 2,3-dichloro-1,4-naphoquinone to nucleophile with *o*-phenylenediamine and benzamidine under the condition of H_2O in the presence of alkali and micelles (SDS) as catalysts, achieving the expected products in excellent yields. It was worth noting that this approach could be applied for the incorporation of simple linear and branched alkyl groups. Moreover, this provided a sustainable and economically cost-effective method for the preparation of phenazine derivatives.

Scheme 1.19



In 2017, Chen and co-workers disclosed an elegant formal synthesis of dibenzo [*a,c*]phenazine (**1.17a**) and tribenzo[*a,c,i*]phenazine (**1.17b**) [73]. As shown in Scheme 1.20, the success of the formation of products was obtained via a one-step sequence which involved in refluxing for 3 h with phenanthrene-9,10-dione (**1.16a**), benzene-1,2-diamine (**1.15a**) or naphthalene-2,3-diamine (**1.15b**) and ethanol as solvent. Remarkably, the reaction process was simple to operate and the reaction time was short. In addition, it was observed that the controllable luminescent behavior of the triplet state between the fluorescence and phosphorescence of phenazine derivatives, which might have potential applications in the design of organic electroluminescent devices and pure organic materials with high triplet yields.

Scheme 1.20

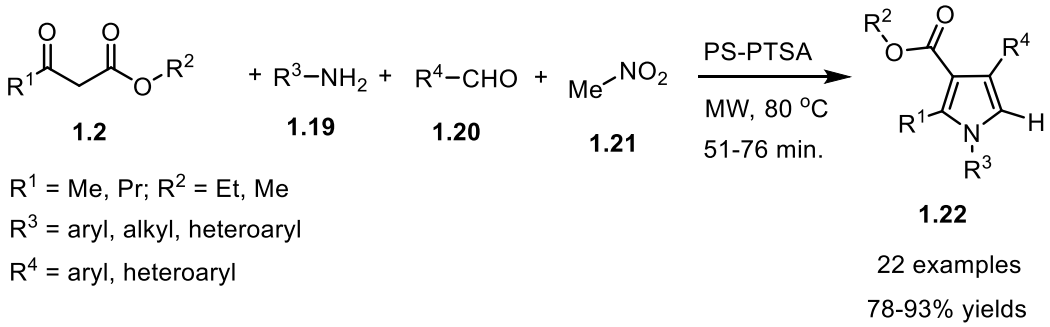


1.4. 1,2-DICARBONYL COMPOUNDS IN THE MULTICOMPONENT SYNTHESIS OF PYRROLE DERIVATIVES

Pyrrole derivatives have widely distributed in nature as a biological molecule such as porphyrin, heme, lamellarins, etc. that involved in primary and secondary metabolic pathways of plants and animal [74]. In addition, this important molecule exhibit a diverse range of biological activities [75]. Owing to their importance several method have been developed time to time for their synthesis. Here, we are summarizing some recent green, sustainable synthetic pathways of pyrroles through multicomponent reaction.

In 2014, Jeong et al. reported a solvent-free microwave assisted convenient synthesis of tetra-substituted pyrroles (**1.22**) by the multicomponent reaction between β-ketoester (**1.2**), amine (**1.19**), aldehyde (**1.20**) and nitroalkane (**1.21**) in presence of free polystyrene supported *p*-toluene sulphonic acid (PS-PTSA) as catalyst (Scheme 1.21) [76]. This procedure involved the condensation and intramolecular cyclisation steps, which was able to produce two new C-N, and two C-C bonds in a single operation. The authors carried out optimization studies and it was observed that using 5 mg of PS-PTSA catalyst at 80 °C under MW irradiation produced better yields of tetra-substituted pyrroles.

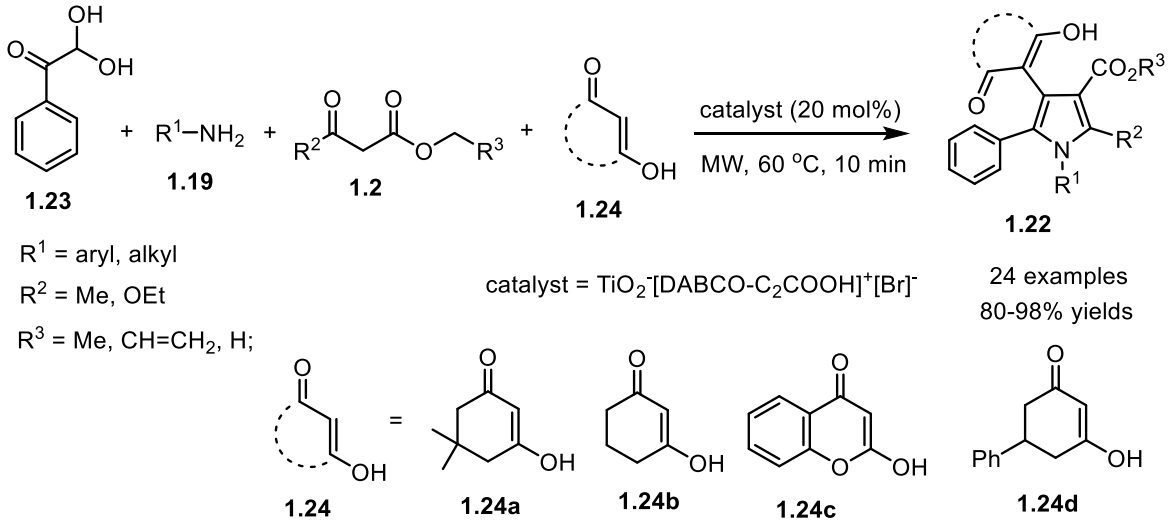
Scheme 1.21



In 2019, Mukhopadhyay et al. firstly used a unique 1,4-diazabicyclo[2.2.2]octane (DABCO) based amphoteric ionic liquid supported TiO_2 nanoparticles, which has been used as catalyst for microwave assisted solvent-free synthesis of N-substituted pyrroles (**1.22**) (Scheme 1.22) [77]. Highly substituted

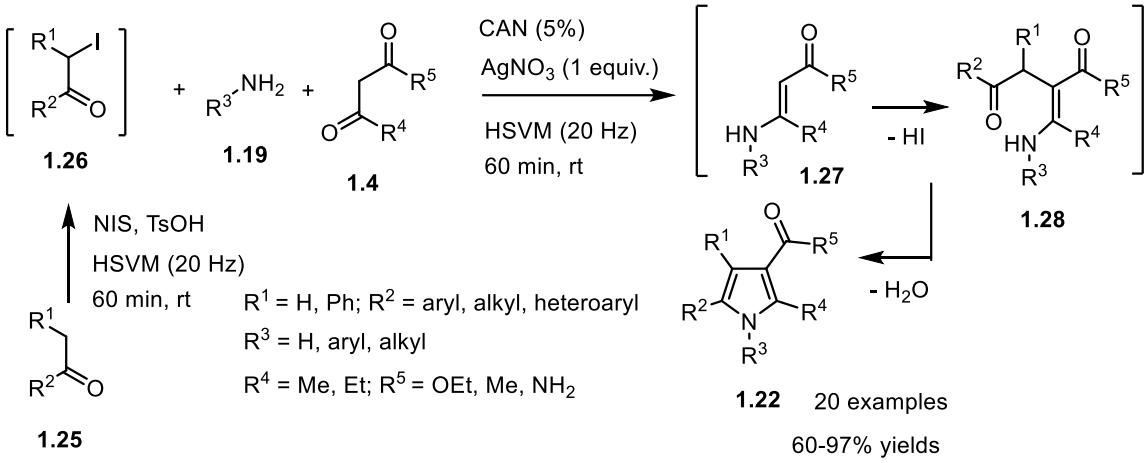
pyrroles were formed by the reaction between cyclic 1,3-diones (**1.24**), β-keto esters (**1.2**), phenyl glyoxal hydrate (**1.23**) and amines (**1.19**) via TiO_2-[DABCO-C_2COOH]$^+$[Br]$^-$ catalysis. Substrate scope was well explored and the desired product was obtained in good to excellent yields. The amplified catalytic features like high efficiency, recyclability and the quasi heterogeneous state of the catalyst makes the system highly green. This combined green catalytic system enabled the synthesis of functionalized pyrrole moieties for the first time, without any chromatographic method under microwave assisted solvent-free conditions. It was observed that microwave irradiation in TiO_2-[DABCO-C_2COOH]$^+$[Br]$^-$ for 10 min. at 60 °C was the best protocol for this transformation. This is attributed to the synergistic catalytic effect of [DABCO$^-$ C_2COOH]$^+$[Br]$^-$ and TiO_2.

Scheme 1.22



Estevez and co-workers disclosed the first multicomponent, solvent-free reaction under high-speed vibration milling (HSVM) conditions to synthesize polysubstituted functionalized pyrroles (**1.22**) (Scheme 1.23) [78]. This method was found efficient in the synthesis of differently substituted pyrroles including alkyl, secondary alkyl and dialkyl amino substituents at the nitrogen atom.

Scheme 1.23

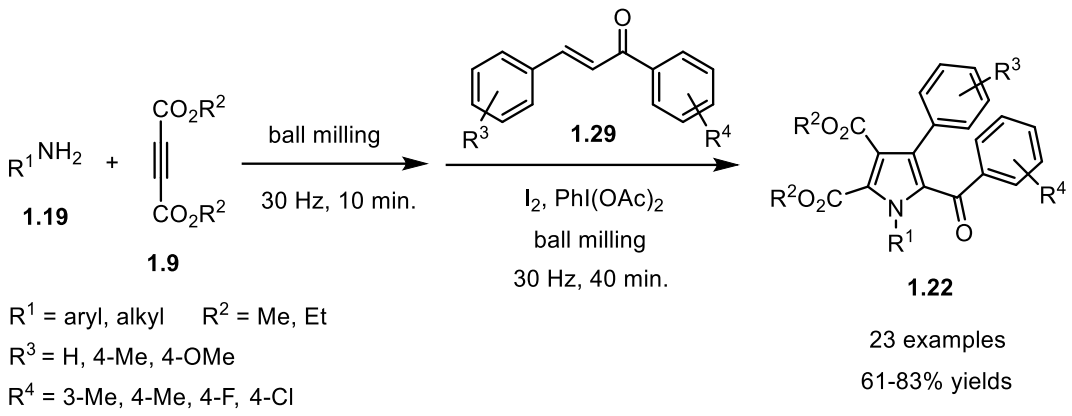


In 2014, the first example for the incorporation of a mechanochemical technique as an only source of energy in atorvastatin lactone oriented synthesis via multicomponent reaction was developed by Estevez *et al*. [79]. The authors established a very short, mechanochemical Hantzsch-type sequential three-component reaction under high-speed vibration milling conditions in the presence of ytterbium triflate and silver nitrate using the substrates 4-methyl-3-oxo-*N*-phenylpentanamide, *tert*-butyl 2-[(4*R*,6*R*)-6-(2-aminoethyl)-2,2-dimethyl-1,3-dioxan-4-yl]acetate and 1-(4-fluorophenyl)-2-iodo-2-phenylethanone and obtained the target compound in 38% overall yield. The authors also attempted a complete solvent-free synthesis of atorvastatin analogues utilizing the same substrates along with CAN and silver nitrate at a high speed vibration of 20 Hz for 1 hour, affording moderate yields of the desired products, but as a regioisomeric mixture.

An I_2/PhI(OAc)$_2$-promoted synthesis of pyrroles (**1.22**) was reported by Xu *et al*. through an efficient one-pot multicomponent reaction of amines (**1.19**) with alkyne esters (**1.9**) and chalcones (**1.29**) under solvent-free conditions under ball milling for the first time (Scheme 1.24) [80]. It was observed that the addition of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to the reaction system could afford synthetically more attractive pyrroles. The reaction was examined with different substrates and shown that the proposed methodology tolerated a good range

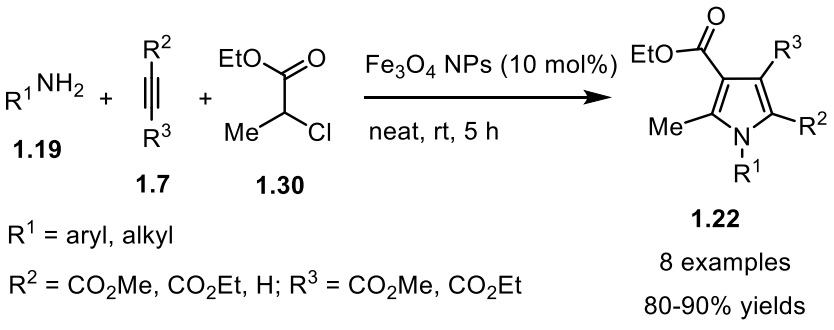
of functional groups. Optimized conditions utilized 0.1 mmol PhI $(OAc)_2$, and 0.8 mmol DDQ at ball milling conditions affording good yields. This strategy featured a highly efficient large-scale friendly, solvent- add metal-free reaction under mild conditions.

Scheme 1.24



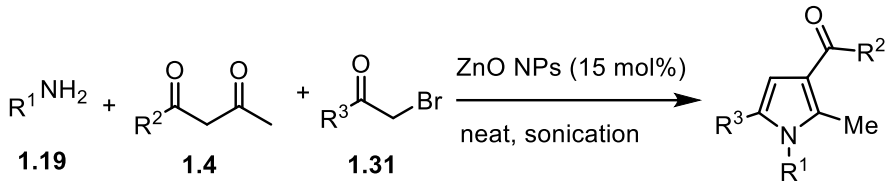
Hossaini *et al.* developed a solvent-free synthesis of 1*H*-pyrrole derivatives using Fe_3O_4 nanoparticles at room temperature using green synthetic protocols (Scheme 1.25) [81]. The reaction of primary amine (**1.19**), ethyl 2-chloroacetoacetate (**1.30**), and activated acetylenic compounds (**1.7**) in the presence of magnetic Fe_3O_4 nanoparticles led to pyrrole derivatives **1.22** in excellent yields It was observed that the reaction initiated with the reaction of activated acetylenic moiety and primary amines to form aminoacrylate. An adduct was formed in the presence of Fe_3O_4 NPs which further on intermolecular cyclisation with the removal of a water molecule yielded the desired product.

Scheme 1.25



A solvent-free ZnO nanoparticles-catalyzed synthesis of 1,2,3,5-tetra-substituted pyrrole derivatives was reported under sonochemical conditions (Scheme 1.26) [82]. This reaction was carried out by the three component one-pot reaction between amines (**1.19**), β-dicarbonyls (**1.4**) and α-bromo ketones (**1.31**) which afforded moderate to good yields. Extensive examinations were done to check the influence of various reaction parameters like solvent, catalyst loading, and time and optimized the amount of catalyst as 15 mol%. This ZnO nanoparticles catalyst was found efficient towards the reaction of primary aromatic amines such as anilines with α-bromo ketones and β-dicarbonyl compounds. The solvent-free conditions, reusability of the catalyst made this reaction highly significant and environmentally friendly.

Scheme 1.26



R^1 = aryl, alkyl; R^2 = OEt, OMe; R^3 = H, OMe, Br, COOEt

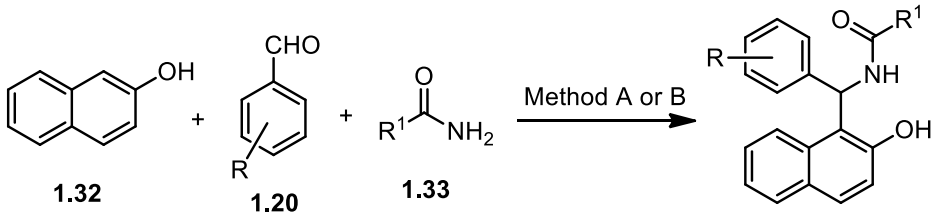
1.5. SELECTED REACTIONS OF MONO-CARBONYL COMPOUNDS WITH *N*-NUCLEOPHILES

1.5.1. Synthesis of 1-Amidoalkyl-2-naphthols

1-Amidoalkyl-2-naphthols have emerged as molecules of great importance mainly due to their hydrolyzed product 1-aminoalkyl-2-naphthols, which possess interesting drug-like properties [83,84]. These derivatives have been evaluated for their potential biological activities, such as hypotensive [85], bradycardic [86], antibiotic [87], analgesic [88], anticonvulsant [89], antitumor [90], anti-anginal [91], antimalarial [92], antipsychotic [93], antirheumatic [94] and antihypertensive [95]. They can be synthesized from the condensation reaction between 2-naphthol, aromatic aldehydes and amides. In this short review, we have discussed the synthesis of this moiety which has been reported in the last decade.

Karimi-Jaberi et al. developed very simple and efficient methods for the high-yielding synthesis of 1-amidoalkyl-2-naphthols (**1.34**) by one-pot three-component coupling of 2-naphthol (**1.32**), various aromatic aldehydes (**1.20**), and amides (**1.33**) using trichloroacetic acid or cobalt(II) chloride as catalyst (Scheme 1.27) [96]. The authors prepared a range of 1-amidoalkyl-2-naphthols under the optimized reaction conditions: 2-naphthol (**1.32**, 1 mmol), aryl aldehydes (**1.20**, 1 mmol), and acetamide (**1.33a**, 1.3 mmol) in the presence of trichloroacetic acid (0.048 g, 30 mol%). A series of 1-amidoalkyl-2-naphthols was prepared in high to excellent yields. The catalyst is readily available and inexpensive and can conveniently be handled and removed from the reaction mixture.

Scheme 1.27



R = H, Me, OMe, NO_2, F, Cl etc.

R^1 = Me, Ph, CH_2=CH

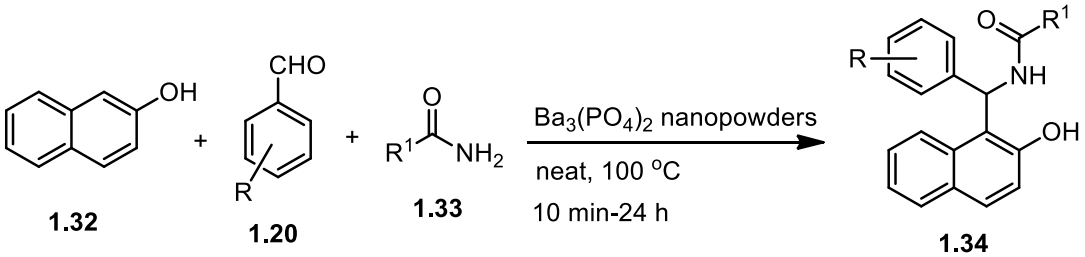
23 examples

Method A: Cl_3CCOOH, neat, 120 ^oC, 1-67 min., 82-99% yields

Method B: $CoCl_2 \cdot 6H_2O$, neat, 120 ^oC, 1-3 h, 68-96% yields

In 2016, $Ba_3(PO_4)_2$ nanopowder was prepared by a simple precipitation method and was used as an efficient catalyst for the preparation of 1-amidoalkyl-2-naphthol derivatives (Scheme 1.28) [97]. It was stated that the use of 0.083 mmol of $Ba_3(PO_4)_2$ as catalyst for the catalytic condensation reaction of aromatic aldehydes (**1.20**), 2-naphthol (**1.32**) and amides (**1.33**) under ambient condition provides high yields of products. In all cases, arylaldehydes carrying either electron-donating or electron-withdrawing groups reacted successfully and gave the products in high yields. However, in the case of alkylaldehydes, complicated products were formed under the optimized conditions, which probably resulted from the aldol formation. The use of cyclohexanecarbaldehyde did not correspond to the expected product.

Scheme 1.28



R = H, Me, NO_2, F, Cl, ^{t}Bu etc.

R^1 = Me, Ph,3-MePh, MeNH

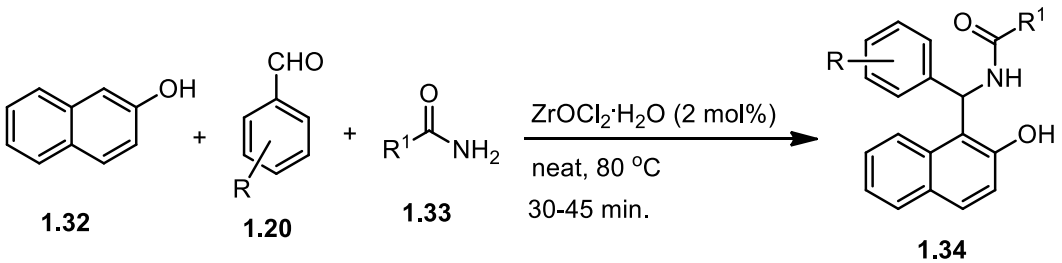
32 examples

up to 94% yields

At the same time, an efficient synthesis of amidoalkyl naphthols (**1.34**) was reported from the reaction of β-naphthol (**1.32**) and various aromatic aldehydes

(**1.20**) and amides (**1.33**) using $ZrOCl_2 \cdot 8H_2O$, an environmentally friendly catalyst under a thermal solvent-free green procedure (Scheme 1.29) [98]. Amidoalkyl naphthols containing electron-withdrawing groups such as nitro group or electron-donating groups such as alkyl and alkoxy groups were formed in a short experimental time (30–45 min) with high yields (83-96%). In addition, urea and different amines such as benzamide and acetamide worked equally. The catalyst $ZrOCl_2 \cdot 8H_2O$ can be reused.

Scheme 1.29



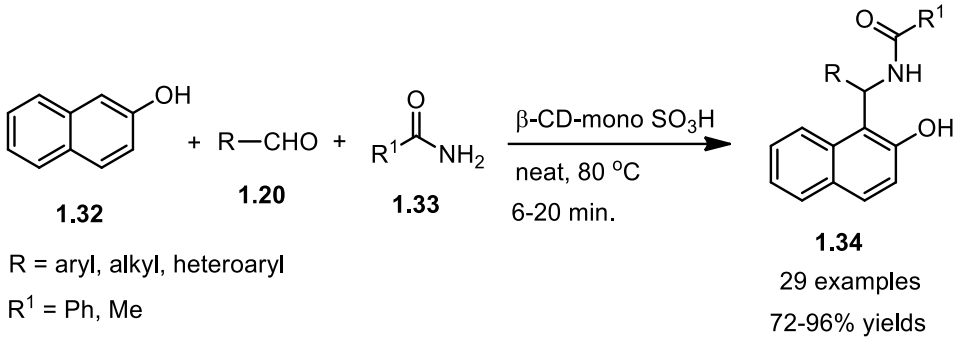
1.32 **1.20** **1.33** **1.34**

R = H, Me, OMe, Cl, Br, F, NO_2,
R^1 = Me, Ph, NH_2

24 examples
82-96% yields

An efficient and rapid approach was developed for the synthesis of 1-amidoalkyl-2-naphthols catalyzed by β-cyclodextrin-monosulphonic acid under solvent-free conditions (Scheme 1.30) [99]. The catalyst can be prepared easily from readily available β-cyclodextrin in a single step procedure and is characterized by ESI-Mass (Electrospray Ionization-Mass), elemental analysis and TGA (Thermogravimetric analysis). A total of 29 compounds were prepared from various aldehydes (**1.20**), amides (**1.33**) and 2-naphthol (**1.32**) using this β-cyclodextrin-monosulphonic acid indicating the broad substrate scope of this method. The catalyst can be reused for further reaction.

Scheme 1.30



1.32 **1.20** **1.33** **1.34**

R = aryl, alkyl, heteroaryl

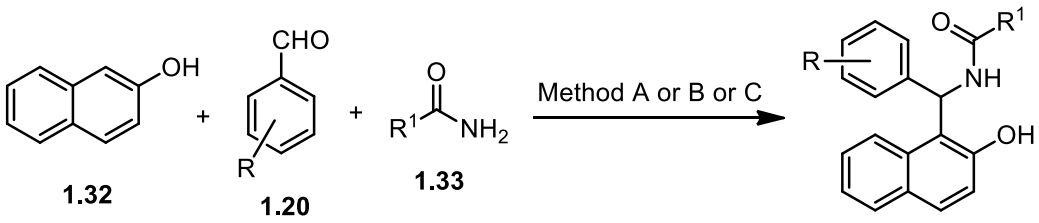
R^1 = Ph, Me

29 examples

72-96% yields

In 2018, a facile, cost-effective and environment-friendly protocol was reported for the synthesis of 1-amidoalkyl-2-naphthols (**1.34**) exploring tannic acid as a novel, cheap and biodegradable catalyst (Scheme 1.31) [100]. β-Naphthol (**1.32**) was condensed with substituted aromatic aldehydes (**1.20**) and various amides (**1.33**) using catalytic amount of tannic acid in the absence of solvent under thermal (hot plate and oil bath) and microwave irradiation techniques. Various functionalities present in the aryl aldehydes, such as methyl, chloro, dimethyl amino, nitro, and methoxy with urea/acetamides/benzamides groups were well tolerated under these conditions. However, the reactions of aliphatic aldehydes failed to give the desired products.

Scheme 1.31



1.32 **1.20** **1.33** **1.34**

R = H, Me, NO_2, Cl, NMe_2, etc.

R^1 = Me, Ph, NH_2, C_6H_4N

16 examples

Method A: Tannic acid (0.03 mmol), MW irradiation, 5-13 min, 82-90% Yields

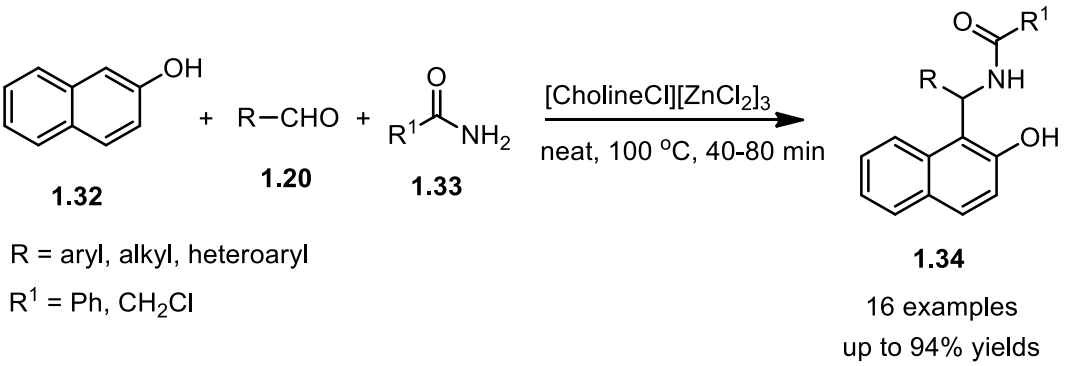
Method B: Tannic acid (0.03 mmol), oil bath, 110-120 °C, 7-20 min, 75-90% Yields

Method C: Tannic acid (0.03 mmol), hot plate, 10-21 min, 47-76% Yields

In 2021, a multicomponent synthesis of 1-amidoalkyl naphthols was reported as an atom-economic procedure catalyzed by a deep eutectic solvent

([CholineCl][$ZnCl_2$]$_3$) (Scheme 1.32) [101]. The reactions proceeded at low temperatures for a short reaction time without the use of toxic and volatile organic solvents. Deep eutectic solvents were capable of not only allowing multicomponent reactions to proceed in high yield but also controlling the selectivity towards desired products. The mechanistic insight was examined by HRMS (ESI) to propose a plausible mechanism. Furthermore, [CholineCl][$ZnCl_2$]$_3$ can be recycled in up to three consecutive cycles with an insignificant loss of catalytic activity under the optimized conditions.

Scheme 1.32



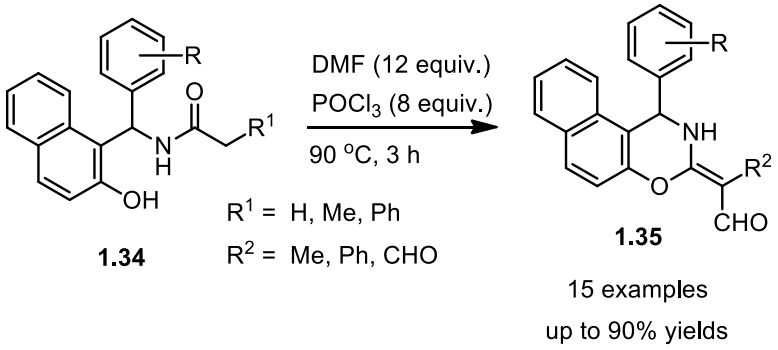
1.5.2. Transformation of 1-Amidoalkyl Naphthols to Oxazines

Further transformation of amidoalkyl naphthols can be done affording the 1,3-oxazine derivatives. The 1,3-oxazines has attracted attention in the past because of their potential as antibiotics [102], antitumor agents [103], analgesics [104], and anticonvulsants [105]. 1,3-Oxazines have generated great interest as anti-psychotic agents and as possible effectors for serotonin and dopamine receptors [106]. In addition, benzo-1,3-oxazines are known to be biologically active as anti-malarial [107], antianginal [108], anti-hypertensive [109] and potent anti-rheumatic agents [110].

In 2009, Perumal et al. reported the first example of the use of the Vilsmeier reagent for the synthesis of oxazine derivatives (**1.35**) from amidoalkyl naphthols (**1.34**) (Scheme 1.33) [111]. The results demonstrated the efficiency and synthetic

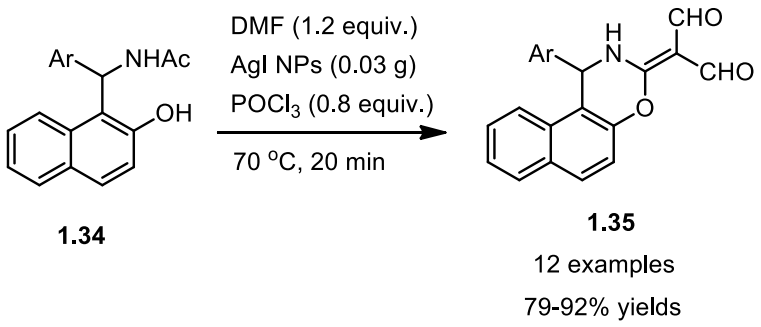
interests of the cyclization reaction with respect to amidoalkyl naphthols bearing various amide groups. It was observed that various amidoalkyl naphthols and amidoalkyl phenols reacted with Vilsmeier reagent to afford a series of substituted oxazines in good yields.

Scheme 1.33



In 2014, Ghomi et al. developed a clean and environment-friendly approach for the synthesis of (amidoalkyl)naphthol and oxazine derivatives with high yields using AgI NPs as catalyst (Scheme 1.34) [112]. The treatment of 2-naphthol, aldehyde and acetamide resulted in 1-(amidoalkyl)-2-naphthols. Then, the prepared (amidoalkyl)naphthols were reacted with Vilsmeier reagent in the presence of AgI NPs to give highly substituted functionalized oxazine derivatives.

Scheme 1.34

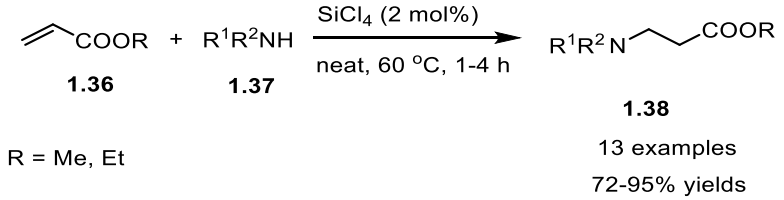


1.5.3. Transformations of Acrylates in Reactions with *N*-Nucleophiles

Reactions between acrylates with amines are the most staright-forward tool for the preparation of acrylamides, and the most common starting materal for that is acroyl chloride [113]. In case of other acrylates the main direction for the reaction is the aza-Michael addition, reaction involving the formation of a C-N bond between *N*-nucleophiles as nitrogen donors and α,β-unsaturated compounds [114]. This reaction is particularly important in the production of antibiotics, anticancer agents and bioactive molecules such as β-amino acid oligomers that can mimic the biological activity of cationic α-helical antimicrobial peptides without getting broken down by the body. Below few selective works on the aza-Michael addition reaction between acrylates and amines will be discussed.

Azizi and co-workers successfully performed a simple, high yielding, and efficient aza-Michael addition of aliphatic and aromatic amines (**1.37**) to α,β-unsaturated carbonyl compounds (**1.36**) by using a catalytic amount of silicon tetrachloride as Lewis acid [115]. The attractive aspect of this reaction is that the use of readily available and inexpensive reagents, solvent-free conditions and simple experimental procedure. In various solvents, such as DCM, acetonitrile, toluene, THF, ethanol, and even water the Michael addition proceeds over longer reaction times to give target adducts (1.38) in lower yields (Scheme 1.35). Unfortunately, the absence of isolated yields (the only NMR or GC yields were given) decreases the synthetic value of this work.

Scheme 1.35



1.36 **1.37** **1.38**

R = Me, Et

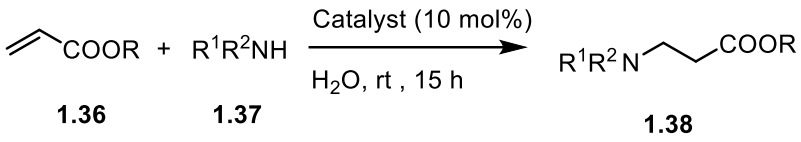
13 examples

72-95% yields

Michael donors (R^1R^2NH): piperidine, pyrrolidine, Et_2N, Bu_2NH, BnN(Me)H, $BnNH_2$, All_2NH, $ZC_6H_4NH_2$: Z = H, 4-OMe, 4-Br, 4-Cl, 4-Me, 2-Me

The reaction of aliphatic amines (**1.37**) with acrylates (**1.36**) was studied in the presence of Lewis acid $FeCl_3 \cdot 6H_2O$ as catalyst (Scheme 1.36). When primary or secondary aromatic amines (aniline, diphenylamine or α-naphthylamine) are used, more highly active catalyst ($RuCl_3$ instead of $FeCl_3$) and another solvent (PEG 2000 instead of water) is required for preparation of β-amino esters (Scheme 1.36) [116].

Scheme 1.36



1.36 **1.37** **1.38**

cat = $FeCl_3 \cdot 6H_2O$ 42-96% yields

Amines = $BuNH_2$, Et,NH, $^iPr_2NH$, Ph_2NH, piperidine, imidazole, ethylcarbamate

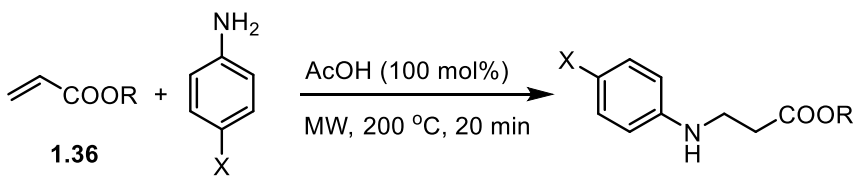
cat = $RuCl_3$, solvent PEG 2000:

Amines = Ph_2NH, aniline, α-naphthylamine

The conjugate nucleophilic addition of aromatic amines (**1.39**) to methyl and ethyl acrylates (**1.36**) in the presence of acetic acid (100 mol%) was reported (Scheme 1.37). The authors claim that the use of microwave irradiation makes it possible to obtain the target adducts (**1.40**) in a shorter reaction time compared to traditional methods [117].

Recently, trifluoromethanesulfonic acid has been successfully used as a catalyst for the addition of substituted anilines to ethyl acrylate. The Michael adducts are obtained in 44-89% yields after refluxing at 100 °C for 16 h [118].

Scheme 1.37



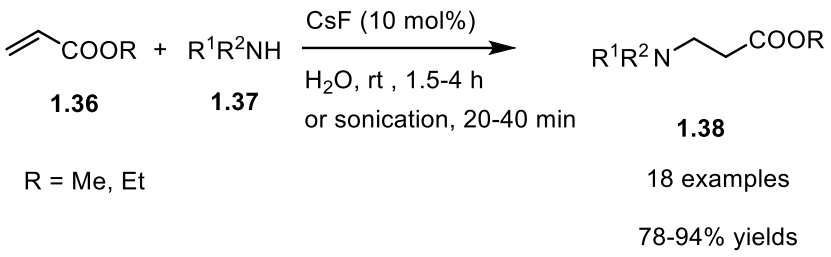
1.36 **1.39** **1.40**

R = Me, Et

X = Cl, Br, Me, OMe, NO_2

A simple alkali metals salts was also used as catalysts for conjugate nucleophilic addition [119]. For example, CsF has been proved to be an efficient catalyst for the synthesis of the derivatives of β-amino acids (esters and nitrile) through the aza-Michael reaction in water at ambient temperature with or without ultrasonic irradiation (Scheme 1.38).

Scheme 1.38

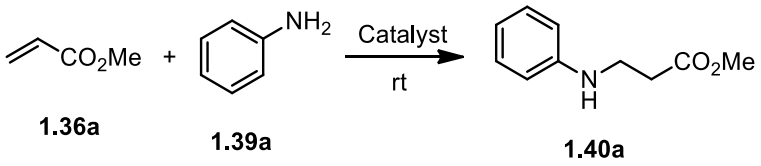


Michael donors (R^1R^2NH): Me_2NH, Et_2NH, piperidine, morpholine, $MeNH_2$, $BuNH_2$, $MeO(CH_2)_2NH_2$

Examples of the successful use of different ionic liquids in the aza-Michael reaction were documented last decade. It is shown that the aza-Michael addition of various amines to electron-deficient alkenes can be catalyzed by both basic and acidic ionic liquids, but ionic liquids having basic properties are more frequently used. The effect of various ionic liquids on the reaction course can be illustrated by examples of the addition of aromatic (aniline) amines (**1.39a**) to methyl acrylate (**1.36a**). The results of the study of these reactions in the absence of ionic liquids or in organic solvents are given for comparison (Table 3).

It worth to mention that, among the all above described examples the ones involving the formation of acroyl amides *via* green/sustainable methods, for instance by using chloride-free methods were not reported.

Table 3. Comparison of results of the study in absence of ionic liquids or in organic solvents



1.36a 1.39a 1.40a

Entry	IL	Conditions	Yields (%)	Ref.
1	-	H_2O, rt, 24 h	0	[120]
2	-	DCM, reflux, 16 h	0	[121]
3	-	EtOH, reflux, 16 h	0	[121]
4	[dbim][OH] (5 mol%)	rt, 45 min	80	[122]
5	[Im][Cl] (30 mol%)	100 °C, 2 h	88	[123]
6	[*n*-Butyl Ur][OH] (5 mol%)	rt, 1 h	75	[124]
7	[Ch][OH] (25 mol%)	H_2O, rt, 75 min	70	[124]
8	[Hmim][TFA]	80 °C, 4 h	90	[125]
9	[TMPSA][HSO_4] (10 mol%)	H_2O, rt, 4 h	88	[126]
10	[DDPA][HSO_4] (10 mol%)	H_2O, rt, 4 h	88	[127]
11	[TMG][Lac] (20 mol%)	rt, 24 h	12	[128]

1.6 CONCLUSION

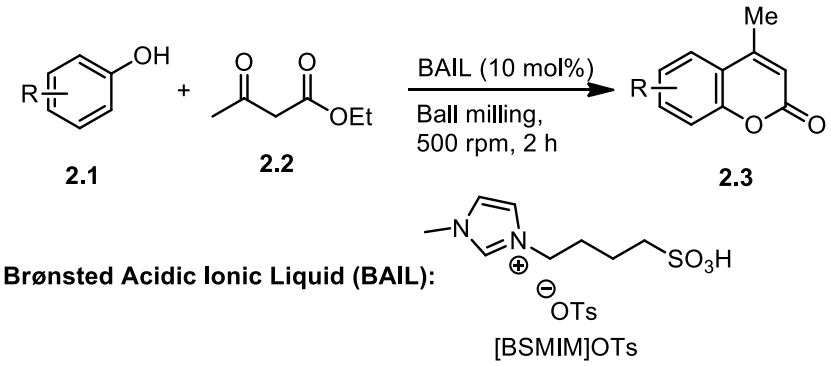
From the literature review, it has been shown that transformations of mono-, 1,2- and 1,3-dicarbonyl compounds in reactions with nucleophiles are convenient tool for the construction of various heterocycles such as coumarins, quinoxalines, phenazines, pyrroles etc., as well as various acyclic scaffolds. Most commonly these reactions are carried out in a solvent media with use of TM-based catalysts and multi-step procedures. And most of these processes result in a generation of large volumes of wastes/side products with high E-factors of the whole reactions. Not much attention in literature is given so far to the green/sustainable synthetic approaches (to the above mentioned scaffolds), such as reactions in an aqueous media, solvent-free reactions, including reactions in ionic liquids/molten salts and/or under the ball milling conditions, one-pot reactions, TM-free processes etc.

CHAPTER 2. RESULTS AND DISCUSSION

2.1. SYNTHESIS OF COUMARIN DERIVATIVES BY THE INTERACTION OF 1,3-DICARBONYL COMPOUNDS WITH PHENOLS AND INVESTIGATION OF THE POSSIBILITY OF FURTHER FUNCTIONALIZATION

The coumarin cycle presents in a large number of bio- and photoactive compounds, and the synthesis of new representatives of this series is relevant. As part of this work, we have studied the applicability of the reactions of 1,3-dicarbonyl compounds under mechanochemical conditions in the absence of a solvent for the synthesis of coumarins. Thus, as part of the work, we developed an efficient, scalable, environmentally friendly protocol for the synthesis of coumarin derivatives (**2.3**) by the Pechman condensation of phenols (**2.1**) and β-ketoesters (**2.2**) of various 1,3-diketones under mechanochemical conditions [17,129]. Further, in order to study the applicability of ionic liquids, the reaction described above was carried out in the absence of a solvent (Scheme 2.1).

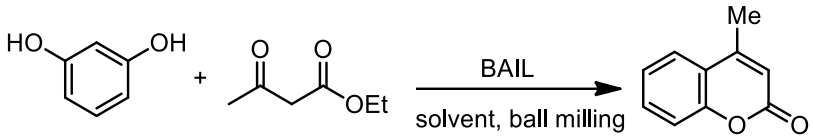
Scheme 2.1



Initially, we carried the reaction taking resorcinol (**2.1a**, 1 mmol), ethyl acetoacetate (**2.2a**, 1.5 mmol), and stirred the mixture adding 10 mol% of [BSMIM]OTs in 1,2-DCE solvent under ball milling conditions. As a result of this, we obtained the desired product **2.3a** with 38% (Table 4, entry 4). After getting this result the reaction was then performed in other available solvents such as water,

ethanol, THF and CH_3CN (Table 4, entry 2-5) to find more amount of yields but unfortunately, the solvents were unable to give a satisfactory amount of yield. Soon after, the reaction was carried out under solvent-free conditions where a very good amount of yield that is 88% was formed (Table 4, entry 6). By prolonging the time hours, the reaction yield was not improved (Table 4, entry 7) and also by decreasing the time, the yield decreased (Table 4, entry 8). Catalyst loading for this reaction was also checked. For 20 mol% of BAIL did not improve much the product formation while 5 mol% was found not enough to get a maximum yield (Table 4, entry 9-10). So the optimized reaction condition was achieved by using 10 mol% BAIL under ball milling condition after 2 h without using any external solvent.

Table 4. Optimization of the reaction conditions[a,b]



2.1a **2.2** **2.3a**

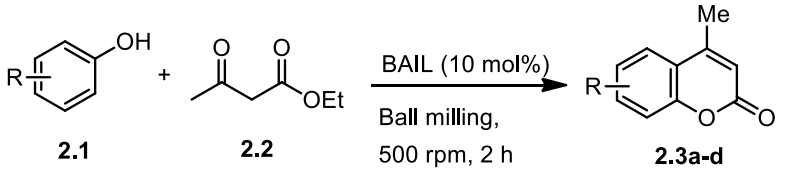
Entry	Catalyst (mol%)	Solvent	Time (h)	Yield (%)[b]
1	BAIL (10)	1,2-DCE	2	38
2	BAIL (10)	H_2O	2	46
3	BAIL (10)	EtOH	2	52
4	BAIL (10)	THF	2	24
5	BAIL (10)	CH_3CN	2	trace
6	**BAIL (10)**	**neat**	**2**	**88**
7	BAIL (10)	neat	3	86
8	BAIL (10)	neat	1	44
9	BAIL (20)	neat	2	89
10	BAIL (5)	neat	2	47

[a]Reaction conditions: resorcinol (**2.1a**, 1 mmol) and ethyl acetoacetate (**2.2**, 1.5 mmol) under ball milling. [b]Isolated yields.

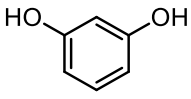
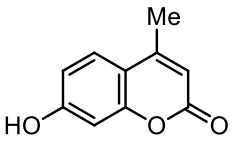
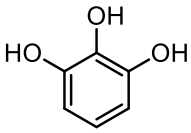
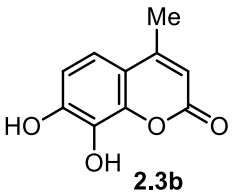
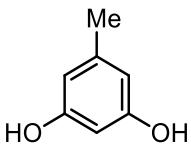
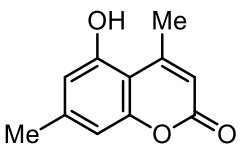
For the evaluation of the generality of our procedure, a range of substituted phenols was subjected to solvent-free under the optimized reaction conditions (Table

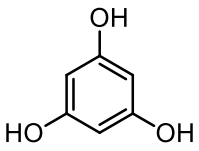
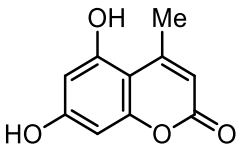
5). After getting product 7-hydroxy-4-methyl-2*H*-chromen-2-one, **2.3a** with 88% yield taking resorcinol, **2.1a** as a phenol substrate we then motivated to use some other substituted phenol for this reaction. The condensation reaction of pyrogallol (**2.1b**) and 5-methylbenzene-1,3-diol reaction (**2.1c**) with ethyl acetoacetate underwent in a good manner and we successfully synthesized the corresponding coumarin derivatives 7,8-dihydroxy-4-methyl-2*H*-chromen-2-one, **2.3b** and 5-hydroxy-4,7-dimethyl-2*H*-chromen-2-one, **2.3c** with 84% and 80% yields respectively. Another phenol derivative phloroglucinol, **2.1d** also gets converted to the respective compounds 5,7-dihydroxy-4-methyl-2H-chromen-2-one, **2.3d** considering 82% yield. The presence of extra hydroxyl group in phenyl ring leads to greater activation of the aromatic ring towards hydroxyalkylation.

Table 5. The Solvent-free Pechmann Condensation of Phenols and *β*-Ketoesters using BAIL in Ball milling[a]



2.1 2.2 2.3a-d

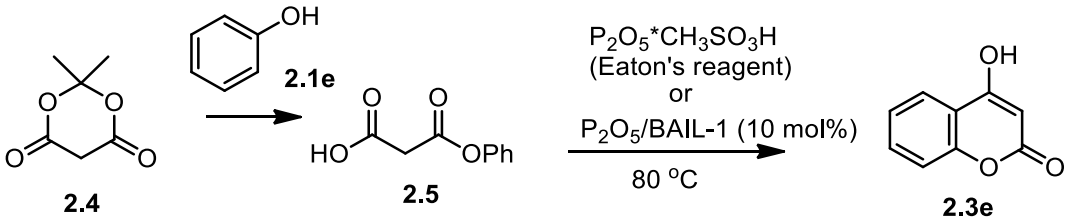
Entry	Phenol	Product (**3**)	Yield[b]
1	 **2.1a**	 **2.3a**	88
2	 **2.1b**	 **2.3b**	84
3	 **2.1c**	 **2.3c**	80

4	 **2.1d**	 **2.3d**	82

[a]Reaction conditions: Phenol (**2.1a**, 1 mmol) and ethyl acetoacetate (**2.2**, 1.5 mmol), BAIL (10 mol%) under ball milling. [b]Isolated yields.

In addition, we synthesized 4-hydroxycoumarin **2.3e** in 50% yield according to the previously described synthesis by the action of Eaton's reagent on malonic acid monophenyl ester, or by heating the latter under the action of P_2O_5 in the presence of BAIL (Scheme 2.2).

Scheme 2.2

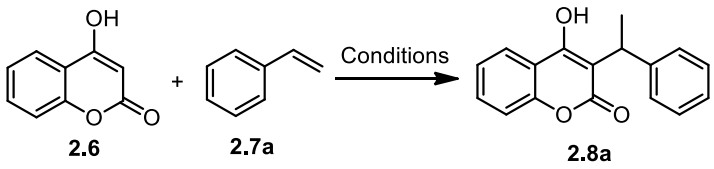


Next, we have described TsOH (*p*-toluenesulfonic acid)-catalyzed mild and efficient methodology for C_3-alkylation of 4-hydroxycoumarin by the reaction with styrenes under neat conditions (Scheme 1) [130].

We have initiated the investigation for the C_3-alkylation of 4-hydroxycoumarin taking 4-hydroxycoumarin (**2.6**, 1 mmol) and styrene (**2.7a**, 1.5 mmol) in presence of 20 mol% of TsOH and the reaction mixture was stirred under aqueous medium at 80 ºC temperature for 4 h (Table 6, entry 1). After getting 61% of moderate yield, we further performed the reaction under ethanolic medium and lower yield was found (Table 6, entry 2). After that, some other organic solvents like 1,2-dichloroethane, 1,4-dioxane, toluene and acetonitrile were introduced to check the activity of the reaction but those resulted in poor product formation (Table 6, entries 3-6). At that point, we were interested to perform the reaction under neat condition, which produced a satisfactory yield (78%) of the desired product (Table

6, entry 7). Then, we investigated the reaction by applying other available Brønsted acids such as trifluoroacetic acid (TFA), HCl, formic acid, acetic acid and benzoic acid but those catalysts were unable to proceed the reaction (Table 6, entry 8-12). Heating plays an important role in this reaction. The yield was not enhanced noticeably by increasing the temperature while a lower yield was obtained after decreasing the temperature (Table 6, entry 13-14). By increasing or decreasing the reaction time the yield was not improved (Table 6, 15-16). We have observed that 20 mol% of TsOH as the catalyst afforded better yield (78%) compared to that of 10 mol% where only 45% yield was obtained (Table 6, entry 17). Even by increasing the catalyst loading the yield did not increase (Table 6, entry 18). After considering above all experiments, the optimized reaction conditions were achieved by taking 4-hydroxycoumarin (**2.6**, 1 mmol) and styrene (**2.7a,** 1.5 mmol) in presence of 20 mol% of TsOH at 80 ºC for 4 h under neat conditions.

Table 6. Optimization of the reaction conditions on model reaction between 4-hydroxycoumarin (**2.6**) and styrene (**2.7a**) in presence of different catalysts[a]



Entry	Catalysts (mol%)	Solvent (2 mL)	Temp. (ºC)	Time (h)	Yield of 2.3a (%)[b]
1	TsOH (20)	H_2O	80 ºC	4	61
2	TsOH (20)	EtOH	80 ºC	4	49
3	TsOH (20)	DCE	80 ºC	4	28
4	TsOH (20)	1,4-dioxane	80 ºC	4	33
5	TsOH (20)	Toluene	80 ºC	4	16
6	TsOH (20)	MeCN	80 ºC	4	21
7	TsOH (20)	neat	80 ºC	4	78
8	TFA (20)	neat	80 ºC	4	trace

9	HCl (20)	neat	80 ºC	4	nr
10	HCO_2H (20)	neat	80 ºC	4	trace
11	AcOH (20)	neat	80 ºC	4	trace
12	$PhCO_2H$ (20)	neat	80 ºC	4	trace
13	TsOH (20)	neat	120 ºC	4	79
14	TsOH (20)	neat	50 ºC	4	37
15	TsOH (20)	neat	80 ºC	5	76
16	TsOH (20)	neat	80 ºC	3	68
17	TsOH (10)	neat	80 ºC	4	45
18	TsOH (30)	neat	80 ºC	4	78

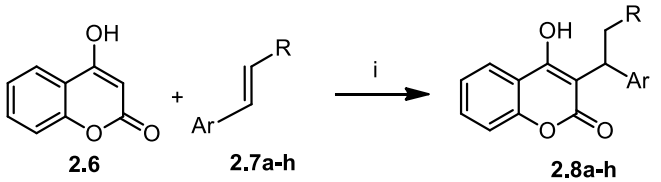
[a] Reaction conditions: **2.6** (1 mmol), **2.7a** (1.5 mmol), catalysts (20 mol%), heating. [b]Isolated yield.

Based on the optimized reaction condition, we checked the scope and limitations of our reaction protocol. For this purpose, we have introduced some substituted styrenes reacting with 4-hydroxycoumarin under the similar conditions as summarized in Scheme 2.3.

As we observed that simple styrene smoothly reacted with 4-hydroxycoumarin and produced 78% of desired product (**2.8a**). Then, 2-methylstyrene (**2.7b**) was introduced for the reaction which afforded the compound **2.8b** with a good yield (70%). After getting this result, the reaction was carried out using 4-methylstyrene (**2.7c**) and we obtained the desired product (**2.8c**) in good yield (75%). We had a choice to check the activity of 4-methoxystyrene (**2.7d**) which gave corresponding product **2.8d** smoothly (77% yield). Therefore, it was notable that the styrene bearing electron-donating group easily underwent the reaction without any obstacles. After getting these satisfying results, we investigated the effect of other substituted styrenes. Performing the reaction with 4-chlorostyrene (**2.7e**) the desired product **2.8e** was obtained in a good amount of yield (74%). Next, 3-bromostyrene (**2.7f**) was tested and 72% yield was formed as a desired product

(**2.8f**). In addition, another electron-withdrawing styrene derivative like 4-flourostyrene (**2.7g**) also gave the desired product (**2.8g**) in 73% yield by the reaction with 4-hydroxycoumarin. With our delight, we have successfully synthesized phenprocoumon **2.8h** in 68% yield by treating *β*-methylstyrene with 4-hydroxycoumarin. Although, 1-nitro-3-vinylbenzene (**2.7i**) and methyl 4-vinylbenzoate (**2.7j**) did not afford the desired products (**2.8i** & **2.8j**) under the optimaized reaction conditions.

Scheme 2.3



2.6 **2.7a-h** **2.8a-h**

2.7a Ar = Ph, R = H — **2.8a** Ar = Ph, R= H, 78%
2.7b Ar = 2-MeC_6H_4, R= H — **2.8b** Ar = 2-MeC_6H_4, R= H, 70%
2.7c Ar = 4-MeC_6H_4, R= H — **2.8c** Ar = 4-MeC_6H_4, R= H, 75%
2.7d Ar = 4-$MeOC_6H_4$, R= H — **2.8d** Ar = 4-$MeOC_6H_4$, R= H, 77%
2.7e Ar = 4-ClC_6H_4, R= H — **2.8e** Ar = 4-ClC_6H_4, R= H, 74%
2.7f Ar = 3-BrC_6H_4, R= H — **2.8f** Ar = 3-BrC_6H_4, R= H, 72%
2.7g Ar = 4-FC_6H_4, R= H — **2.8g** Ar = 4-FC_6H_4, R= H, 73%
2.7h Ar = C_6H_5, R= Me — **2.8h** Ar = C_6H_5, R= Me, 68%
2.7i Ar = 3-$NO_2C_6H_4$, R= H — **2.8i** Ar = 3-$NO_2C_6H_4$, R= H, 0%
2.7j Ar = 4-$CO_2EtC_6H_4$, R= H — **2.8j** Ar = 4-$CO_2EtC_6H_4$, R= H, 0%

Reagents and optimal conditions: i, **2.6**/**2.7** = 1:1.5 (mol/mol), TsOH (20 mol%), neat, 80 °C, 4 h (6 h for **2.3f**).

Next, we were interested to produce anticoagulant drug phenprocoumon (**2.8h**) in gram scale range and for that purpose, the reaction between 4-hydroxycoumarin (10 mmol) and *β*-methylstyrene (**2.7h**, 15 mmol) was performed in the presence of TsOH (20 mol%) under the optimized reaction conditions. As a result, 1.7 g (61%) of the desired product **2.8h** has been isolated successfully.

We have developed another similar catalytic method for direct C_3-alkylation of 4-hydroxycoumarins using styrene the presence of $BF_3{\cdot}Et_2O$ without any solvent and under 80 °C temperature (Scheme 2.4) [131].

Scheme 2.4

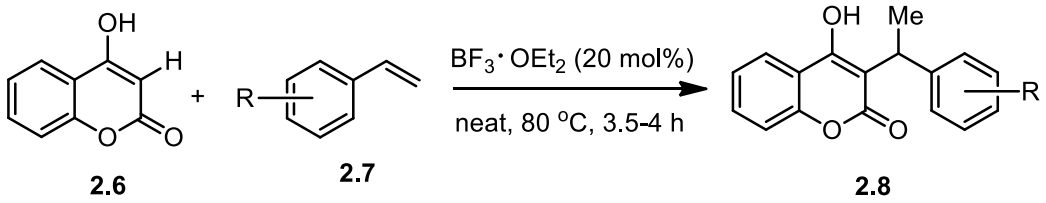
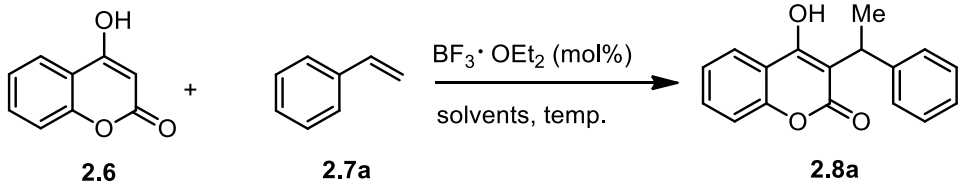


Table 7. Optimization of the reaction conditions[a]



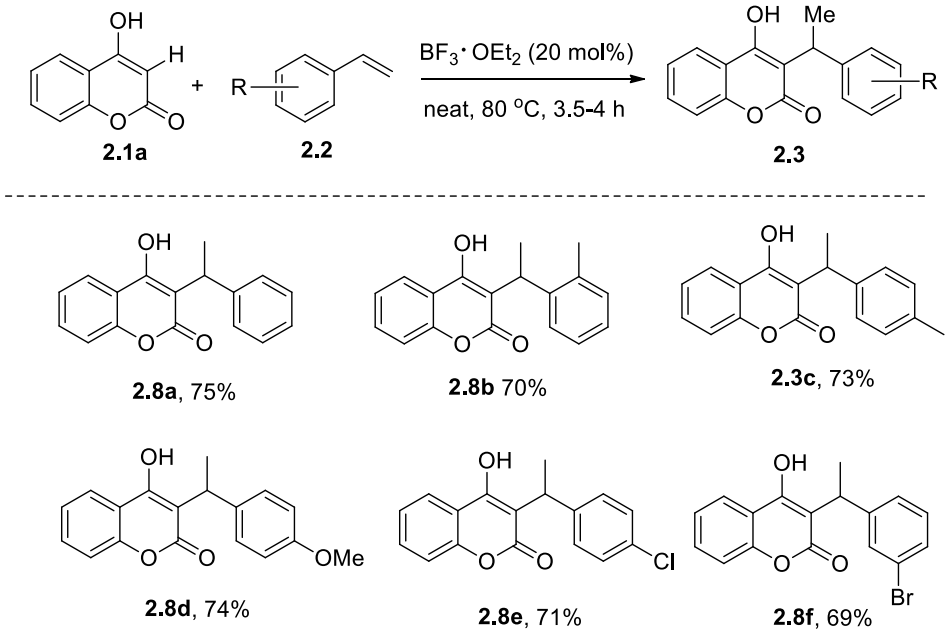
Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Yield (%)[b]
1	BF_3 .OEt_2 (20)	1,2-DCE	80 °C	54
2	BF_3 .OEt_2 (20)	MeCN	80 °C	30
3	BF_3 .OEt_2 (20)	toluene	80 °C	22
4	BF_3 .OEt_2 (20)	THF	80 °C	15
5	BF_3 .OEt_2 (20)	H_2O	80 °C	traces
6	BF_3 .OEt_2 (20)	neat	80 °C	75
7	BF_3 .OEt_2 (20)	neat	100 °C	75
8	BF_3 .OEt_2 (10)	neat	80 °C	41
9	BF_3 .OEt_2 (40)	neat	80 °C	76

[a]Reaction conditions: 4-hydroxycoumarin (**2.6**, 1 mmol) and styrene (**2.7a**, 1 mmol), $BF_3.Et_2O$ (20 mol%), stirred for 4 h. [b]Isolated yields.

Under the optimized reaction condition, 4-hydroxycoumarin **2.6** reacted with styrene **2.7a** led to the different type of product 4-hydroxy-3-(1-phenylethyl)-2*H*-

chromen-2-one **2.8a** with 75% yield (Table 8). Following this result, **6** was then allowed to react with *ortho*-, *meta*- or *para*-substituted styrene. **2.6** afforded enough to react with styrene containing either electron-donating or withdrawing groups. *Para* and *ortho*-substituted vinylbenzene (4-CH_3, 2-CH_3) gave the products **2.8c** and **2.8b** in 73% and 70% yields respectively. Upon reaction with 4-methoxysytrene 4-hydroxycoumarin was converted to the desired product **2.8d** in 74% yield. The products **2.8e** in 71% yield and **2.8f** in 69% yield were obtained when 4-Cl and 3-Br styrene were subjected to react with **2.1a**.

Table 8. Synthesis of C_3-alkylation derivatives of 4-hydroxycoumarins[a,b]

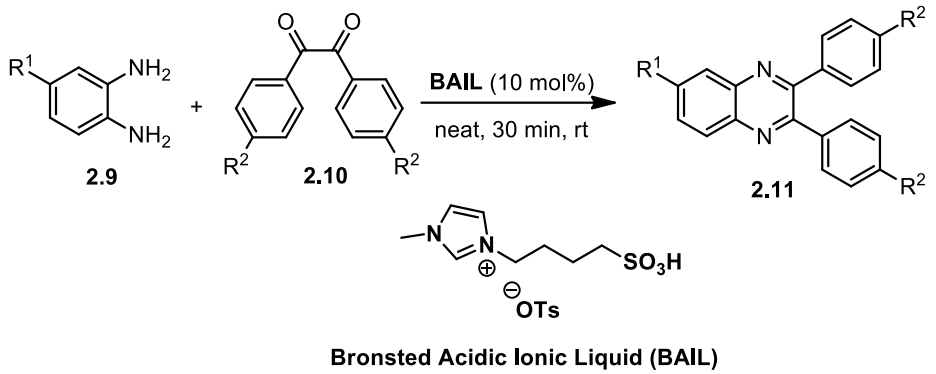


[a]Reaction conditions: 4-hydroxycoumarin (**2.6**, 1 mmol) and styrenes (**2.7**, 1 mmol), $BF_3.Et_2O$ (20 mol%), [b]Isolated yields.[c]stirred for 4 h.

2.2. SYNTHESIS OF 1,4-DIAZINES AND THEIR ANNELATED (AZA)DERIVATIVES BY REACTION OF 1,2-DICARBONYL COMPOUNDS WITH 1,2-DIAMINES

1,2-Dicarbonyl compounds are convenient synthons for the synthesis of 1,4-diazines and their annelated derivatives. In the framework of this work, we synthesized quinoxaline derivatives using Brønsted acidic ionic liquid (BAIL) [132,133]. The reaction has been performed by adding *o*-phenylenediamine (**2.9**) and 1,2-dicarbonyl compound (**2.10**) in the presence of 10 mol% of ILs under the neat condition and at room temperature (Scheme 2.5).

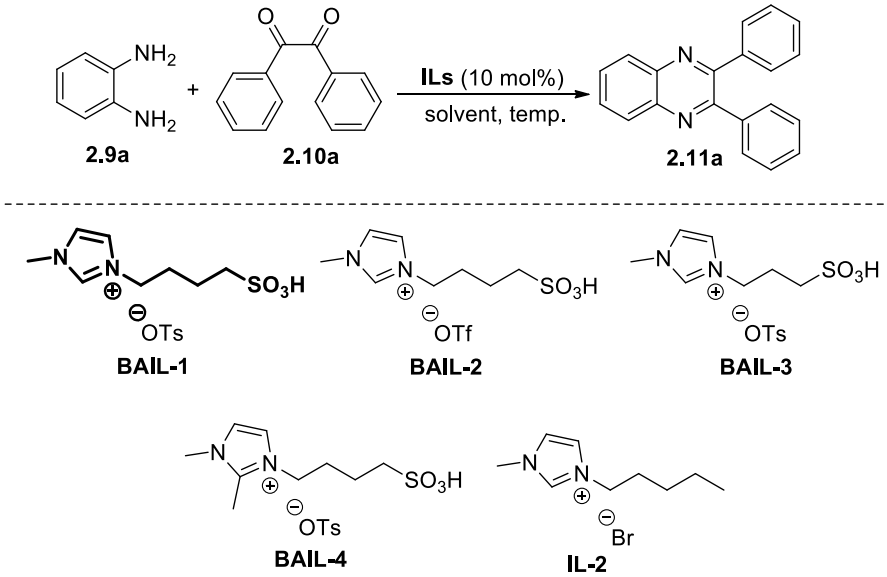
Scheme 2.5



We started the reaction with *o*-phenylenediamine (**2.9a**, 1mmol) and benzil (**2.10a**, 1mmol) adding 10 mol% of BAIL-1 and stirred the mixture at room temperature and the product **2.11a** was obtained with 86% yield (Table 9, entry 1). For further we have applied the other ionic liquids to the reaction the check the product formation. Under a similar condition, the same reaction was performed with various ionic liquids. BAIL-2, BAIL-3, and BAIL-4 (Table 9, entry 2-4) gave the desired product but it was less to some extent than when BAIL-1 was used. Ionic liquid IL-2 was also introduced but we obtained a trace amount of desired product (Table 9, entry 5). After studying the catalyst effect, we were interested to find the effect of solvent on this reaction. A solvent like water and ethanol were poured as a medium of that reaction lower yields were resulted (Table 9, entry 6, 7). The reaction

was also performed increasing the temperature to 60 ^{o}C and the yield of the desired product did not exceed. (Table 9, entry 8).

Table 9. Optimization of the reaction conditions[a]



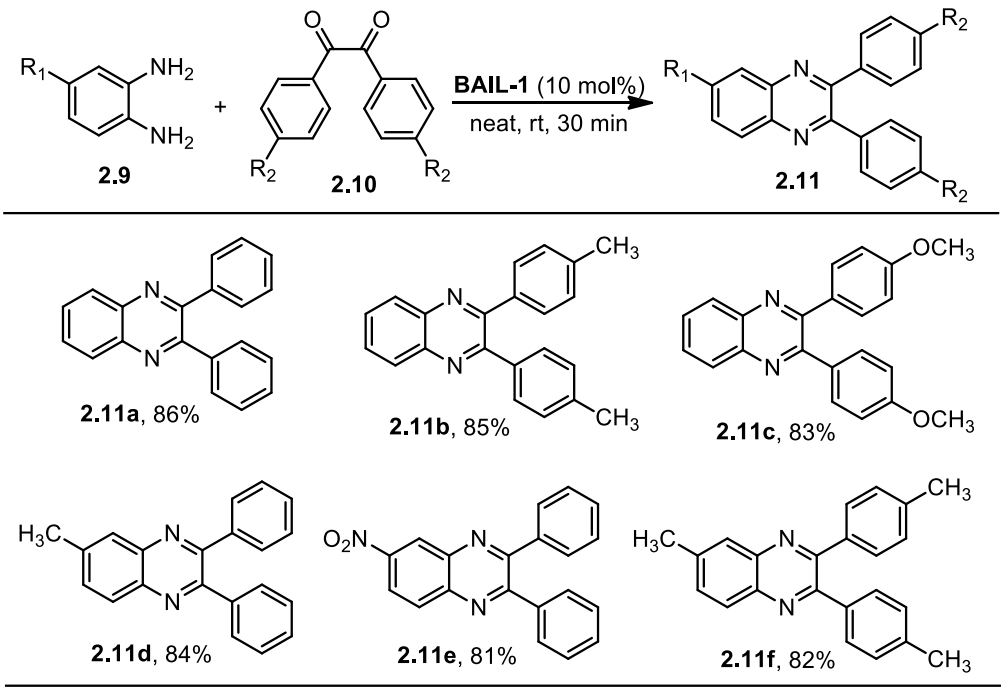
Entry	Catalysts (10 mol%)	Solvents	Temp. (^{o}C)	Yields[b] (%)
1	BAIL-1	neat	rt	86
2	BAIL-2	neat	rt	82
3	BAIL-3	neat	rt	79
4	BAIL-4	neat	rt	83
5	IL-2	neat	rt	trace
6	BAIL-1	H_2O	rt	41
7	BAIL-1	EtOH	rt	49
8	BAIL-1	neat	60 ^{o}C	85

[a]Reaction conditions: *o*-phenylenediamine (**2.9a**, 1.0 mmol) and benzil (**2.10a**, 1.0 mmol), BAIL-1 (10 mol%), stirred for 30 min. [b]Isolated yields.

Employing the present protocol, we propagated the substrate scopes (Table 10). We performed the reaction *o*-phenylenediamine and substituted benzil. 1,2-Di-

p-tolylethane-1,2-dione on reaction with phenylenediamines under this condition desired product **2.11b** was obtained in 85% yield. 4-Methoxy substituted benzil gave the targeted product **2.11c** with high yield. We also reacted to the substituted phenyl diamine like 4-methylbenzene-1,2-diamine and 4-nitrobenzene-1,2-diamine underwent the reaction with benzil to give **2.11d** and **2.11e** with excellent yields. When 4-methylbenzene-1,2-diamine reacted with dimethyl substituted benzyl **2.11f** was formed as a product with 82% yield.

Table 10. Substrates scope[a]



[a]Reaction conditions: *o*-phenylenediamine (**2.9**, 1.0 mmol) and benzil (**2.10**, 1.0 mmol), BAIL-1 (10 mol%).[b] Isolated yields.

After synthesizing the substrates, we were interested to recover the used BAIL catalyst and successfully recuperate it for further reaction. Actually, we were able to recollect the catalyst five times and each time the reaction was catalyzed efficiently with very good yields. A reusable catalytic system that can catalyse these types of reactions is the main advantage of this ionic liquid. From the viewpoint of atom

economy and energy efficiency, we figure out this reusability of the catalyst as shown in Table 11 and Figure 1.

Table 11. Recycling studies of catalyst for model reaction[a]

Run Times	**Time[b] (mins)**	**Yields[c]**
1	30	86
2	30	81
3	30	77
4	45	74
5	60	72

[a]Reaction of *o*-phenylenediamine (**2.9a**, 1.0 mmol) and benzil (**2.10a**, 1.0 mmol), BAIL-1 (10 mol%). [b]Reaction progress monitored by TLC. [c]Isolated yield.

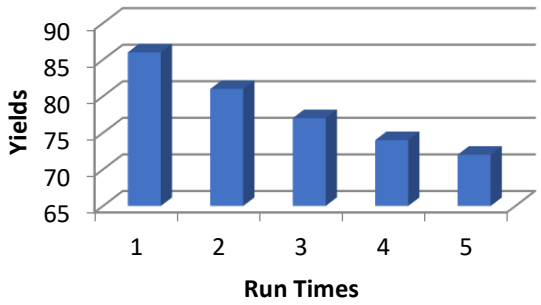
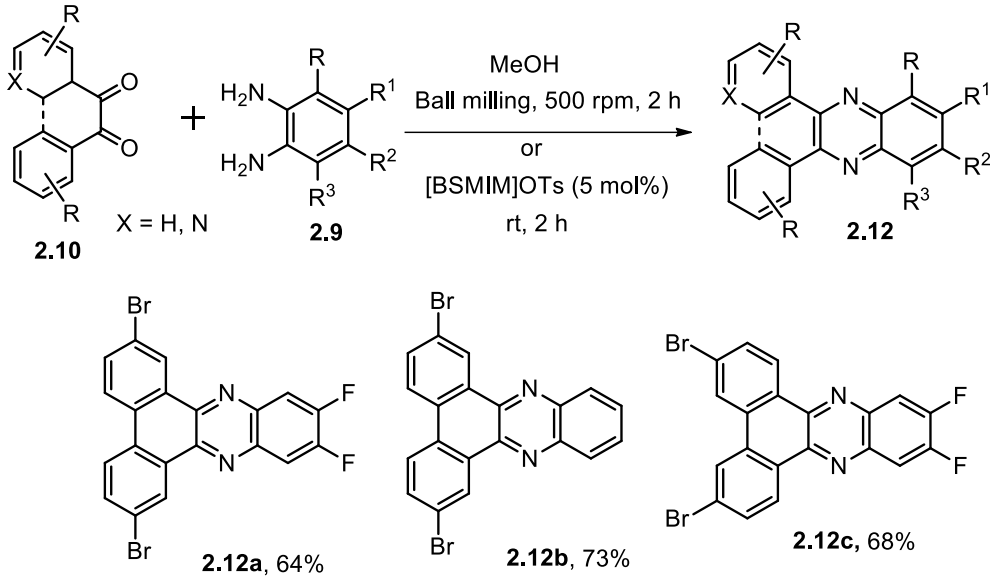


Figure 1. The reusability of BAIL-1 under optimized reaction conditions.

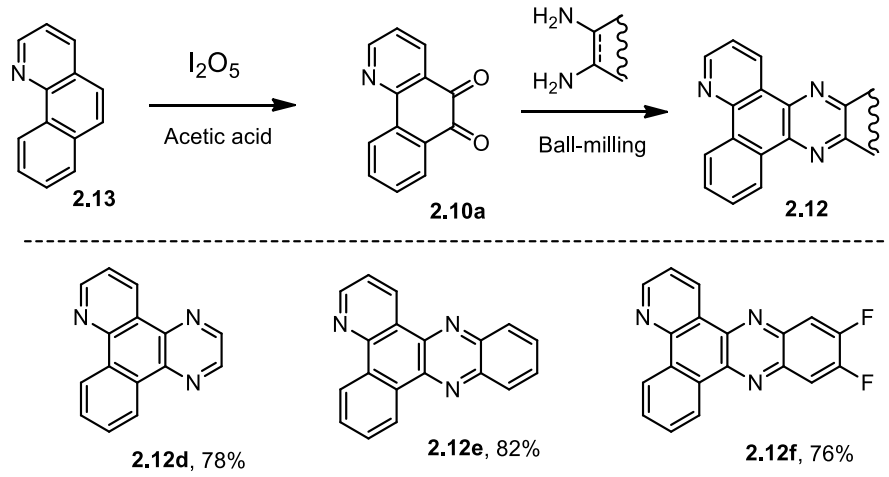
In addition, we have also synthesized several phenazine derivatives in high percentage of yields under mechanochemical conditions or in presence of 5 mol% [BSMIM]OTs catalyst at room temperature (Scheme 2.6) [134,135].

Scheme 2.6



As a follow-up to our research, we synthesized benzo[*f*]pyrido[2,3-*h*]quinoxaline **2.12d** and benzo[*c*]pyrido[3,2-*a*]phenazines **2.12e-f** in up to 82% yields under mechanochemical conditions (Scheme 2.7).

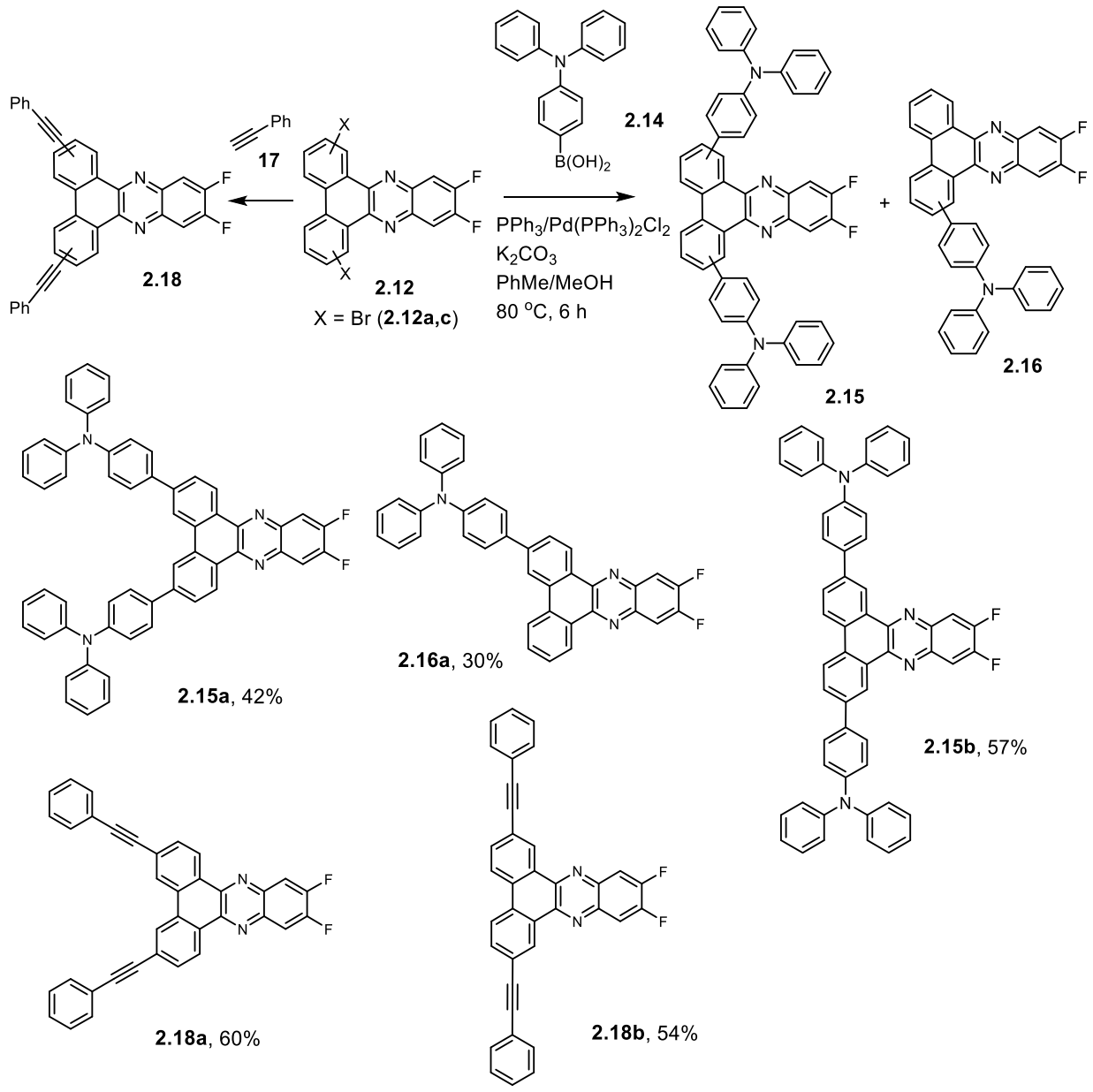
Scheme 2.7



To expand the conjugation system of the obtained quinoxalines for bromine-substituted quinoxalines **2.12a,c**, we carried out their further functionalization using the Suzuki cross-coupling procedure using 4-(diphenylamino)phenylboronic acid **2.14** with the formation of products of mono- and disubstitution of the boron atom in the aromatic ring **2.15-2.16**, as well as the Sonogashira procedure with the

formation of 11,12-difluoro-3,6-bis(phenylethynyl)dibenzo[*a*,*c*]phenazine **2.18** (Scheme 2.8). These compounds are promising push-pull Y- and T-fluorophores.

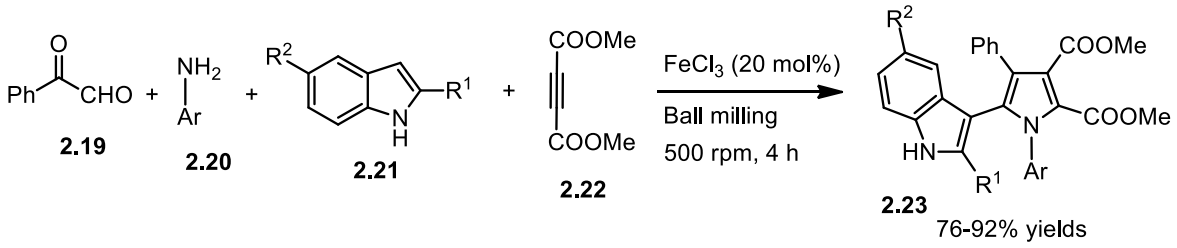
Scheme 2.8



2.3. MECHANOCHEMICAL SYNTHESIS OF MULTI-SUBSTITUTED PYRROLES

In continuation of the work on the use of mechanosynthesis, we investigated the possibility of using another 1,2-dicarbonyl, phenylglyoxal **2.19**, in a multicomponent reaction using *N*-nucleophiles, aromatic amines, *C*-nucleophiles, indoles and dimethyl ester of acetylenedicarboxylic acid, in the presence of a Lewis acid, iron(III) chloride, under mechanochemical conditions (Scheme 2.9) [136,137]. To the best of our knowledge, there is no other process available in the literature to explore this multicomponent synthesis by mechanochemical activation within a short reaction time.

Scheme 2.9



For our initial study, we have optimized the reaction conditions by varying different catalysts. For the study, phenyl glyoxal (**2.19**), *p*-toluidine (**2.20a**), indole (**2.21a**) and dimethylacetylenedicarboxylate (**2.22**) were selected as the model substrates and the reaction was carried out. The reaction was conducted at different conditions with variation of catalyst, catalyst loading, speed of rotation and time. The results are summarized in Table 12. Preliminary optimization experiments indicated that in the absence of any catalyst the reaction did not proceed and the desired product, dimethyl 5-(1*H*-indol-3-yl)-4-phenyl-1-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxylate **2.23a** was not obtained under solvent-free ball milling condition (Table 12, entry 1). Based on our previous experiences in iron-catalyzed reactions we used 20 mol% of $FeCl_3$ as catalyst and the desired product **2.23a** was obtained in 86% yield after 4 h under ball milling in 500 rpm speed (Table 12, entry 2). Next,

we shifted to iron salts as catalyst. $FeCl_3$ was found to be the most effective one among various iron salts such as $FeCl_3$, $FeBr_3$, $Fe(OTf)_3$ (Table 12, entries 3-4). However, other common Lewis acids were not effective for this conversion (Table 12, entries 5–6). All the reactions were carried out under solvent-free conditions. Although, by adding very less amount of CH_3CN as solvent (0.2 mL for 1 mmol reaction) increased the yield slightly (Table 12, entry 7). By increasing the time, the yield was not improved noticeably (Table 12, entry 8). 20 mol% was required as optimum amount of catalyst and increasing the amount of catalyst did not improve the yields while decreasing the amount of catalyst decreased the yields (Table 12, entries 9-10). Finally, the optimized conditions were achieved using 20 mol% $FeCl_3$ under solvent-free conditions for 4 h.

Table 12. Optimization of the reaction conditions for model reaction between **2.19**, **2.20a**, **2.21a**, and **2.22**[a]

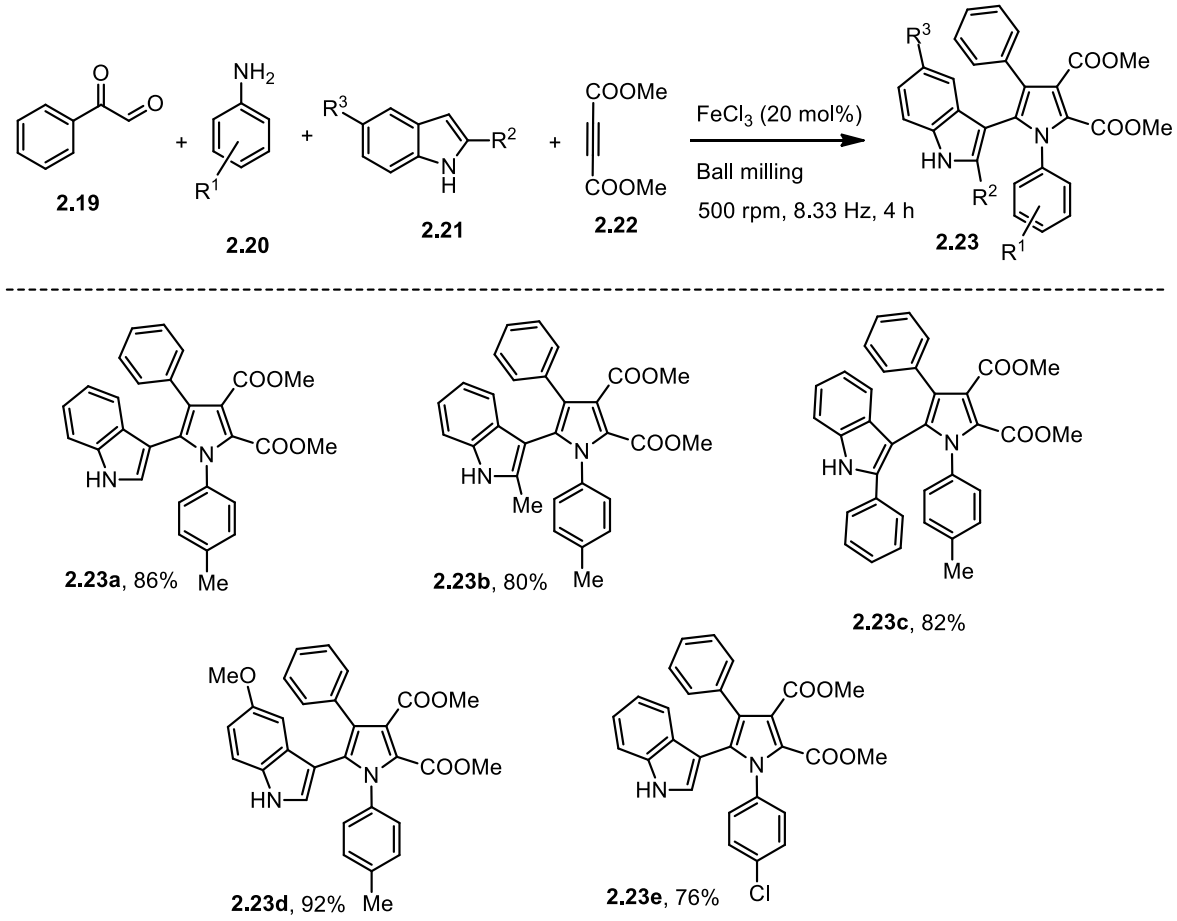
Entry	Catalyst	Catalyst loading	Rotation	Time	Yield of **2.23a**, %[b]
1	-	-	500 rpm	5 h	0
2	$FeCl_3$	20 mol%	500 rpm	4 h	86
3	$FeBr_3$	20 mol%	500 rpm	4 h	32
4	$Fe(OTf)_3$	20 mol%	500 rpm	4 h	18
5	$AlCl_3$	20 mol%	500 rpm	4 h	ND[c]
6	$BF_3{\cdot}OEt_2$	20 mol%	500 rpm	4 h	ND[c]
7	$FeCl_3$	20 mol%	500 rpm	4 h	87[d]
8	$FeCl_3$	20 mol%	500 rpm	6 h	85
9	$FeCl_3$	30 mol%	500 rpm	4 h	86
10	$FeCl_3$	10 mol%	500 rpm	4 h	54
11	$FeCl_3$	20 mol%	500 rpm	4 h	84[e]

[a]Reaction conditions: A mixture of **2.19** (1 mmol), **2.20a** (1 mmol), **2.21a** (1 mmol) and catalyst was ball milled for 30 min. Then **2.22** (1 mmol) was added and

further ball milled for 3.5 h. [b]All are isolated yields. [c]ND = Not detected in TLC. [d]0.2 mL CH_3CN was used as solvent. [e]Reaction was carried out on 10 mmol scale.

Based on the optimized reaction conditions, we checked the scope of our reaction procedure (see Scheme 2.10). During optimization we have observed that *p*-toluidine gave the desired product (**2.23a**) with excellent yields (86%). Methyl and phenyl-substituted indoles at 2-position reacted with phenyl glyoxal, *p*-toluidine and dimethylacetylenedicarboxylate very smoothly in good to excellent yields (**2.23b** & **2.23c**, 80% & 82% respectively). 5-Methoxy indole also gave good result with *p*-toluidine (**2.23d**, 92%). In addition, 4-chloroaniline was also used to react with other reactants where 76% yield was obtained (**2.23e**).

Scheme 2.10

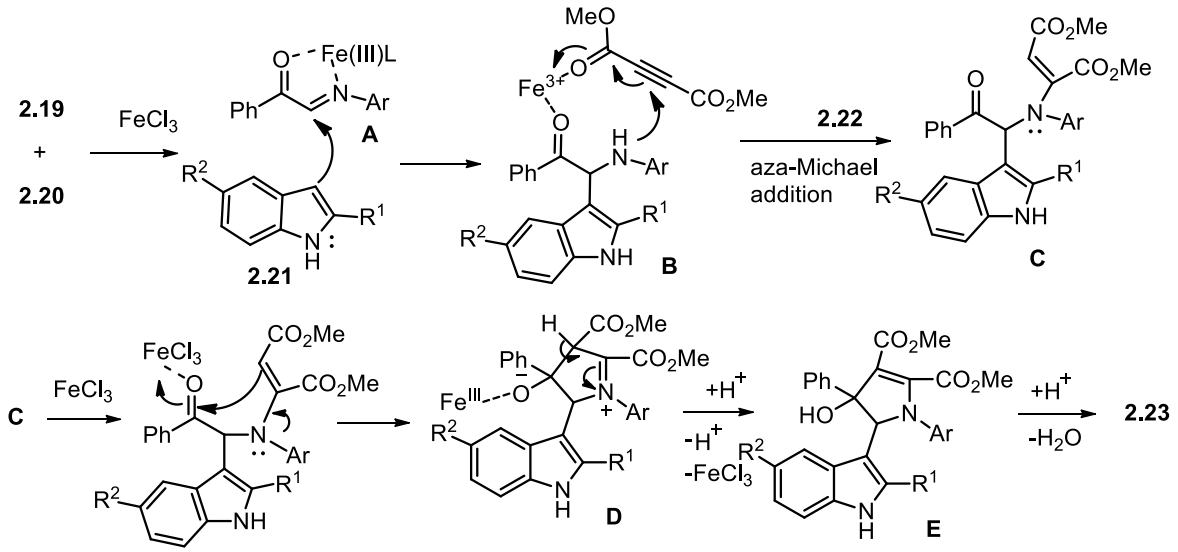


Reagents and optimized conditions: i, $FeCl_3$ (20 mol%), ball milling (500 rpm), room temperature, 4 h.

All these reactions were performed under an open atmosphere and are not sensitive to air and moisture. In addition, the reaction is highly regio-selective. No other regio-isomer was isolated under the present reaction conditions. The reaction conditions are mild and give no decomposition of the products or polymerization of the starting materials. We have not observed any by-products for all reaction combinations which are supported by high yields and regio-selectivity of the protocol. All of the known synthesized compounds have been characterized by spectral data and the new compound by spectral and analytical data.

Furthermore, the potential synthetic applicability of this method was investigated on the gram scale using the model reaction. The reaction could afford 3.9 g of **2.23a** in 84% yield without any significant loss of its efficiency, demonstrating the potential applications of the present method for a large-scale synthesis of pyrrole derivatives (Table 9, entry 11).

Scheme 2.11



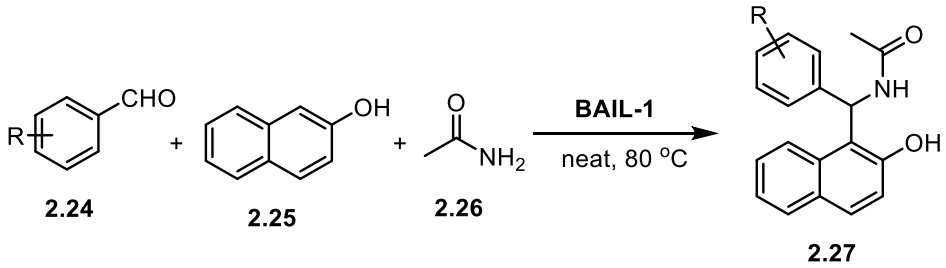
We have proposed a plausible reaction mechanism for this multicomponent cascade reaction as depicted in Scheme 2.11. Initially, phenylglyoxal (**2.19**) and aniline (**2.20**) form C-acylimine intermediate **A** which undergoes nucleophilic addition by the indole nucleophile **2.21** (facilitated by the Fe salt) [138] to produce the intermediate **B**. Iron-catalyzed, aza-Michael addition of amine **B** with activated

alkyne (**2.22**) gives the Michael adduct **C** [139], which further undergoes cascade cyclization to produce a cyclic iminium in presence of $FeCl_3$ [140]. Deprotonation of iminium intermediate (**D**) afforded the intermediate **E** which gave the final product **2.23** by the removal of water.

2.4. REACTIONS OF MONOCARBONYL COMPOUNDS WITH *N*-NUCLEOPHILES: SYNTHESIS OF AMIDOALKYL NAPHTHOLS

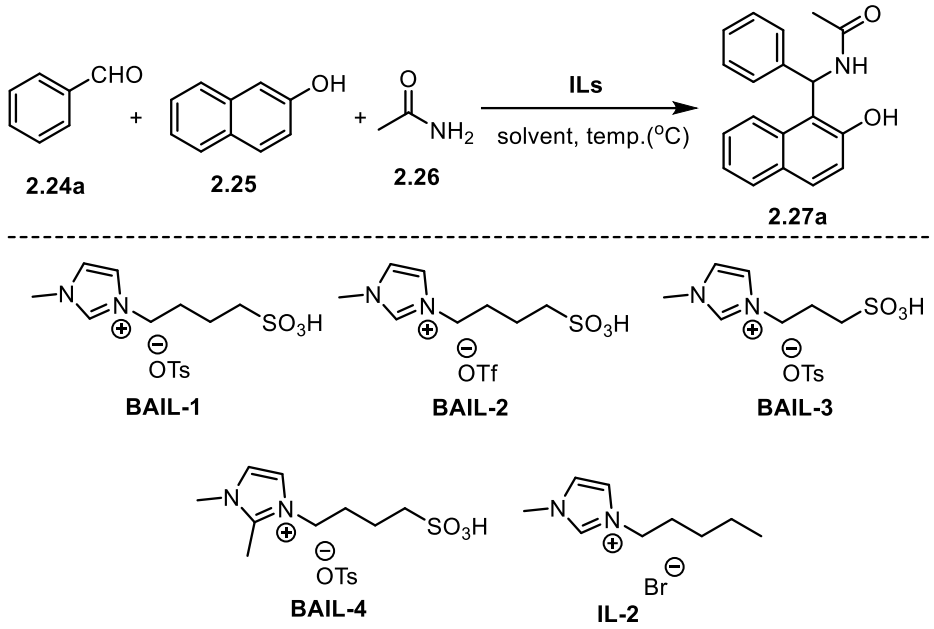
Additionally, within the framework of the work, the synthesis of 1-amidoalkyl-2-naphthols **2.27** was carried out by a three-component reaction between such a typical representative of monocarbonyl compounds as benzaldehyde **2.24**, and β-naphthol **2.25** and acetamide **2.26** in presence of Brønsted acidic ionic liquid (BAIL) (Scheme 2.12) [141].

Scheme 2.12



For the preliminary investigation, a reaction of benzaldehyde (**2.24a**), *β*-naphthol (**2.25**), and acetamide (**2.26**) in the presence of BAIL-1 catalyst was carried out under the solvent-free condition (The results are summarized in Table 13) and 85% of *N*-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)acetamide **2.27a**, was obtained. Encouraged by results, some other ionic liquids like BAIL-2, BAIL-3 and BAIL-4 were also introduced but they did not exceed the yield formation as we obtained by use of BAIL-1. One another ionic liquid IL-2 was also used and at that time the product formation was less than 5%. One protic solvent water and aprotic solvent 1,2-DCE were also tried to enhance the product formation, but they gave a lower extent of desired products. To get more yield the reaction was then performed at 100 ºC and the product formation was not increased.

Table 13. Optimization of the reaction conditions[a]

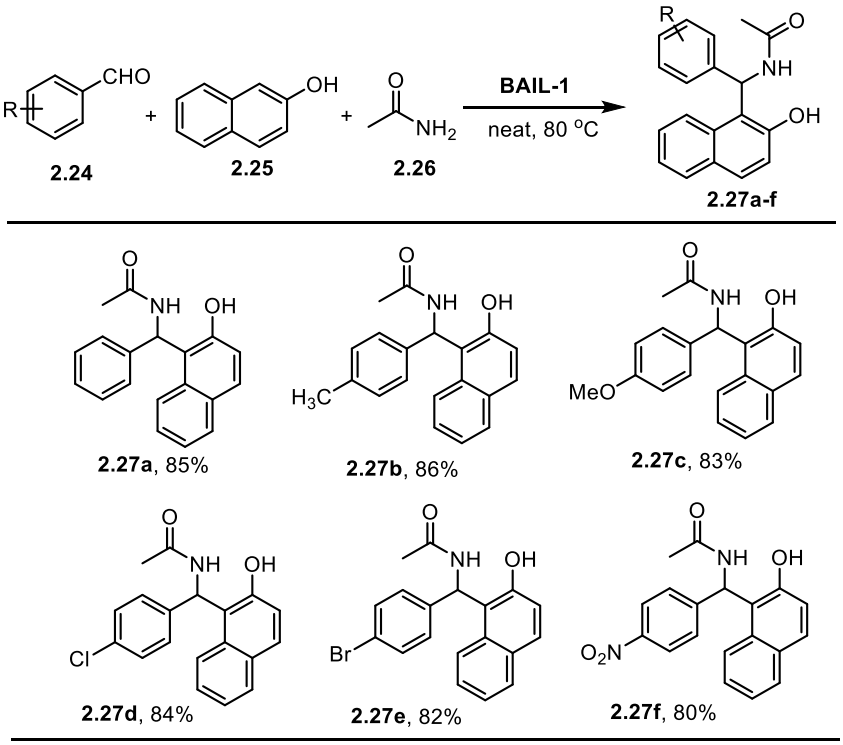


Entry	Catalysts (10 mol%)	Solvents	Temp. (°C)	Yields[b] (%)
1	BAIL-1	neat	80 °C	85
2	BAIL-2	neat	80 °C	82
3	BAIL-3	neat	80 °C	79
4	BAIL-4	neat	80 °C	77
5	IL-2	neat	80 °C	trace
6	BAIL-1	H_2O	80 °C	51
7	BAIL-1	DCE	80 °C	38
8	BAIL-1	neat	100 °C	85

[a]Reaction conditions: benzaldehyde (**2.24a**, 1 mmol), *β*-naphthol (**2.25**, 1 mmol) and acetamide (**2.26**, 1 mmol), solvent-free or with solvent (2 mL), BAIL-1 (10 mol%), stirred for 1h. [b]Isolated yield.

By applying the optimized condition we then explored the substrate scope using various types of aromatic aldehydes (Table 14). As we obtained a promising yield using benzaldehyde, some other substituted benzaldehydes like 4-methyl or 4-methoxy benzaldehyde were taken for this reaction and respective products **2.27b** and **2.27c** were formed in good yield. Benzaldehyde with 4-chloro and 4-bromo substituents also underwent the reaction to give the corresponding products **2.27d** and **2.27e** with an excellent amount yields. 4-Nitrobenzaldehyde reacted under a similar condition to form **2.27f** with 80% of the desired product. So, aromatic aldehydes carrying both electron-donating or electron-withdrawing substituents groups reacted successfully and gave the products in high yields.

Table 14. Synthesis of 1-amidoalkyl-2-naphthols catalyzed by BAIL-1[a,b]



[a]Reaction conditions: aldehydes (**2.24**, 1 mmol), *β*-naphthol (**2.25**, 1 mmol) and acetamide (**2.26**, 1 mmol), BAIL-1 (10 mol%). [b]Isolated yield.

Our next target was the reusability of the catalyst and for that, we used benzaldehyde, *β*-naphthol and acetamide as model substrates. The catalyst was easily recovered by filtration after the reaction followed by vacuum operation and

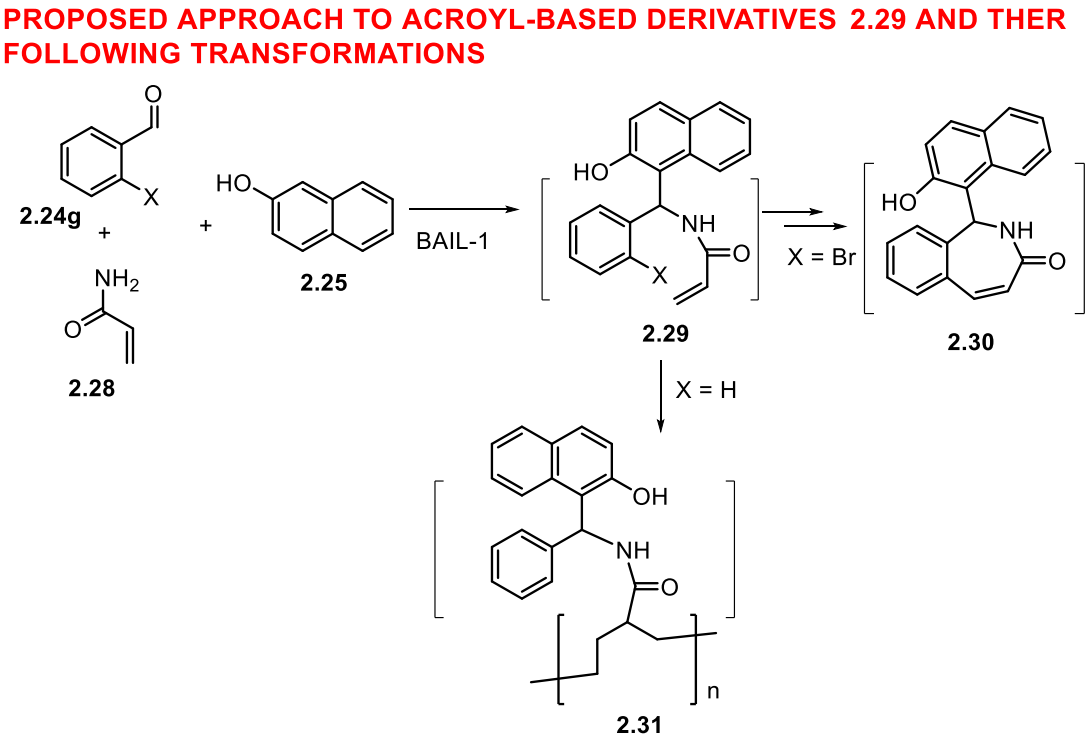
the resulting catalyst was reused directly for the further run. This process was repeated five times and the worked with the same efficiency for each time it was used (Table 15).

Table 15. Recycling studies of catalyst for model reaction[a]

Run Times	Time[b] (h)	Yields[c]
1	1	85
2	1	81
3	1	76
4	1.5	74
5	2	70

[a]Reaction conditions: Benzaldehyde (**2.24a**, 1 mmol), *β*-naphthol (**2.25**, 1 mmol) and acetamide (**2.26**, 1 mmol), BAIL-1 (10 mol%). [b]Reaction progress monitored by TLC. [c]Isolated yield.

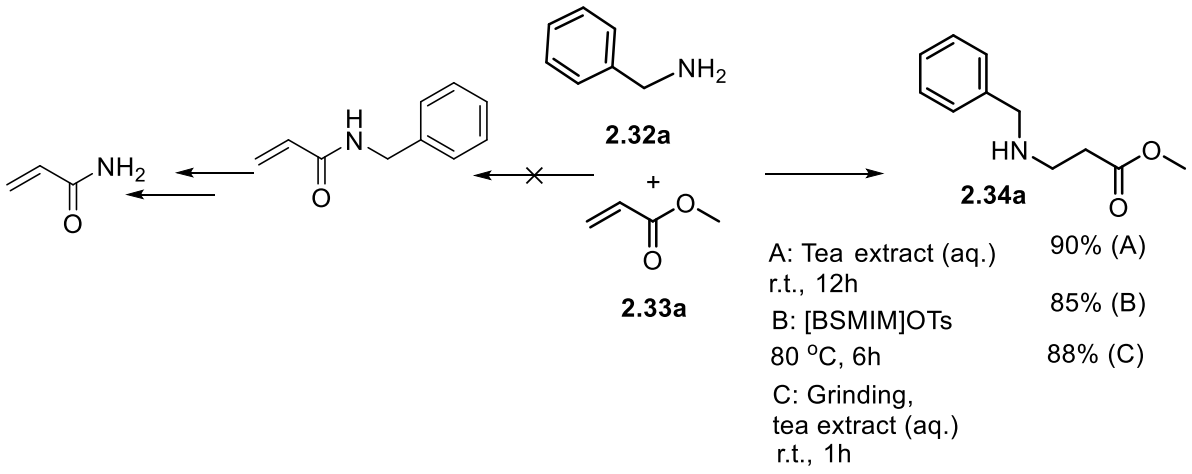
Scheme 2.13



In our opinion, the most promising would be the further development of the applicability of this reaction, for example, we were planning to obtain *N*-((2-hydroxynaphthalene-1-yl)(aryl)(methyl)acrylamide **2.29**, and, by means of further Heck reaction, benzazepine derivatives **2.30**, or, by means of polymerization reaction, naphthyl-substituted fluorescent polymers **2.31** (Scheme 2.13).

According to a literature, the most typical method for obtaining acrylamides is the reaction of acroyl chloride with amines in, in the most cases, in chlorinated solvents. As part of the work, we made an attempt to implement a "green" method for the synthesis of acrylamide using acrylic acid methyl ester. For this purpose, a model study of the interaction of acrylic acid derivatives with amines in the presence of tea extract as a green catalyst was carried out [142,143]. However, we found that under these conditions, the reaction between benzylamine **2.32a** and methyl acrylate **2.33a** did not lead to the expected acrylamide, but to the formation of methyl 3-(benzylamino)propanoate **2.34a** in 90% yield (way A) (Scheme 2.14). The same results were observed upon carring out the reaction in the media of ionic liquid, [BSMIM]OTs (way B), and upon grinding the reagents in the presence of tea extract (way C).

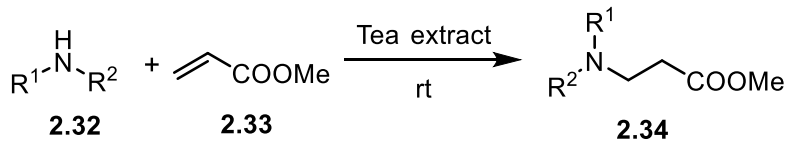
Scheme 2.14



A similar result was obtained upon the interaction (way A) of other amines with an acrylic acid esters, as well as with its nitrile, which was studied to expand

the applicability of the reaction. Interestingly, from the recent research we observed according to normal expectation that the extraction of normal tea is acidic in nature [144]. This observation motivated us to investigate the catalytic role of tea extract for such organic reaction. So, in continuation of our research to develop green methodology, we have observed that tea extract is very useful as solvent as well as catalyst for conjugate addition of a variety of amines to Michael acceptor (methyl acrylate) (Scheme 2.15).

Scheme 2.15



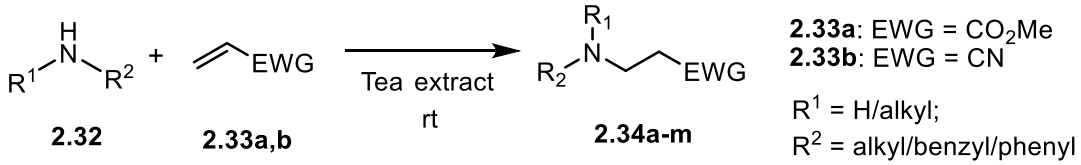
2.32 **2.33** **2.34**

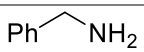
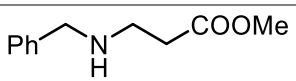
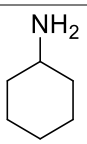
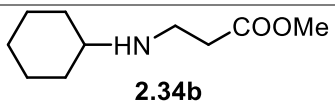
R^1 = H/alkyl; R^2 = alkyl/benzyl/phenyl

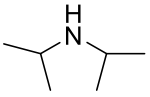
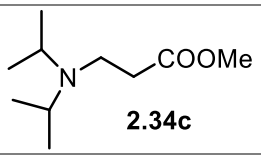
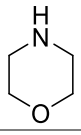
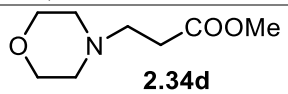
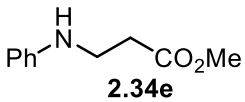
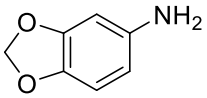
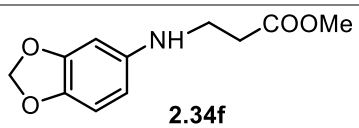
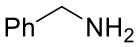
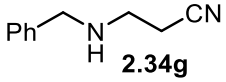
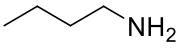
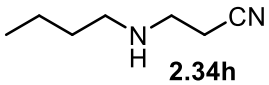
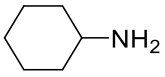
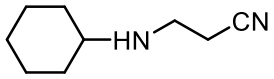
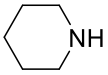
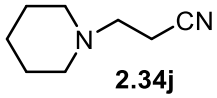
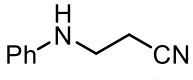
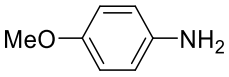
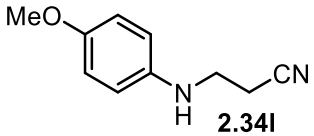
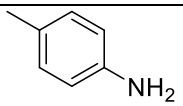
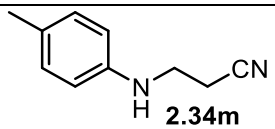
First of all, we prepared the required tea extract. In a typical experimental procedure, 2 g of tea leaves were dissolved in 20 mL of water and boiled it for 10-15 min. After filtration we got the extract which was used for the said reactions. It was observed that 2 mL of tea extract is sufficient to get the best result. Several structurally varied amines were coupled with the wide range of α,β-ethylenic compounds and the results are summarized in Table 16. A variety of aliphatic amines was examined to prove the general applicability of this present procedure and the corresponding Michael adducts were isolated in excellent yields within a short reaction time. The aliphatic primary amines such as benzylamine, butylamine and cyclohexylamine were treated with different Michael acceptors and corresponding monoadducts were isolated in good yields (Table 16, entries 1-4). The reaction of open chain bulky secondary amine like diisopropylamine proceeded very well (Table 16, entry 3). Cyclic secondary amines such as piperidine and morpholine underwent facile additions with acrylic esters and acrylonitrile respectively (Table 16, entries 4 and 10). Aromatic amines are less reactive than aliphatic amines and took long reaction time. Both activated and weakly activated anilines were

investigated. The reactions proceeded smoothly at room temperature and the products were obtained in excellent yields. Several substituted anilines such as methyl and methoxy anilines underwent efficient additions with acrylonitrile and methyl acrylate giving only monoadduct in high yields under present reaction conditions (Table 16, entries 12,13). Acid sensitive functional group in aniline such as 3,4-(methylenedioxy)aniline also reacted well to give the desired product in good yields keeping methylenedioxy group unaffected (Table 16, entry 6). With regard to Michael acceptors, a wide range of structurally diverse electron deficient alkenes was used such as α,β-unsaturated nitrile and carboxylic ester. In general, the reactions are very clean. Both aliphatic and aromatic amines give the products in equally fair yields. In particular, in the case of primary amines the method produces the corresponding β-amino derivatives without the problem of double-conjugate addition. We have not observed any by-products for all reaction combinations which are supported by high yields of the protocol. All of the known synthesized compounds have been characterized by spectral data and the new compounds by spectral and analytical data.

Table 16. Substrate scope[a]



Entry	*N*-nucleophile	Acrylate	Products	Time	Yields, %
1			 2.34a	40 min	90
2			 2.34b	50 min	90

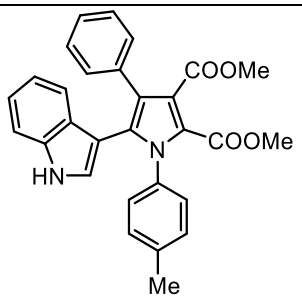
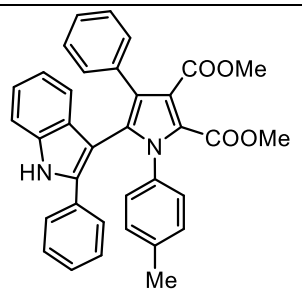
3			 **2.34c**	20 min	94
4			 **2.34d**	20 min	90
5			 **2.34e**	20 h	85
6			 **2.34f**	12 h	88
7			 **2.34g**	20 h	92
8			 **2.34h**	20 min	96
9			 **2.34i**	20 min	96
10			 **2.34j**	10 min	96
11			 **2.34k**	18 min	75
12			 **2.34l**	24 h	75
13			 **2.34m**	24 h	80

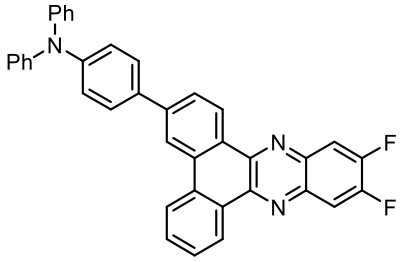
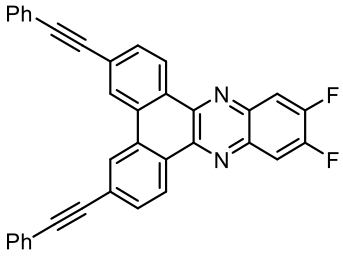
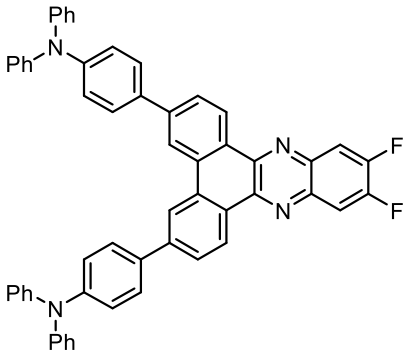
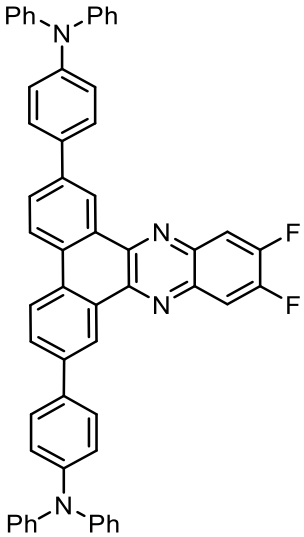
[a]Reaction conditions: 2 mmol of amine and 2 mmol of alkene were stirred in 2 mL of tea extract at room temperature. [b]Isolated yields.

2.5. STUDY OF THE PHOTOPHYSICAL AND COORDINATION PROPERTIES OF SOME OF THE OBTAINED COMPOUNDS

The compounds obtained in the framework of the work are polynuclear azaaromatic structures with a developed conjugation system. It was quite expected to expect the manifestation of promising photophysical properties in some of the obtained products. Thus, in THF solutions, multisubstituted pyrroles exhibit intense blue fluorescence with emission maxima lying in the region of 440-445 nm, which allows them to be classified as so-called. "true-blue" fluorophores. Phenazine **2.18** exhibits intense emission at 437 nm (quantum yield up to 9%). The most promising are fluorophores based on phenazines **2.15–2.16** mono- and difunctionalized with triphenylamine fragments. For them, we recorded orange fluorescence in the region of 608-616 nm with a quantum yield of up to 15% (Table 17, figures 2-3). It should also be noted that, in the absence of phenylethynyl and triphenylamine fragments, the starting 1,4-diazines, as well as their aza- and annelated analogs, did not exhibit significant photophysical properties.

Table 17. Photophysical properties of some of the obtained compounds

Fluorophores	λ_{abs}	λ_{em}	**Φ, %**	**Structures**
2.23a	289	445	-	
2.23c	305	439	-	

2.16a	258, 281sh, 337, 420	608	6.30	
2.18	276, 319sh, 396, 409	437	9.69	
2.15a	258, 268, 287, 335, 432	613	6.75	
2.15b	263sh, 300, 337	395, 411sh	46.85	

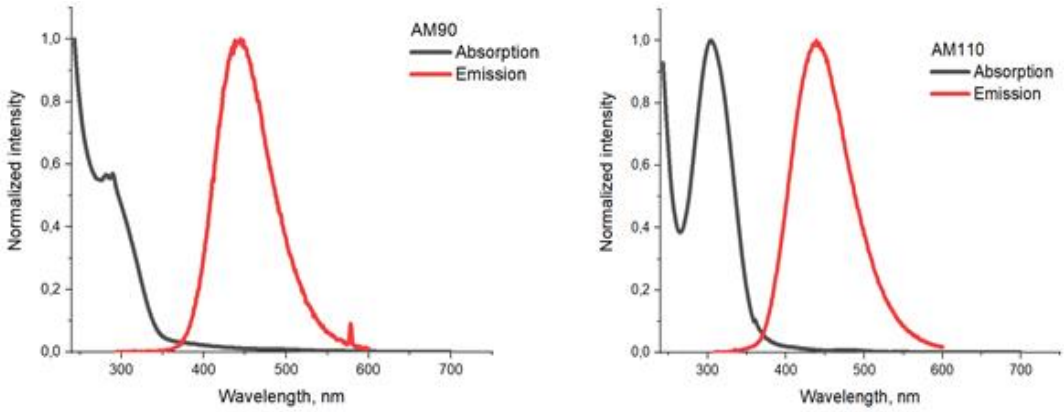


Figure 2. Absorption (black) and emission spectra of the obtained compounds: a) **2.23a** b) **2.23c**

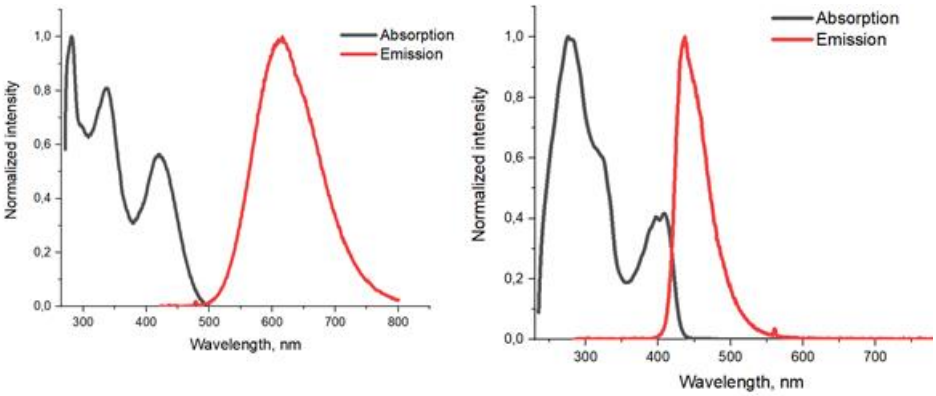


Figure 3. Absorption (black) and emission spectra of the obtained compounds: a) **2.16a**; b) **2.18**

The results obtained make it promising to search for new representatives of fluorophores in these series.

Fluorescent detection of nitroaromatic compounds

Indole derivatives are known to exhibit a fluorescent response to nitroaromatic explosive compounds. As part of our work, we evaluated the possibility of using previously selected fluorophores as chemosensors for the fluorescent detection of nitro-containing (explosive) substances. Thus, products **2.23a** and **2.23c** in a THF solution (10^{-6} M) demonstrate an intense “turn-off” response to 2,4-dinitrotoluene (DNT) and picric acid (PA) with Stern–Volmer quenching constants in the range of

1.2 – 6.2*10^4 M^{-1} (Table 18), which is much higher than the values described for known chemosensors.

Table 18. Quenching constants of compounds **2.23a** and **2.23c** in the presence of DNT and PA

Compounds	**DNT**	**PA**
2.23a	1.17*10^4 M^{-1}	6.14*10^4 M^{-1}
2.23c	1.75*10^4 M^{-1}	3.47*10^4 M^{-1}

Thus, the search for chemosensors for nitro-explosives in the series of compounds obtained is very promising.

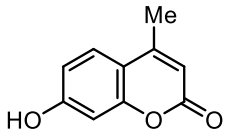
CHAPTER 3. EXPERIMENTAL PART

General Information

^{1}H NMR spectra (400 MHz) were recorded on a Bruker DRX-400 Avance (400 MHz) spectrometer as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (δ) and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet) and coupling constants *J* were given in Hz. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ solution. Chemical shifts are expressed in parts per million (δ) and are referenced to $CDCl_3$ (δ = 77.16) as internal standard. For some compounds DMSO-d_6 was used. Elemental analyses were performed on a PE 2400 II CHN-analyzer (Perkin Elmer). All chemical shifts are given relative to residual signals of solvent. Mass-spectra were recorded on MicrOTOF-Q II (Bruker Daltonics), electrospray as a method of ionization UV–vis absorption spectra were recorded on the Shimadzu UV-1800 spectrophotometer, and emission spectra were measured on the Horiba FluoroMax-4 by using quartz cells with 1 cm path length at room temperature. Absolute quantum yields of luminescence of target compounds in solution were measured by using the Integrating Sphere Quanta-φ of the Horiba-Fluoromax-4 at room temperature. The fluorometric titra-tion was performed by the single-point methodology using Horiba FluoroMax 4. All yields refer to the isolated products. TLC was done using silica gel coated glass plates (Merck, Silica gel G for TLC). For the column chromatography Silica gel (60-120 mesh, Merck) was used. Petroleum ether refers to the fraction boiling in the range of 60-80 °C unless otherwise mentioned. All solvents were dried and distilled before use. Commercially available substrates were freshly distilled before the reaction. Solvents, reagents and chemicals were purchased from Aldrich, Merck, Alfa Aesar and Spectrochem Chemicals. All reactions involving moisture-sensitive reactants were executed using oven-dried glassware. Brønsted acidic ionic liquids were prepared according to the previously reported method [145]. For the ball-milling experiments Retsch PM100 planetary mill apparatus was employed using four balls (stainless steel, size 10 mm) at room temperature and the milling frequency of 8.33 Hz (500 rpm).

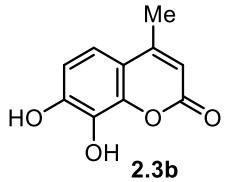
3.1. Synthesis of Coumarin Derivatives

3.1.1. General Procedure for the Synthesis of Compounds 2.3. In a 50 mL grinding jar a mixture of phenol (**2.1a**, 1 mmol), ethyl acetoacetate (**2.2**, 1.5 mmol) and BAIL (10 mol%) was ball milled for 2 h at 500 rpm at room temperature (a 30 min interval). After completion of the reaction (monitored by thin-layer chromatography), the resulting paste or solid was transferred from the jar to a 30 mL beaker using 10-15 mL of ethanol or ethanol-water 1:1 mixture and the mixture was heated to reflux (complete dissolution may not occur, but it is sufficient to dissolve unreacted starting materials). Then the reaction mixture was cooled and the coumarin **2.3** was filtered off and dried to get the pure product.



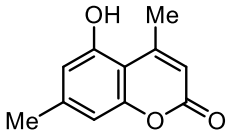
2.3a

7-Hydroxy-4-methyl-2*H*-chromen-2-one (2.3a): White solid, mp. 186-188 °C; Yield: 88%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.56 (s, 1H), 7.53-7.49 (m, 1H), 6.78-7.74 (m, 1H), 6.67 (s, 1H), 5.98 (s, 1H), 2.32 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.2, 160.3, 154.7, 153.4, 126.6, 112.9, 112.1, 110.2, 102.3, 18.0. Anal. Calcd. For $C_{10}H_8O_3$: C, 68.18; H, 4.58%; Found: C, 68.14; H, 4.48%.



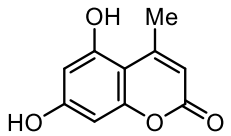
2.3b

7,8-Dihydroxy-4-methyl-2*H*-chromen-2-one (2.3b): White solid, mp. 242–244 °C; Yield 89%. 1 Yield: 84%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.92 (s, 1H), 9.44 (s, 1H), 7.06-7.02 (m, 1H), 6.79-7.77 (m, 1H), 6.08 (s, 1H), 2.32 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.2, 153.9, 149.2, 143.2, 132.0, 115.3, 112.8, 112.0, 110.0, 18.1. Anal. Calcd. For $C_{10}H_8O_4$: C, 62.50; H, 4.20%; Found: C, 62.44; H, 4.28%.



2.3c

5-Hydroxy-4,7-dimethyl-2*H*-chromen-2-one (2.3c): White solid, mp. 255–257 °C; Yield: 80%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.42 (s, 1H), 6.56-6.53 (m, 1H), 5.99 (s, 1H), 2.47 (m, 3H), 2.22 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.9, 156.4, 154.7, 154.5, 142.7, 111.8, 107.6, 106.7, 23.6, 21.2. Anal. Calcd. For $C_{11}H_{10}O_3$: C, 69.46; H, 5.30%; Found: C, 69.55; H, 5.41%.



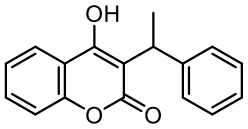
2.3d

5,7-Dihydroxy-4-methyl-2*H*-chromen-2-one (2.3d): White solid, mp. 280–282 °C; Yield: 82%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.50 (s, 1H), 10.25 (s, H), 6.23 (s, 1H), 6.12 (s, 1H), 5.80 (s, 1H), 2.46 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.5, 160.4, 158.4, 157.0, 155.4, 109.2, 102.6, 99.4, 95.0, 23.7. Anal. Calcd. For $C_{10}H_8O_4$: C, 62.50; H, 4.20%; Found: C, 62.42; H, 4.28%.

3.2. C_3-alkylation of 4-hydroxycoumarin in presence of TsOH

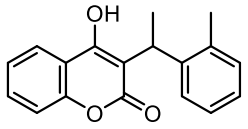
3.2.1. General procedure for the synthesis of compounds 2.8a-h:

A mixture of 4-hydroxycoumarin **2.6** (162 mg, 1 mmol), styrene **2.7a-h** (1.5 mmol) and TsOH (0.034 g, 20 mol%) was stirred at 80 °C for 4-6 h (TLC control). After completion, the reaction mixture was cooled and extracted with ethyl acetate (3×15 mL) and water (2×10 mL). The organic layer was separated and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure on rotary evaporator, the crude product was purified by column chromatography on silica gel (60–120 mesh) using petroleum ether/ethyl acetate (94:6 to 92:8 v/v) as eluent to afford the pure products.



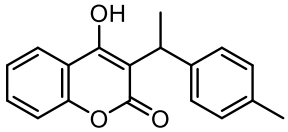
2.8a

4-Hydroxy-3-(1-phenylethyl)-2*H*-chromen-2-one (2.8a): White solid, mp. 203-205 ºC, 207 mg, Yield: 78%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.65-7.63 (m, 1H, ArH), 7.53-7.49 (m, 3H, ArH), 7.47-7.43 (m, 2H, ArH), 7.38-7.31 (m, 2H, ArH), 7.24-7.20 (m, 1H, ArH), 5.92 (s, 1H, OH), 4.76-4.71 (m, 1H, CH), 1.66 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.6, 159.8, 152.6, 141.6, 132.0, 129.9, 128.1, 127.4, 124.0, 123.0, 116.5, 116.2, 110.2, 34.7, 16.6. Anal. Calcd. For $C_{17}H_{14}O_3$: C, 76.68; H, 5.30%; Found: C, 76.78; H, 5.34%.



2.8b

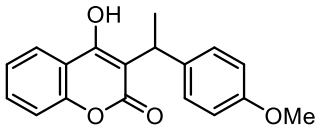
4-Hydroxy-3-(1-(*o*-tolyl)ethyl)-2*H*-chromen-2-one (2.8b): White solid, mp. 163-165 ºC, 196 mg, Yield: 70%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71-7.65 (m, 2H, ArH), 7.55-7.50 (m, 1H, ArH), 7.45-7.41 (m, 1H, ArH), 7.37-7.29 (m, 3H, ArH), 7.26-7.22 (m, 1H, ArH), 6.37 (s, 1H, OH), 4.73-4.68 (m, 1H, CH), 2.27 (s, 3H, CH_3), 1.72 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.2, 159.8, 152.6, 140.1 139.0, 132.1, 131.8, 128.3, 127.6, 124.7, 123.9, 123.0 116.4, 116.1, 108.2, 33.4, 19.7, 17.4. Anal. Calcd. For $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%; Found: C, 77.04; H, 5.78%.



2.8c

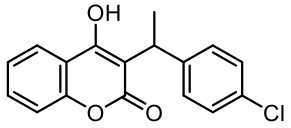
4-Hydroxy-3-(1-(*p*-tolyl)ethyl)-2*H*-chromen-2-one (2.8c): White solid, mp. 166-168 ºC, 210 mg, Yield: 75%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.70-7.68 (m, 1H, ArH), 7.52-7.47 (m, 1H, ArH), 7.38 (d, J = 8 Hz, 2H, ArH), 7.30-7.27 (m, 1H, ArH), 7.24-7.20 (m, 3H, ArH), 6.45 (s, 1H, OH), 4.72-4.66 (m, 1H, CH), 2.35 (s, 3H, CH_3), 1.65

(d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.7, 159.9, 152.6, 138.5, 137.7, 131.8, 130.5, 127.3, 123.9, 123.0, 116.4, 116.3, 110.2, 34.3, 21.1, 16.7. Anal. Calcd. For $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%; Found: C, 77.17; H, 5.82%



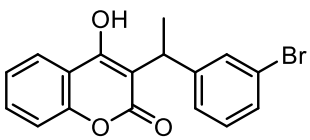
2.8d

4-Hydroxy-3-(1-(4-methoxyphenyl)ethyl)-2*H*-chromen-2-one (2.8d): White solid, 168-170 ºC, mp. 227 mg, Yield: 77%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73-7.71 (m, 1H, ArH), 7.53-7.49 (m, 1H, ArH), 7.43-7.41 (m, 2H, ArH), 7.31-7.29 (m, 1H, ArH), 7.26-7.22 (m, 1H, ArH), 6.96-6.94 (m, 2H, ArH), 6.64 (s, 1H, OH), 4.71-4.65 (m, 1H, CH), 3.82 (s, 3H, OCH_3), 1.67 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.6, 159.8, 159.4, 152.7, 133.0, 131.9, 128.6, 123.9, 123.0, 116.5, 116.3, 115.3, 110.2, 55.5, 34.0, 16.9. Anal. Calcd. For $C_{18}H_{16}O_4$: C, 72.96; H, 5.44%; Found: C, 72.90; H, 5.35%.



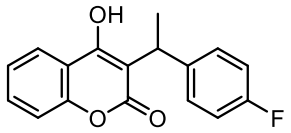
2.8e

3-(1-(4-Chlorophenyl)ethyl)-4-hydroxy-2*H*-chromen-2-one (2.8e): White solid, mp. 185-187 ºC, 222 mg, Yield: 74%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72-7.70 (m, 1H, ArH), 7.55-7.50 (m, 1H, ArH), 7.42-7.35 (m, 4H), 7.31-7.27 (m, 1H, ArH), 7.25-7.23 (m, 1H, ArH), 6.36 (s, 1H, OH), 4.71-4.66 (m, 1H, CH), 1.66 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.5, 159.9, 152.6, 140.4, 133.7, 132.2, 129.7, 128.8, 124.1, 123.0, 116.6, 116.0, 109.8, 34.0, 16.7. Anal. Calcd. For: $C_{17}H_{13}ClO_3$: C, 67.90; H, 4.36%; Found: C, 67.81; H, 4.45%.



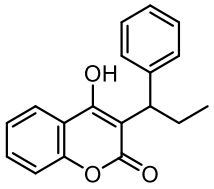
2.8f

3-(1-(3-Bromophenyl)ethyl)-4-hydroxy-2*H*-chromen-2-one (2.8f): White solid, mp. 205-207 ºC, 247 mg, Yield: 72%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72-7.70 (m, 1H, ArH), 7.61-7.60 (m, 1H, ArH), 7.55-7.51 (m, 1H, ArH), 7.46-7.40 (m, 2H, ArH), 7.32-7.23 (m, 3H, ArH), 6.26 (s, 1H, OH), 4.73-4.68 (m, 1H, CH), 1.66 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.3, 159.8, 152.7, 144.5, 132.2, 131.1, 130.9, 130.6, 126.0, 124.1, 123.9, 122.9, 116.7, 116.0, 109.7, 34.3 16.6. Anal. Calcd. for $C_{17}H_{13}BrO_3$: C, 59.15; H, 3.80%; Found: C, 59.07; H, 3.88%.



2.8g

3-(1-(4-Fluorophenyl)ethyl)-4-hydroxy-2*H*-chromen-2-one (2.8g): White solid, mp. 184-186 ºC, 207 mg, Yield: 73%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75-7.73 (m, 1H, ArH), 7.60-7.55 (m, 1H, ArH), 7.53-7.49 (m, 2H, ArH), 7.36 (d, J = 7.6 Hz, 1H, ArH), 7.35-7.28 (m, 1H, ArH), 7.19-7.14 (m, 2H, ArH), 6.15 (s, 1H, OH), 4.78-4.72 (m, 1H, CH), 1.71 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.3 (d, J = 246 Hz), 159.8, 152.6, 137.3 (d, J = 2 Hz), 132.1, 129.1 (d, J = 7 Hz), 124.1, 123.0, 116.7 (d, J = 19 Hz), 116.6, 116.0, 109.9, 34.0, 16.9. Anal. Calcd. for $C_{17}H_{13}FO_3$: C, 71.82; H, 4.61%; Found C, 71.76; H, 4.68%.



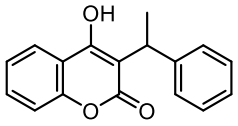
2.8h

4-Hydroxy-3-(1-phenylpropyl)-2*H*-chromen-2-one (2.8h): White solid, mp. 176-178 ºC, 190 mg, Yield: 68%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66-7.64 (m, 1H, ArH), 7.53-7.47 (m, 3H, ArH), 7.44-7.40 (m, 2H, ArH), 7.34-7.30 (m, 2H, ArH), 7.24-7.20 (m, 1H, ArH), 6.12 (s, 1H, OH), 4.53 (t, J = 15.2 Hz, 1H, CH), 2.29-2.22 (m, 1H, CH_2), 2.12-2.05 (m, 1H, CH_2), 1.08 (t, J = 14.4 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.6, 159.1, 151.0, 138.5, 132.0, 129.9, 127.9, 128.8, 124.0, 122.9,

116.8, 116.5, 108.3, 41.8, 24.1 12.4. Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%; Found: C, 77.20; H, 5.87%.

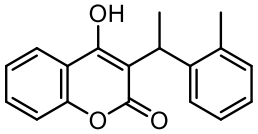
3.3. C_3-alkylation of 4-hydroxycoumarin in presence of $BF_3 \cdot OEt_2$

3.3.1. Typical procedure for the synthesis of compound 2.8a: A mixture of 4-hydroxycoumarin **2.6** (1 mmol, 162 mg), styrene **2.7a** (1 mmol, 104 mg) and $BF_3.OEt_2$ (20 mol%)was allowed to stir at 80 °C for 3.5 h. After completion indicated by TLC, the reaction mixture was cooled to room temperature and diluted with ethyl acetate (10 mL) and water. Then the mixture was dried over anhydrous Na_2SO_4 and the organic layer was filtered. After evaporation of the solvent, the crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (6% to 8%) to afford the pure corresponding product **2.8a**. The identity and purity of the product were confirmed by ^1H and ^{13}C NMR spectroscopic analysis.



2.8a

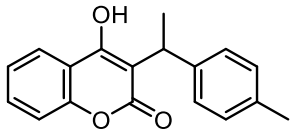
4-Hydroxy-3-(1-phenylethyl)-2*H*-chromen-2-one (2.8a): 231 mg, Yield: 76%; ^1H NMR ($CDCl_3$, 400 MHz):δ7.65-7.63 (m, 1H), 7.53-7.49 (m, 3H), 7.47-7.43 (m, 2H), 7.38-7.31 (m, 2H), 7.24-7.20 (m, 1H), 5.92 (s, 1H), 4.76-4.71 (m, 1H), 1.66 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):δ 163.6, 159.8, 152.6, 141.6, 132.0, 129.9, 128.1, 127.4, 124.0, 123.0, 116.5, 116.2, 110.2, 34.7, 16.6.



2.8b

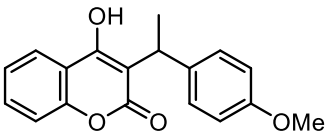
4-Hydroxy-3-(1-(o-tolyl)ethyl)-2*H*-chromen-2-one (2.8b): 196 mg, Yield: 70%; ^1H NMR ($CDCl_3$, 400 MHz):δ 7.71-7.65 (m, 2H), 7.55-7.50 (m, 1H), 7.45-7.41 (m,

1H), 7.37-7.29 (m, 3H), 7.26-7.22 (m, 1H), 6.37 (s, 1H), 4.73-4.68 (m, 1H), 2.27 (s, 3H), 1.72 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):*δ* 163.2, 159.8, 152.6, 140.1, 139.0, 132.1, 131.8, 128.3, 127.6, 124.7, 123.9, 123.0 116.4, 116.1, 108.2, 33.4, 19.7, 17.4.



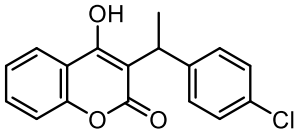
2.8c

4-Hydroxy-3-(1-(*p*-tolyl)ethyl)-2*H*-chromen-2-one (2.8c): 204 mg, Yield: 73%; ^{1}H NMR ($CDCl_3$, 400 MHz):*δ* 7.70-7.68 (m, 1H), 7.52-7.47 (m, 1H), 7.38 (d, *J* = 8 Hz, 2H), 7.30-7.27 (m, 1H), 7.24-7.20 (m, 3H), 6.45 (s, 1H), 4.72-4.66 (m, 1H), 2.35 (s, 3H), 1.65 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):*δ* 163.7, 159.9, 152.6, 138.5, 137.7, 131.8, 130.5, 127.3, 123.9, 123.0, 116.4, 116.3, 110.2, 34.3, 21.1, 16.7.



2.8d

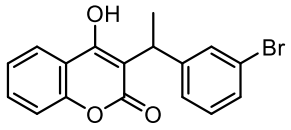
4-Hydroxy-3-(1-(4-methoxyphenyl)ethyl)-2*H*-chromen-2-one (2.8d): 219 mg, Yield: 74%; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.73-7.71 (m, 1H), 7.53-7.49 (m, 1H), 7.43-7.41 (m, 2H), 7.31-7.29 (m, 1H), 7.26-7.22 (m, 1H), 6.96-6.94 (m, 2H), 6.64 (s, 1H), 4.71-4.65 (m, 1H), 3.82 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):*δ* 163.6, 159.8, 159.4, 152.7, 133.0, 131.9, 128.6, 123.9, 123.0, 116.5, 116.3, 115.3, 110.2, 55.5, 34.0, 16.9.



2.8e

3-(1-(4-Chlorophenyl)ethyl)-4-hydroxy-2*H*-chromen-2-one (2.8e): 213 mg, Yield: 71%; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.72-7.70 (m, 1H), 7.55-7.50 (m, 1H),

7.42-7.35 (m, 4H), 7.31-7.27 (m, 1H), 7.25-7.23 (m, 1H), 6.36 (s, 1H), 4.71-4.66 (m, 1H), 1.66 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):δ 163.5, 159.9, 152.6, 140.4, 133.7, 132.2, 129.7, 128.8, 124.1, 123.0, 116.6, 116.0, 109.8, 34.0, 16.7.

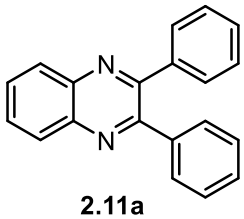


2.8f

3-(1-(3-Bromophenyl)ethyl)-4-hydroxy-2*H*-chromen-2-one (2.8f): 238 mg, Yield: 69%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72-7.70 (m, 1H), 7.61-7.60 (m, 1H), 7.55-7.51 (m, 1H), 7.46-7.40 (m, 2H), 7.32-7.23 (m, 3H), 6.26 (s, 1H), 4.73-4.68 (m, 1H), 1.66 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):δ 163.3, 159.8, 152.7, 144.5, 132.2, 131.1, 130.9, 130.6, 126.0, 124.1, 123.9, 122.9, 116.7, 116.0, 109.7, 34.3 16.6.

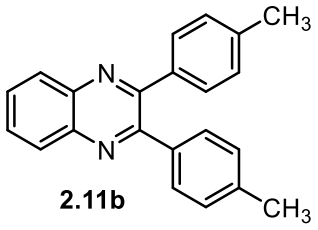
3.4. Synthesis of 1,4-diazines and their annelated (aza)derivatives in presence of BAIL-1

3.4.1. General procedure for the synthesis of substrate 2.11a: A mixture of *o*-phenylenediamine (**2.9a**, 1.0 mmol) and benzil (**2.10a**, 1.0 mmol), and BAIL-1 (10 mol%) was stirred without solvent at room temperature for 0.5 h. After TLC checked, indicating the completion the reaction mixture was then cooled and diluted with a sufficient amount of ethyl acetate (10 mL) and water. After that, the mixture was collected over anhydrous Na_2SO_4, and the organic layer was filtered. Evaporating the solvent, the residue product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate to afford the pure corresponding product **2.11a**.



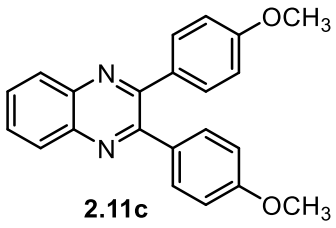
2.11a

2,3-Diphenyl-quinoxaline (2.11a): White solid, mp. 121-123 ºC; 242 mg, Yield: 86%; ^{1}H NMR (CDCl3, 400 MHz): δ 8.21-8.18 (m, 2H), 7.77-7.75 (m, 2H), 7.56-753 (m, 4H), 7.37-7.7.32 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.5, 141.3, 139.15, 130.1, 130.0, 129.3, 128.9, 128.4. Anal. Calcd. For $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92%; Found: C, 85.17; H, 5.09; N, 9.97%.



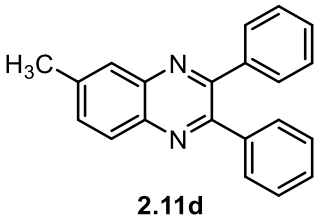
2.11b

2,3-Di-*p*-tolylquinoxaline (2.11b): White solid, mp. 135-137 ºC; 263 mg, Yield: 85%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18-8.14 (m, 2H), 7.76-7.73 (m, 2H), 7.46-7.43 (m, 4H), 7.17-7.14 (m, 4H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.2, 140.9, 138.4, 136.1, 129.5, 129.4, 128.8, 128.6, 21.1. Anal. Calcd. For $C_{22}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03%; Found: C, 85.05; H, 5.78; N, 9.09%.



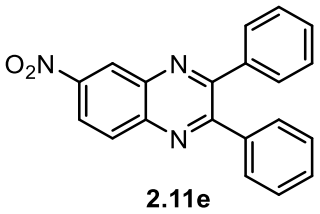
2.11c

2,3-Bis(4-methoxyphenyl)quinoxaline (2.11c): White solid, mp. 135-137 ºC; 283 mg, Yield: 83%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15-8.12 (m, 2H), 7.75-7.72 (m, 2H), 7.51-7.48 (m, 4H), 6.90-6.86 (m, 4H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.0, 152.8, 140.9, 131.5, 131.0, 129.3, 128.7, 113.5, 55.2. Anal. Calcd. For $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18%; Found: C, 77.86; H, 5.42; N, 8.30%.



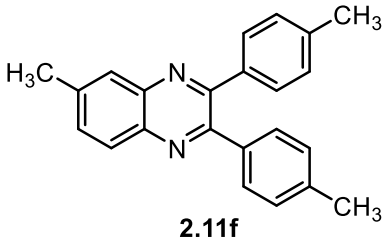
2.11d

6-Methyl-2,3-diphenylquinoxaline (2.11d): White solid, mp. 114-116 ºC; 248 mg, Yield: 84%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06 (d, J = 11.4 Hz, 1H), 7.96 (s, 1H), 7.54-7.49 (m, 5H), 7.36-7.32 (m, 6H), 2.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.1, 152.2, 140.9, 140.2, 139.4, 139.0, 132.0, 130.6,129.6, 129.1, 128.9, 128.4, 128.3 (2C), 127.9, 127.1, 127.3, 126.9, 126.8, 21.6. Anal. Calcd. For $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45%; Found: C, 85.20; H, 5.52; N, 9.32%.



2.11e

6-Nitro-2,3-diphenylquinoxaline (2.11e): White solid, mp. 192-194 ºC; 264 mg, Yield: 81%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.09-9.06 (m, 1H), 8.56-8.52 (m, 1H), 8.31-8.28 (m, 1H), 7.60-7.35 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.2, 139.9, 137.9, 137.7, 130.8, 130.7, 130.5, 129.7, 129.6, 129.5, 129.2, 128.7, 128.5, 128.2, 127.2, 127.1, 124.2, 123.1. Anal. Calcd. For $C_{20}H_{13}N_3O_2$: C, 73.38; H, 4.00; N, 12.84%; Found: C, 73.30; H, 4.14; N, 12.80%.



2.11f

6-Methyl-2,3-di-*p*-tolylquinoxaline (2.11f): Pale yellow solid, mp. 137-139 ºC; 265 mg, Yield: 82%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05-8.01 (m, 1H); 7.92 (s, 1H), 7.59-7.41 (m, 5H), 7.16-7.13 (m, 4H), 2.61 (s, 3H), 2.40 (s, 6H); ^{13}C NMR

($CDCl_3$, 100 MHz):δ 153.2, 152.3, 140.9, 139.8, 139.3, 138.3, 138.2, 136.2, 131.7, 129.5, 128.7, 128.3, 127.6, 21.7, 21.1. Anal. Calcd. For $C_{23}H_{20}N_2$: C, 85.15; H, 6.21; N, 8.63%; Found: C, 85.28; H, 6.31; N, 8.72%.

3.5. Synthesis of 1,4-diazines and their annelated (aza)derivatives under ball milling

3.5.1. General procedure for the synthesis of compounds 2.12 under ball milling

In a 50 mL grinding jar a mixture of dicarbonyl compounds (**2.10**, 2 mmol), diamines (2 mmol) and methanol (0.5 mL) was grinded for 2 h at 500 rpm (a 30 min intervals). After completion of the reaction (monitored by thin-layer chromatography), the resulting paste or solid was transferred from the jar to a 30 mL beaker using 10-15 mL of ethanol or ethanol-water 1:1 mixture and the mixture was heated to reflux (complete dissolution may not occur, but it is sufficient to dissolve unreacted starting materials). Then the reaction mixture was cooled and the desired products **2.12** were filtered off and dried to get the pure product.

3.5.2. General procedure for the synthesis of compounds 2.12 in presence of [BSMIM]OTs.

A mixture of dicarbonyl compounds (**2.10**, 2 mmol), diamines (2 mmol) and [BSMIM]OTs (5 mol%) in methanol (2 mL) was stirred at room temperature for 2 h. After completion of the reaction (monitored by thin-layer chromatography), the resulting paste or solid was transferred from the jar to a 30 mL beaker using 10-15 mL of ethanol or ethanol-water 1:1 mixture and the mixture was heated to reflux (complete dissolution may not occur, but it is sufficient to dissolve unreacted starting materials). Then the reaction mixture was cooled and the desired products **2.12** were filtered off and dried to get the pure product.

3.5.3. General procedure for the synthesis of benzo[*h*]quinoline-5,6-dione 2.10a.

Benzo[*h*]quinoline-5,6-dione was synthesized following a literature method [146]. Benzo[*h*]quinoline (3.6 g, 20 mmol) and iodopentoxide (8.2 g, 25 mmol) were added to a 250 mL round-bottom flask with glacial acetic acid (50 mL). The orange mixture was heated at reflux (118 °C) for 3 h, resulting in a dark purple solution. The product was precipitated by the addition of deionized water (~75 mL) and left to stand overnight at room temperature. The precipitate was isolated by vacuum filtration using a medium glass-sintered frit and subsequently dissolved in chloroform (300 mL) to give a dark red solution that was washed with 100 mL of sat. $NaHCO_3$ and 100 mL of sat. $Na_2S_2O_3$. The organic layer was dried with anhydrous $NaSO_4$, and the solvent was removed by rotary evaporation to give the analytically pure product.

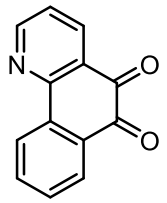
3.5.4. General procedure for the synthesis of 2.15 & 2.16.

A mixture of corresponding bromo-substituted phenazine **2.12** (1 mmol), boronic acid **2.14** (1.1 mmol), $Pd(PPh_3)_2Cl_2$ (2 mol%), PPh_3 (3 mol%) and K_2CO_3 (2 equiv.) was stirred in toluene/MeOH mixture (1:1, 3 mL) at 80 °C for 6 h (TLC control). After completion, the reaction mixture was cooled and extracted with ethyl acetate (3×15 mL) and water (2×10 mL). The organic layer was separated and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure on rotary evaporator, the crude product was purified by column chromatography on silica gel (60–120 mesh) using petroleum ether/ethyl acetate as eluent to afford the pure products.

3.5.5. General procedure for the synthesis of 2.18.

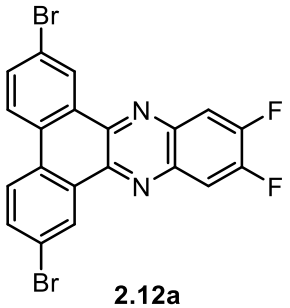
To a degassed (argon) suspension of bromo-substituted phenazine **2.12** (1 mmol), $PdCl_2(PPh_3)_2$ (0.01 mmol) and CuI (0.01 mmol) in DMF (15 mL) phenyl acetyelene (1.5 mmol) and triethylamine (2 mmol) were added. The mixture was heated at 60 °C under argon until the starting material had been consumed (TLC). After completion, the reaction mixture was cooled and extracted with ethyl acetate (3×20 mL) and water (2×20 mL). The organic layer was separated and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure on rotary evaporator, the

crude product was purified by column chromatography on silica gel (60–120 mesh) using petroleum ether/ethyl acetate as eluent to afford the pure products.



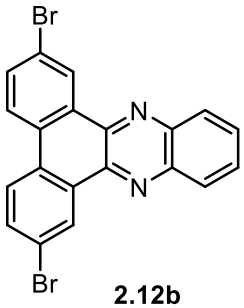
2.10a

Benzo[*h*]quinoline-5,6-dione (2.10a). Brown solid, Yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (d, *J* = 4 Hz, 1H), 8.70 (d, *J* = 8 Hz, 1H), 8.41 (d, *J* = 8 Hz, 1H), 8.21 (d, *J* = 8 Hz, 1H), 7.81 (t, *J* = 8 Hz, 1H), 7.59 (t, *J* = 8 Hz, 1H), 7.44-7.41 (m, 1H); Anal. Calcd. For $C_{13}H_7NO_2$: C, 74.64; H, 3.37; N, 6.70%; Found: C, 74.55; H, 3.45; N, 6.79%.



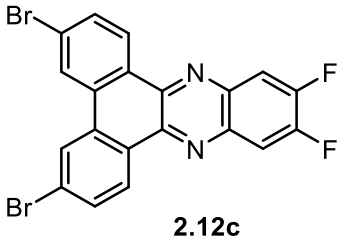
2.12a

2,7-Dibromo-11,12-difluorodibenzo[*a,c*]phenazine (2.12a): Yellow solid, Yield 64%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 2H), 8.38 (s, 2H), 8.07 (d, 2H), 7.91 (d, 2H). Anal. Calcd. For $C_{20}H_8Br_2F_2N_2$: C, 50.67; H, 1.70; N, 5.91%; Found: C, 50.80; H, 1.82; N, 5.85%.



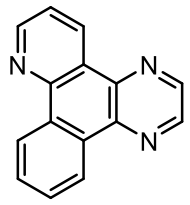
2.12b

2,7-Dibromodibenzo[*a,c*]phenazine (2.12b): Yellow solid, Yield 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.46 (d, 2H, J = 2.2 Hz), 8.29 (m, 4 H), 7.83 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 133.7, 132.2, 130.8, 130.4, 129.8, 129.4, 124.9, 123.2, 100.3. Anal. Calcd. For $C_{20}H_{10}Br_2N_2$: C, 54.83; H, 2.30; N, 6.39%; Found: C, 54.95; H, 2.22; N, 6.52%.



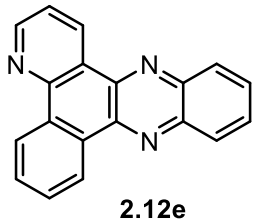
2.12c

3,6-Dibromo-11,12-difluorodibenzo[*a,c*]phenazine (2.12c): Orange solid, Yield 68%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.17 (d, J = 9.2 Hz, 2H), 9.10 (s, 2H), 8.39-8.33 (m, 2H), 8.06-8.04 (m, 2H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -129.08. Anal. Calcd. For $C_{20}H_8Br_2F_2N_2$: C, 50.67; H, 1.70; N, 5.91%; Found: C, 50.75; H, 1.82; N, 5.80%.



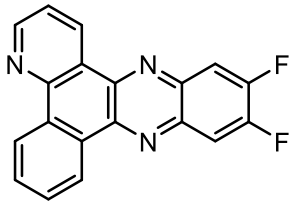
2.12d

Benzo[f]pyrido[2,3-h]quinoxaline (2.12d): White solid, Yield 78%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.44 (d, J = 8 Hz, 1H), 9.30 (d, J = 8 Hz, 1H), 9.21 (d, J = 8 Hz, 1H), 9.10 (d, J = 4 Hz, 1H), 8.95 (d, J = 16 Hz, 2H), 7.91 - 7.84 (m, 2H), 7.72-7.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.98, 147.76, 144.19, 143.71, 141.65, 140.55, 133.26, 132.36, 131.17, 129.92, 129.40, 125.03, 124.80, 124.69, 122.72. Anal. Calcd. For $C_{15}H_9N_3$: C, 77.91; H, 3.92; N, 18.17%; Found: C, 77.80; H, 3.84; N, 18.26%.



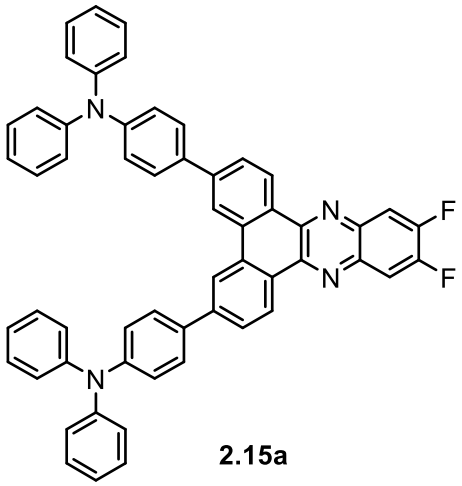
2.12e

Benzo[*a*]pyrido[2,3-*c*]phenazine (2.12e): Brown solid, Yield 82%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.59 (d, *J* = 8 Hz, 1H), 9.37 (d, *J* = 8 Hz, 1H), 9.22 (d, *J* = 8 Hz, 1H), 9.07 (d, *J* = 4 Hz, 1H),8.37-8.32 (m, 2H), 7.90-7.87 (m, 4H), 7.69-7.66 (m, 1H). Anal. Calcd. For $C_{19}H_{11}N_3$: C, 81.12; H, 3.94; N, 14.94%; C, 81.23; H, 3.81; N, 14.80%.



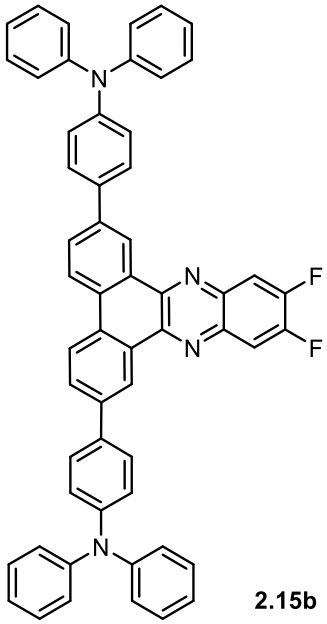
2.12f

11,12-Difluorobenzo[*a*]pyrido[2,3-*c*]phenazine (2.12f): Brown solid, Yield 76%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.52 (d, *J* = 8 Hz, 1H), 9.30 (d, *J* = 8 Hz, 1H), 9.23 (d, *J* = 8 Hz, 1H), 9.08 (d, *J* = 4 Hz, 1H), 8.10-8.02 (m, 2H), 7.92-7.84 (m, 2H), 7.70-7.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.50, 131.09 (2C), 130.96, 130.23, 129.84, 125.57 (2C), 125.52, 125.21, 125.17, 123.03 (2C), 121.14, 114.81, 114.62, 114.58, 114.43, 114.41. Anal. Calcd. For $C_{19}H_9F_2N_3$: C, 71.92; H, 2.86; N, 13.24%; Found: C, 71.80; H, 2.76; N, 13.12%.



2.15a

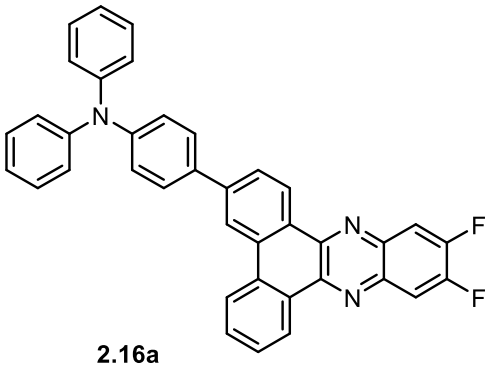
4,4'-(11,12-difluorodibenzo[*a,c*]phenazine-3,6-diyl)bis(*N*,*N*-diphenylaniline) (2.15a). Brown solid, Yield 42%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.22 (d, *J* = 8 Hz, 2H), 8.65 (s, 2H), 7.96-7.86 (m, 4H), 7.67 (d, *J* = 8 Hz, 4H), 7.31 (t, *J* = 8 Hz, 8H), 7.24-7.18 (m, 12H), 7.08 (t, *J* = 8 Hz, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -129.81; Anal. Calcd. For $C_{56}H_{36}F_2N_4$: C, 83.77; H, 4.52; N, 6.98%; Found: C, 83.67; H, 4.43; N, 6.90%.



2.15b

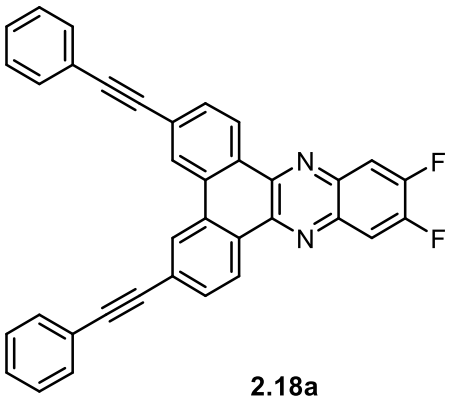
4,4'-(11,12-Difluorodibenzo[*a,c*]phenazine-2,7-diyl)bis(*N*,*N*-diphenylaniline) (2.15b). Brown solid, Yield 57%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.55 (s, 2H), 8.59-8.58 (m, 2H), 8.07-8.03 (m, 4H), 7.78 (d, *J* = 8 Hz, 4H), 7.33-7.30 (m, 8H), 7.20-7.18 (m, 12H), 7.09-7.06 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -129.45; Anal.

Calcd. For $C_{56}H_{36}F_2N_4$: C, 83.77; H, 4.52; N, 6.98%; Found: C, 83.86; H, 4.60; N, 6.90%.



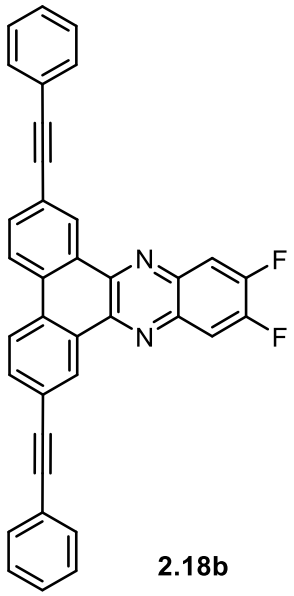
2.16a

4-(11,12-Difluorodibenzo[*a,c*]phenazin-3-yl)-*N*,*N*-diphenylaniline (2.16a). Brown solid, Yield 30%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.32 (t, *J* = 4 Hz, 1H), 9.30 (s, 1H), 8.70 (s, 1H), 8.62 (d, *J* = 8 Hz, 1H), 8.00 (t, *J* = 8 Hz, 2H), 9.93 (d, *J* = 8 Hz, 1H), 7.81-7.69 (m, 4H), 7.34-7.30 (m, 4H), 7.25-7.18 (m, 6H), 7.08 (t, *J* = 8 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -129.57, -129.76. Anal. Calcd. For $C_{38}H_{23}F_2N_3$: C, 81.56; H, 4.14; N, 7.51%; Found: C, 81.65; H, 4.26; N, 7.64%.



2.18a

11,12-Difluoro-3,6-bis(phenylethynyl)dibenzo[*a,c*]phenazine (2.18a): Yellow gummy, Yield 60%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 8.80 (s, 2H), 8.71-8.62 (m, 2H), 8.10-8.05 (m, 2H), 7.78-7.66 (m, 6H), 7.55-7.49 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -129.10; Anal. Calcd. For $C_{36}H_{18}F_2N_2$: C, 83.71; H, 3.51; N, 5.42%; Found: C, 83.82; H, 3.59; N, 5.35%.

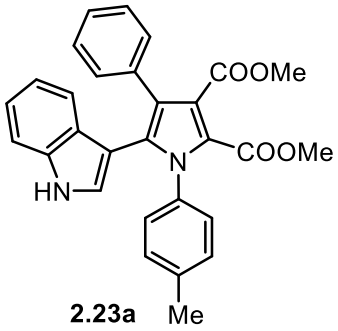


2.18b

11,12-Difluoro-2,7-bis(phenylethynyl)dibenzo[*a,c*]phenazine (2.18b). Yellow gummy; Yield 54%; ^{1}H NMR: (400 MHz, $CDCl_3$): δ 9.35 (s, 2H), 8.30 (d, *J* = 8 Hz, 4H), 8.05-8.00 (m, 4H), 7.89-7.86 (m, 4H), 7.69-7.68 (m, 2H), 7.50-7.44 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -127.64; Anal. Calcd. For $C_{36}H_{18}F_2N_2$: C, 83.71; H, 3.51; N, 5.42%; Found: C, 83.78; H, 3.42; N, 5.51%.

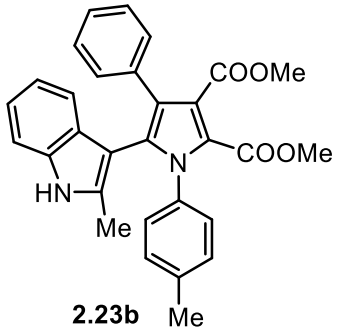
3.6. Mechochemical synthesis of multi-substituted pyrroles:

3.6.1. General Procedure for the Synthesis of Compounds 2.23. In a 50 mL grinding jar a mixture of phenyl glyoxal (**2.19**, 1 mmol), aniline (**2.20**, 1 mmol), indole (**2.21**, 1 mmol) and $FeCl_3$ (20 mol%) was ball milled for 30 min. Then dimethylacetylenedicarboxylate (**2.22**, 1 mmol) was added and further ball milled for 3.5 h at 500 rpm at room temperature (a 30 min interval). After completion of the reaction (monitored by thin-layer chromatography), the reaction mixture was extracted with ethyl acetate (2 × 15 mL). The organic layer was washed with water (2 × 10 mL) and dried over anhydrous Na_2SO_4. Then, it was concentrated under reduced pressure to obtain the crude residue which was subjected to column chromatography using petroleum ether−ethyl acetate as the eluent to obtain the analytically pure product.



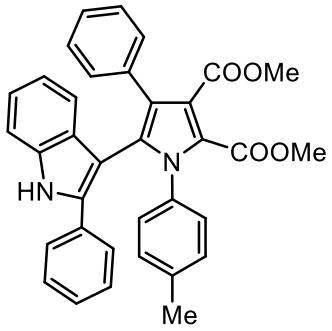
2.23a

Dimethyl 5-(1*H*-indol-3-yl)-4-phenyl-1-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxylate (2.23a): White solid, mp. 185-187 °C, 398 mg (86% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (brs, 1H), 7.26-7.25 (m, 3H), 7.22-7.10 (m, 7H), 7.08-7.02 (m, 2H), 6.90-6.87 (m, 1H), 6.74 (s, 1H), 8.85 (s, 3H), 3.73 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 160.6, 138.0, 135.9, 135.3, 133.9, 131.9, 129.2, 128.9, 127.9, 127.2, 126.5, 126.1, 123.9, 122.9, 122.5, 122.0, 119.8, 111.0, 105.7, 52.4, 51.9, 21.1. Anal. Calcd. for $C_{29}H_{24}N_2O_4$: C, 74.98; H, 5.21; N, 6.03%; Found: C, 74.92; H, 5.16; N, 6.09%.



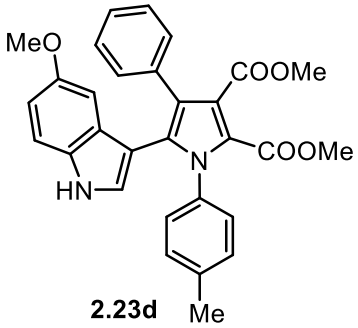
2.23b

Dimethyl 5-(2-methyl-1*H*-indol-3-yl)-4-phenyl-1-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxylate (2.23b): Gray solid, mp. 220-222 °C, 382 mg (80% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (brs, 1H), 7.16-7.09 (m, 3H), 7.05-7.00 (m, 3H), 6.97-6.85 (m, 6H), 3.77 (s, 3H), 3.66 (s, 3H), 2.12 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 160.9, 138.0, 135.9, 135.7, 135.1, 134.2, 131.7, 129.7, 129.1, 128.9, 128.1, 127.3, 126.6, 125.3, 123.5, 122.2, 121.3, 120.0, 119.1, 110.3, 103,1, 52.3, 51.9, 21.1, 12.2. Anal. Calcd. for $C_{30}H_{26}N_2O_4$: C, 75.30; H, 5.48; N, 5.85%; Found: C, 75.24; H, 5.40; N, 5.79%.



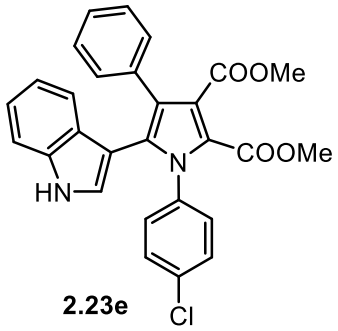
2.23c

Dimethyl 4-phenyl-5-(2-phenyl-1*H*-indol-3-yl)-1-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxylate (2.23c): Brown gummy mass, 443 mg (82% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06-8.00 (m, 2H), 7.61-7.59 (m, 2H), 7.39-7.36 (m, 4H), 7.16-7.07 (m, 4H), 6.74-6.68 (m, 4H), 6.57-6.55 (m, 2H), 5.45 (s, 1H), 3.82 (s, 3H), 3.59 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 163.5, 152.1, 146.7, 139.9, 136.2, 136.0, 135.3, 131.3, 129.1, 128.7, 128.5, 128.3, 127.9, 127.1, 125.8, 123.2, 122.5, 122.2, 120.4, 111.0, 106.6, 104.3, 83.7, 53.0, 51.0, 20.8. Anal. Calcd. For $C_{35}H_{28}N_2O_4$: C, 77.76; H, 5.22; N, 5.18%; Found: C, 77.68; H, 5.17; N, 5.25%.



2.23d

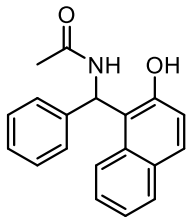
Dimethyl 5-(5-methoxy-1*H*-indol-3-yl)-4-phenyl-1-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxylate (2.23d): White solid, mp. 195-197 °C, 455 mg (92% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (brs, 1H), 7.26-7.24 (m, 2H), 7.14-7.11 (m, 3H), 7.10−7.02 (m, 5H), 6.68-6.62 (m, 2H), 6.36 (s, 1H), 3.82 (s, 3H), 3.70 (s, 3H), 3.50 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 160.5, 154.2, 138.2, 135.8, 133.9, 131.8, 130.0, 129.1, 129.0, 128.9, 127.9, 127.2, 126.5, 126.1, 123.1, 122.7, 122.5, 113.0, 111.3, 105.7, 100.7, 56.0, 53.0, 51.4, 21.9. Anal. Calcd. For $C_{30}H_{26}N_2O_5$: C, 72.86; H, 5.30; N, 5.66%; Found: C, 72.80; H, 5.21; N, 5.75%.



2.23e

Dimethyl 1-(4-chlorophenyl)-5-(1*H*-indol-3-yl)-4-phenyl-1*H*-pyrrole-2,3-dicarboxylate (2.23e): Pale yellow solid, mp. 212-214 °C, 368 mg (76% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (brs, 1H), 7.26-7.07 (m, 12H), 6.94-6.90 (m, 1H), 6.76 (s, 1H), 3.86 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 160.8, 137.7, 135.8, 134.7, 134.1, 132.2, 130.1, 129.7, 129.1, 128.5, 127.6, 127.2, 126.4, 124.8, 123.9, 123.0(2C), 120.8, 120.3, 111.5, 106.4, 52.2, 51.8. Anal. Calcd. For $C_{28}H_{21}ClN_2O_4$: C, 69.35; H, 4.37; N, 5.78%; Found: C, 69.30; H, 4.45; N, 5.87%.

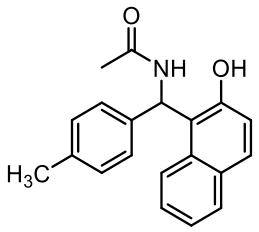
3.7. Synthesis of amidoalkyl naphthols (2.27): A mixture of aldehyde (**2.24**, 1 mmol), 2-naphthol (**2.25**, 1 mmol), amide (**2.26**, 1.2 mmol) and [BSMIM]OTs (10 mol%) was stirred at 80 ^{o}C in an oil bath. After the completion of the reaction was monitored by TLC, water and ethyl acetate were added and the product was washed and then purified by column chromatography (Hexane: EtOAc).



2.27a

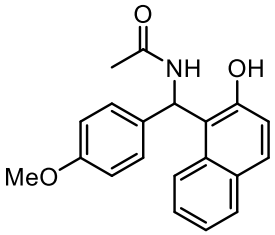
***N*-((2-Hydroxynaphthalen-1-yl)(phenyl)methyl)acetamide** (**2.27a)**: White solid, mp. 228-230 °C; Yield 85%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.99 (s, 1H), 8.44 (d, *J* =8.4 Hz, 1H), 7.82-7.76 (m, 3H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.27-7.21 (m, 4H), 7.17-7.12 (m, 4H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.8, 153.6, 143.1, 132.8, 129.7, 129.1, 128.9, 128.7, 128.4, 126.8, 126.5, 123.9, 122.8, 119.3,

119.0, 48.7, 23.1. Anal. Calcd. For $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81%; Found: C, 78.25; H, 5.98; N, 4.73%.



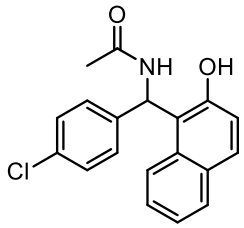
2.27b

***N*-[(4-Methyl phenyl)-(2-hydroxy-naphthalen-1-yl)-methyl]-acetamide** (**2.27b**): White solid, mp. 224-226 °C; Yield 86%; ^{1}H NMR (400 MHz, DMSO-d_6):δ 9.95 (s, 1H), 8.37 (d, J = 8.2 Hz, 1H), 7.83 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.38-7.35 (m, 1H), 7.24 (t, J = 7.2 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 7.10–7.04 (m, 5H), 2.23 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.1, 153.0, 143.3, 139.5, 135.0, 132.3, 129.0, 128.5, 128.3, 126.2, 126.0, 123.1, 122.4, 118.9, 118.5, 47.8, 22.8, 20.5. Anal. Calcd. For $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59%; Found: C, 78.77; H, 6.43; N, 4.62%.



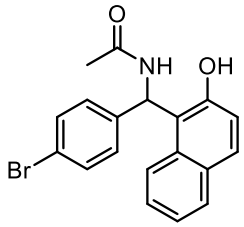
2.27c

***N*-((2-Hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)acetamide** (**2.27c**): White solid, mp. 160-162 °C; Yield 83%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.01 (s, 1H), 8.37 (d, J = 8.2 Hz, 1H), 7.83-7.79 (m, 2H), 7.75 (d, J = 8.8 Hz, 1H), 7.30-7.12 (m, 3H), 7.10–6.98 (m, 4H), 3.83 (s, 3H), 1.965 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.6, 159.0, 153.1, 143.3, 139.5, 135.0, 132.3, 129.0, 128.3, 126.2, 126.0, 123.1, 122.4, 118.9, 118.5, 116.1, 56.4, 47.8, 20.5. Anal. Calcd. For $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36%; Found: C, 74.84; H, 5.86; N, 4.25%.



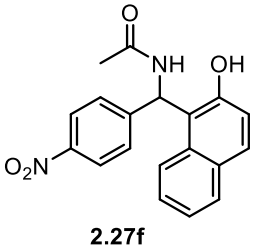
2.27d

***N*-((4-Chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl)acetamide** (**2.27d**): Grey solid, mp. 234-236 °C; Yield 84%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.09 (s, 1H); 8.76 (d, *J* =8.8 Hz, 1H), 7.81-7.78 (m, 3H), 7.41-7.16 (m, 8H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.1, 153.8, 141.9, 132.7, 132.1, 130.1, 129.2, 128.9, 128.5, 128.4, 127.0, 126.3, 123.4, 118.9, 118.5, 48.4, 22.9. Anal. Calcd. For $C_{19}H_{16}ClNO_2$: C, 70.05; H, 4.95; N, 4.30%; Found: C, 70.14; H, 4.90; N, 4.22%.



2.27e

***N*-((4-Bromophenyl)(2-hydroxynaphthalen-1-yl)methyl)acetamide** (**2.27e**): White solid, mp. 229-231 °C; Yield 82%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.78 (s, 1H), 7.68-7.62 (m, 2H), 8.28 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 10 Hz, 1H), 7.36-700 (m, 8H), 1.98 (s, 3H),^{13}C NMR (100 MHz, DMSO-d_6): δ 168.5, 152.8, 140.0, 133.3, 131.1, 130.2, 129.4, 128.8, 128.4, 127.0, 123.9, 122.4, 121.3, 118.8, 117.9, 46.7, 23.4. Anal. Calcd. For $C_{19}H_{16}BrNO_2$: C, 61.64; H, 4.36; N, 3.78%; Found: C, 61.54; H, 4.31; N, 3.67%.



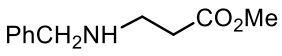
2.27f

***N*-[(4-Nitro-phenyl)-(2-hydroxy-naphthalen-1-yl)-methyl]-acetamide** (**2.27f**): Light yellow solid, mp. 238-240 °C; Yield 80%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.08 (s, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.06–8.03 (m, 2H), 7.90 (s, 1H), 7.81 (t, *J* = 8.8 Hz, 2H), 7.60–7.54 (m, 2H), 7.40 (t, *J* = 7.4, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 8.8, 1H), 7.20 (d, *J* = 8.0, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.0, 153.3, 147.8, 145.4, 132.8, 132.2, 129.9, 129.5, 128.7, 126.8, 122.5, 121.2, 120.4, 118.6, 117.8, 47.7, 22.6. Anal. Calcd. For $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.80; N, 8.33%; Found: C, 67.95; H, 4.88; N, 8.43%.

3.8. Conjugate addition of a variety of amines to Michael acceptor

3.8.1. Preparation of tea extract: 2 g of tea leaves (any marketed) were dissolved in 20 mL of water and boiled it for 10-15 min. After filtration we got the extract which was used for the reactions.

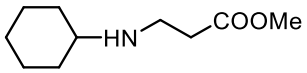
3.8.2. General procedure for the synthesis of β-amino derivatives (2.34): A mixture of amine (2 mmol) and alkene (2 mmol) was stirred in 2 mL of tea extract at room temperature as required for completion (TLC). After completion of the reaction the reaction mixture was extracted with ethyl acetate (40 mL). The extract was washed with water (2 x 10 mL) and brine solution (1 x 10 mL) and dried over anhydrous sodium sulphate. Evaporation of solvent followed by short column chromatography of the crude product over silica gel (hexane/ ethyl acetate) furnished the analytically pure product. The known compounds have been identified by comparison of spectra data (IR and NMR). The spectral and analytical data of the compounds which are not readily found provided below.



2.34a

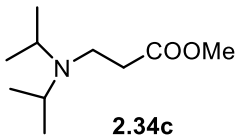
Methyl 3-(benzylamino)propanoate (2.34a): Yellow oil, Yield 90%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.23 (m, 5H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 2H), 2.90 (t, *J* = 6.3 Hz, 2H), 2.53 (t, *J* = 6.3 Hz, 2H), 1.66 (s, 1H), 1.25 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$): δ 172.79, 140.17, 128.42, 128.09, 126.96, 60.41, 53.77, 44.51, 34.79, 14.23; Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%; Found: C, 68.47; H, 7.90; N, 7.36%.



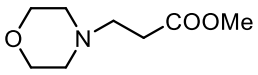
2.34b

Methyl 3-(cyclohexylamino)propanoate (2.34b): Yellow oil, Yield 90%; ^{1}H NMR (300 MHz, CDCl3) δ: 1.019-1.242 (m, 2H), 1.568-1.648 (m, 2H), 1.680-1.722 (m, 2H), 1.841-1.866 (m, 2H), 2.341-2.472 (m, 1H), 2.494 (t, *J* = 6.4 Hz, 2H), 2.881 (t, *J* = 6.8 Hz, 2H), 3.655 (s, 3H); Anal. Calcd. For $C_{10}H_{19}NO_2$: C, 64.83; H, 10.34; N, 7.56%; Found: C, 64.90; H, 10.30; N, 7.64%.



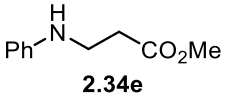
2.34c

Methyl 3-(diisopropylamino)propanoate (2.34c): White gummy, Yield 94%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (d, *J* = 6.4 Hz, 12H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.63 (t, *J* = 5.9 Hz, 2H), 2.68 (hept, *J* = 6.6 Hz, 2H), 3.49 (s, 3H). Anal. Calcd. For $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30; N, 7.48%; Found: C, 64.21; H, 11.42; N, 7.40%.



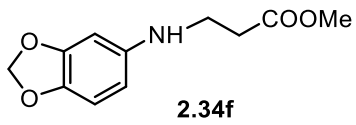
2.34d

Methyl 3-morpholinopropanoate (2.34d): Yellow oil, Yield 90%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (t, *J* = 4.4 Hz, 4H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.60 (t, *J* = 7.2 Hz, 2H), 3.61 (t, *J* = 4.4 Hz, 4H), 3.63 (s, 3H); Anal. Calcd. For $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09%; Found: C, 55.47; H, 8.73; N, 8.09%.



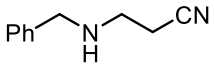
2.34e

Methyl 3-(phenylamino)propanoate (2.34e): Yellow gummy, Yield 85%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.23 (dd, *J* = 8.0, 7.4 Hz, 2H), 6.77 (dd, *J* = 7.4, 7.4 Hz, 2H), 6.67 (d, *J* = 8.0 Hz, 1H), 4.09 (brs, 1H), 3.74 (s, 3H), 3.49 (t, *J* = 6.4 Hz, 2H), 2.65 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.7, 147.5, 129.1, 117.5, 112.8, 51.4, 39.1, 33.4. Anal. Calcd. For $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%; Found: C, 67.11; H, 7.42; N, 7.76%.



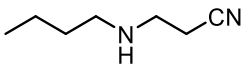
2.34f

Methyl 3-(benzo[*d*][1,3]dioxol-5-ylamino)propanoate (2.34f): Light yellow gummy, Yield 88%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.64 (d, *J* = 8.3 Hz, 1H), 6.25 (d, *J* = 2.3 Hz, 1H), 6.04 (dd, *J* = 8.3, 2.3 Hz, 1H), 5.82 (d, *J* = 0.8 Hz, 2H), 3.68 (d, *J* = 0.7 Hz, 3H), 3.35 (t, *J* = 6.4 Hz, 2H), 2.58 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.59, 148.19, 143.15, 139.62, 108.40, 104.51, 100.38, 96.10, 51.48, 40.24, 33.41. Anal. Calcd. For $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27%; Found: C, 59.28; H, 5.95; N, 6.20%.



2.34g

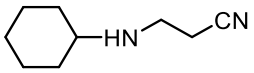
3-(Benzylamino)propanenitrile (2.34g): Pale yellow oil, Yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.28 (m, 4H), 7.27-7.19 (m, 1H), 3.79 (s, 2H), 2.86 (td, *J* = 6.6, 2.6 Hz, 2H), 2.44 (td, *J* = 6.6, 2.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 128.3, 127.8, 126.9, 118.6, 52.8, 44.1, 18.5. Anal Calcd. For: $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48%; Found: C, 74.77; H, 7.68; N, 17.40%.



2.34h

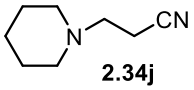
3-(Butylamino)propanenitrile (2.34h): Light yellow oil, Yield 96%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.9 (t, *J* = 6.6 Hz, 2H), 2.6 (t, *J* = 7.1 Hz, 2H), 2.5 (t, *J* = 6.6

Hz, 2H), 2.1 (brs, 1H), 1.7-1.5 (m, 2H), 1.3-1.1 (m, 2H), 0.9 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 112.2, 52.3, 46.7, 34.3, 30.1, 21.5, 14.1. Anal. Calcd. For $C_7H_{14}N_2$: C, 66.62, H, 11.18, N, 22.20%; Found: C, 66.92, H, 11.34, N, 22.47%.



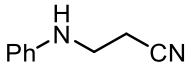
2.34i

3-(Cyclohexylamino)propanenitrile (2.34i): Colorless oil; 1H NMR (300 MHz, $CDCl_3$): δ 2.85 (t, *J* = 5.1 Hz, 2H), 2.45 (t, *J* = 5.1 Hz, 2H), 2.43(m, 1H) 1.80-1.63 (m, 5H), 1.25-1.16 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 119.2, 58.7, 43.4, 34.7 (2C), 26.1, 25.3 (2C), 18.2. Anal. Calcd. For $C_9H_{16}N_2$: C, 71.01; H, 10.59; N, 18.40 %; Found: C, 60.82; H, 10.35; N, 18.13 %.



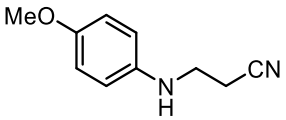
2.34j

3-(Piperidin-1-yl)propanenitrile (2.34j): Yellow oil, Yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.8 (t, *J* = 6.7 Hz, 2H), 2.7-2.5 (m, 6H), 1.3-1.1 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.2, 52.7, 49.5, 26.4, 25.2, 18.5; Anal Calcd. For $C_8H_{14}N_2$: C, 69.52, H, 10.21, N, 20.27%; Found: C, 69.84, H, 10.52, N, 20.63%.



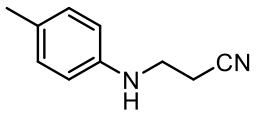
2.34k

3-(Phenylamino)propanenitrile (2.34k): Thick brown oil, Yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (t, *J* = 8.0 Hz, 2H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 2H), 3.90 (br, 1H), 3.45 (t, *J* = 6.5 Hz, 2H), 2.56 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1, 129.5, 118.7, 113.1, 39.8, 18.2. Anal Calcd. For $C_9H_{10}N_2$: C, 73.94; H, 6.89; N, 19.16%; Found: C, 73.77; H, 6.80; N, 19.32%.



2.34l

3-(4-Methoxy-phenylamino)-propanenitrile (2.34l): Colorless liquid, Yield 75%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.80 (d, *J* = 5.1 Hz, 2H), 6.61 (d, *J* = 5.1 Hz, 2H), 3.75 (s, 3H), 3.47 (t, *J* = 4.8 Hz, 2H), 2.61 (t, *J* = 4.8 Hz, 2H), (N-H) not identified; ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.9, 140.3, 118.5, 115.1 (2C), 114.8 (2C), 55.8, 40.8, 18.2. Anal. Calcd. For $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90 %; Found: C, 67.98; H, 6.53; N, 15.62%.



2.34m

3-(4-Methyl-phenylamino)-propanenitrile (2.34m): Colorless liquid, Yield 80%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (d, *J* = 6.0 Hz, 2H), 6.53 (d, *J* = 6.0 Hz, 2H), 3.47 (d, *J* = 5.1 Hz, 2H), 2.60 (d, *J* = 5.1 Hz, 2H), 2.24 (s, 3H) (N-H) not identified; ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.9, 130.2 (2C), 127.7, 118.5, 113.2 (2C), 40.0, 20.4, 18.0. Anal. Calcd. For $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48 %. Found: C, 74.63; H, 7.38; N, 17.16 %.

Conclusions:

1. The applicability of reactions of mono- and dicarbonyl compounds with *N*-, *O*-, *C*-centered nucleophiles under mechanical activation conditions and in ionic liquids has been demonstrated for the synthesis of practically useful compounds (ligands, fluorophores and drug candidates):

1.1. A method has been developed for the synthesis of 4-substituted coumarins by reacting 1,3-dicarbonyl compounds with phenols as 1,3-*C*-,*O*-dinucleophiles under mechanical activation conditions, as well as under the solvent-free condition in ionic liquids environment.

1.2. For the first time, direct C3-functionalization of 4-hydroxycoumarins was carried out in reactions with substituted styrenes in the absence of a solvent or in ionic liquids.

1.3. A method has been developed for the synthesis of new derivatives of quinoxalines, phenazines and their polycyclic and aza derivatives by the reaction of 1,2-dicarbonyl compounds and 1,2-diamines in the absence of a solvent under mechanochemical conditions or in ionic liquids.

1.4. An effective method has been developed for the construction of new tetrasubstituted pyrrole derivatives through a multicomponent reaction under mechanochemical conditions.

1.5. An effective method has been developed for the synthesis of 1-amidoalkyl-2-naphthols by a multicomponent reaction in ionic liquids.

1.6. A method has been developed for the synthesis of β-aminopropionic acid derivatives by reacting acrylic acid derivatives with amines under conditions of catalysis with ionic liquids, catalysis with tea extract, and mechanical activation.

2. Among the obtained compounds, derivatives of indolyl-substituted pyrroles and dibenzophenazines, promising blue and orange fluorophores were discovered.

3. The applicability of indolyl-substituted pyrroles for fluorescent “turn-off” detection of explosive components in solutions with quenching constants up to 10^4-10^5 M^{-1} has been demonstrated, which exceeds those for known compounds.

Recommendations, prospects for the further development of the topic:

As a part of further development of the topic, we can consider further expanding the series of fluorophores based on phenazines and quinoxalines, as well as multisubstituted pyrroles. It is also promising to search for drug candidates among the obtained compounds.

References:

1. Stanchev S. Investigation of the antioxidant properties of some new 4-hydroxycoumarin derivatives / S. Stanchev, V. Hadjimitova, T. Traykov, T. Boyanov, I. Manolov // Eur. J. Med. Chem. – 2009. – Vol. 44. – P. 3077-3082.
2. Sashidhara K.V. Synthesis and antihyperlipidemic activity of novel coumarin bisindole derivatives / K. V. Sashidhara, A. Kumar, M. Kumar, A. Srivastava, A. Puri // Bioorg. Med. Chem. Lett. – 2010. – Vol. 20. – P. 6504-6507.
3. Keri R.S. Analgesic, anti-pyretic and DNA cleavage studies of novel pyrimidine derivatives of coumarin moiety / R. S. Keri, K. M. Hosamani, R. V. Shingalapur, M. H. Hugar // Eur. J. Med. Chem. – 2010. – Vol. 45. – P. 2597-2605.
4. Cohen A.J. Critical review of the toxicology of coumarin with special reference to interspecies differences in metabolism and hepatotoxic response and their significance to man / A. J. Cohen // Food Cosmet. Toxicol. – 1979. – Vol. 17. – P. 277-289.
5. Basile A. Antimicrobial and antioxidant activities of coumarins from the roots of Ferulago campestris (Apiaceae) / A. Basile, S. Sorbo, V. Spadaro, M. Bruno, A. Maggio, N. Faraone, S. Rosselli //Molecules. – 2009. – Vol. 14. – P. 939-952.
6. Bigi F. Montmorillonite KSF as an inorganic, water stable, and reusable catalyst for the knoevenagel synthesis of coumarin-3-carboxylic acids / F. Bigi, L. C. Hesini, R. Maggi, G. Sartori // J. Org. Chem. – 1999. – Vol. 64. – P. 1033-1035.
7. Donnelly B.J. Dalbergia Species-VI: The occurrence of melannein in the genus Dalbergia / B. J. Donnelly, D. M. X. Donnelly, A. M. O. Sullivan // Tetrahedron. – 1968. – Vol. 24. – P. 2617-2622.
8. Pechmann V.H. Neue bildungsweise der cumarine. Synthese des daphnetins. I / V. H. Pechmann // Ber. Dtsch. Chem. Ges. – 1884. – Vol. 17. – P. 929-936.

9. Yavari I. A new and efficient route to 4-carboxymethylcoumarins mediated by vinyltriphenylphosphonium salt / I. Yavari, R. H. Shoar, A. Zonuzi // Tetrahedron Lett. – 1998. – Vol. 39. – P. 2391-2392.
10. Cairns N. Tandem thermal Claisen-Cope rearrangements of coumarate derivatives. Total synthesis of the naturally occurring coumarins: suberosin, demethylsuberosin, ostruthin, balsamiferone and gravelliferone / N. Cairns, L. M. Harwood, D. P. Astles // J. Chem. Soc., Perkin Trans. 1. – 1994. – Vol. 1. – P. 3101-3107.
11. Shirner R.L. The Reformatsky reaction / R. L. Shirner // Org. React. – 1942. – Vol. 1. – P. 1-37.
12. Von Pechmann H. Ueber die verbindungen der phenole mit acetessigäther / H. Von Pechmann, C. Duisberg // Ber. Dtsch. Chem. Ges. – 1883. – Vol. 16. – P. 2119-2128.
13. Sharma D. A facile synthesis of 2*H*-chromen-2-ones via Pechmann condensation under solvent free conditions using grinding technique / D. Sharma, S. Kumar // Green Process Synth. – 2013. – Vol. 2. – P. 151-155.
14. Rezayati S. One-pot synthesis of coumarin derivatives using butylenebispyridinium hydrogen sulfate as novel ionic liquid catalyst / S. Rezayati, F. Sheikholeslami-Farahani, F. Rostami-Charati, S. A. S. Abad // Res. Chem. Intermed. – 2016. – Vol. 42. – P. 4097-4107.
15. Taib L.A. Solvent-free synthesis of 4-substituted coumarins catalyzed by novel brønsted acidic ionic liquids with perchlorate anion: a convenient and practical complementary method for Pechmann condensation / L. A. Taib, M. Keshavarz, A. Parhami // Reaction Kinetics, Mechanisms and Catalysis. – 2021. – Vol. 133. – P. 383-403.
16. Uroos M. Green synthesis of coumarin derivatives using Brønsted acidic pyridinium based ionic liquid [MBSPy][HSO_4] to control an opportunistic human and a devastating plant pathogenic fungus *Macrophomina phaseolina* / M. Uroos, A. Javaid, A. Bashir, J. Tariq, I. H. Khan, S. Naz, S. Fatima, M. Sultan // RSC Adv. – 2022. – Vol. 12. – P. 23963-23972.

17. Sharapov A.D. Mechanochemical synthesis of coumarins via Pechmann condensation under solvent-free conditions: an easy access to coumarins and annulated pyrano[2,3-*f*] and [3,2-*f*]indoles / A. D. Sharapov, R. F. Fatykhov, I. A. Khalymbadzha, V. V. Sharutin, S. Santra, G. V. Zyryanov, O. N. Chupakhin, B. C. Ranu // Green Chem. – 2022. – Vol. 24. – P. 2429-2437.
18. Becerra-Anaya S.J. A simple and effective protocol for the Pechmann reaction to obtain 4-methylcoumarin derivatives using a high-speed mixer ball mill process / S. J. Becerra-Anaya, D. R. Merchán Arenas, V. V. Kouznetsov // Chemistry. – 2023. – Vol. 5. – P. 1077-1088.
19. Yao X. Highly efficient addition of activated methylene compounds to alkenes catalyzed by gold and silver / X. Yao, C. J. Li // J. Am. Chem. Soc. – 2004. – Vol. 126. – P. 6884-6885.
20. Yao X. Highly efficient, reversible addition of activated methylene compounds to styrene derivatives catalyzed by silver catalysts / X. Yao, C. J. Li // J. Org. Chem. – 2005. – Vol. 70. – P. 5752-5755.
21. Rueping M. An efficient metal-catalyzed hydroalkylation / M. Rueping, B. J. Nachtsheim, A. Kuenkel // Synlett. – 2007. – Vol. 2007. – P. 1391-1394.
22. Li Y. Efficient copper(II)-catalyzed addition of activated methylene compounds to alkenes. Y. Li, Z. Yu, S. Wu // J. Org. Chem. – 2008. – Vol. 73. – P. 5647-5650.
23. Wang G.-W. Solvent-free hydroalkylation of olefins with 1, 3-diketones catalyzed by phosphotungstic acid / G. –W. Wang, Y. – B. Shen, X. –L. Wua, L. Wang // Tetrahedron Lett. – 2008. – Vol. 49. – P. 5090-5093.
24. Liu P.N. Perchloric acid catalyzed homogeneous and heterogeneous addition of β-dicarbonyl compounds to alcohols and alkenes and investigation of the mechanism / P. N. Liu, L. Dang, Q. W. Wang, S. L. Zhao, F. Xia, Y. J. Ren, X. Q. Gong, J. Q. Chen // J. Org. Chem. – 2010. – Vol. 75. – P. 5017-5030.
25. Yadav J.S. Iodine as a versatile catalyst for the hydroalkylation of vinyl arenes with 1, 3-diketones. / B. V. S. Reddy, T. S. Rao, K. Bhavani, A. Raju // Tetrahedron Lett. – 2010. – Vol. – 51. – P. 2622-2624.

26. Boosa M. HY and Hβ zeolites mediated C–C bond formation via addition/substitution reaction of 1,3-dicarbonyl compounds to alcohols and alkenes / M. Boosa, D. R. Yennamaneni, D. Chevella, V. Amrutham, K. S. Gajula, R. Madasu, V. Akula, N. Nama // Catal. Lett. – 2023. – Vol. 153. – P. 1349-1358.
27. Nakamura M. Indium-catalyzed addition of active methylene compounds to 1-alkynes / M. Nakamura, K. Endo, E. Nakamura // J. Am. Chem. Soc. – 2003. – Vol. 125. – P. 13002-13003.
28. Endo K. Indium-catalyzed 2-alkenylation of 1, 3-dicarbonyl compounds with unactivated alkynes / K. Endo, T. Hatakeyama, M. Nakamura, E. Nakamura // J. Am. Chem. Soc. – 2007. – Vol. 129. – P. 5264-5271.
29. Sau M.C. Addition of 1, 3-dicarbonyl compounds to terminal alkynes catalyzed by a cationic cobalt(III) complex / M. C. Sau, M. Bhattacharjee // RSC Adv. – 2020. – Vol. 10. – P. 36014-36019.
30. Pennington-Boggio M.K. A ruthenium-catalyzed coupling of alkynes with 1, 3-diketones / M. K. Pennington-Boggio, B. L. Conley, T. J. Williams // J. Organomet. Chem. – 2012. – Vol. 716. – P. 6-10.
31. Cao H. DABCO-catalyzed C-C bond formation reaction between electron-deficient alkynes and 1, 3-dicarbonyl compounds / H. Cao, H. Zhong, Y. Lin, L. Yang // Tetrahedron. – 2012. – Vol. 68. – P. 4042-4047.
32. Beck T.M. Regioselective rhodium-catalyzed addition of β-keto esters, β-keto amides, and 1, 3-diketones to internal alkynes / T. M. Beck, B. Breit // Eur. J. Org. Chem. – 2016. – Vol. 2016. – P. 5839-5844.
33. Luo Y. Copper-free Sonogashira reactions of 4-hydroxycoumarins with alkynes / Y. Luo, J. Wu // Tetrahedron. – 2009. – Vol. 65. – P. 6810-6814.
34. Chatterjee R. Vinylation of carbonyl oxygen in 4-hydroxycoumarin: Synthesis of heteroarylated vinyl ethers / R. Chatterjee, S. Santra, G. V. Zyryanov, A. Majee // Synthesis. – 2019. – Vol. 51. – P. 2371-2378.
35. Tan X.-c. Atom-economical chemoselective synthesis of furocoumarins via cascade palladium catalyzed oxidative alkoxylation of 4-oxohydrocoumarins

and alkenes / X. -c. Tan, H. -y. Zhao, Y. -m. Pan, N. Wu, H. -s. Wang, Z. -f. Chen // RSC Adv. – 2015. – Vol. 5. – P. 4972-4975.

36. Soleymani M. The chemistry and applications of the quinoxaline compounds, The chemistry and applications of the quinoxaline compounds. M. Soleymani, M. Chegeni // Curr. Org. Chem. – 2019. – Vol. 23. – P. 1789-1827.
37. Tariq S. Quinoxaline: an insight into the recent pharmacological advances, Quinoxaline: An insight into the recent pharmacological advances / S. Tariq, K. Somakala, M. Amir // Eur. J. Med. Chem. – 2018. – Vol. 143. – P. 542-557.
38. Jiang X. Functionalized quinoxalinones as privileged structures with broad-ranging pharmacological activities / X. Jiang, K. Wu, R. Bai, P. Zhang, Y. Zhang // Eur. J. Med. Chem. – 2022. – Vol. 229. – P. 114085.
39. Ingle R. Sulphonamido-quinoxalines: search for anticancer agent, Sulphonamido-quinoxalines: Search for anticancer agent / R. Ingle, R. Marathe, D. Magar, H. M. Patel, S. J. Surana // Eur. J. Med. Chem. – 2013. – Vol. 65. – P. 168-186.
40. El Newahie A.M.S. Quinoxaline-based scaffolds targeting tyrosine kinases and their potential anticancer activity / A. M. S. El Newahie, N. S. M. Ismail, D. A. Abou El Ella, K. A. M. Abouzid // Arch. Pharm. – 2016. – Vol. 349. – P. 309-326.
41. Ibrahim M.K. Design, synthesis, molecular modeling and antihyperglycemic evaluation of novel quinoxaline derivatives as potential PPARγ and SUR agonists / M. K. Ibrahim, I. H. Eissa, A. E. Abdallah, A. M. Metwaly, M. M. Radwan, M. A. El-Sohly // Bioorg. Med. Chem. – 2017. – Vol. 25. – P.1496-1513.
42. Shintre S.A. Synthesis, in vitro antimicrobial, antioxidant, and antidiabetic activities of thiazolidine–quinoxaline derivatives with amino acid side chains, S. A. Shintre, D. Ramjugernath, M. S. Islam, R. Mopuri, C. Mocktar, N. A. Koorbanally // Med. Chem. Res. – 2017. – Vol. 26. – P. 2141-2151.

43. El-Helby A.G.A. Quinoxalin-2(1*H*)-one derived AMPA-receptor antagonists: Design, synthesis, molecular docking and anticonvulsant activity / A. G. A. El-Helby, R. R. A. Ayyad, K. El-Adl, A. Elwan // Med. Chem. Res. – 2017. – Vol. 26. – P. 2967-2984.
44. Guillon J. Synthesis of new piperazinyl-pyrrolo[1,2-*a*]quinoxaline derivatives as inhibitors of Candida albicans multidrug transporters by a Buchwald-Hartwig cross-coupling reaction, / J. Guillon, S. Nim, S. Moreau, L. Ronga, S. Savrimoutou, E. Thivet, M. Marchivie, A. Di Pietro, R. Prasad, M.L. Borgne // RSC Adv. – 2020. – Vol. 10. – P. 2915-2931.
45. Keri R.S. Quinoxaline and quinoxaline-1,4-di-*N*-oxides: an emerging class of antimycobacterials / R. S. Keri, S. S. Pandule, S. Budagumpi, B. M. Nagaraja // Arch. Pharm. – 2018. – Vol. 351. – P. e1700325.
46. Shekhar A.C. Emergence of pyrido quinoxalines as new family of antimalarial agents / A. C. Shekhar, P. S. Rao, B. Narsaiah, A. D. Allanki, P. S. Sijwali // Eur. J. Med. Chem. – 2014. – Vol. 77. – P. 280-287.
47. Cogo J. Synthesis and biological evaluation of novel 2,3-disubstituted quinoxa- line derivatives as antileishmanial and antitrypanosomal agents / J. Cogo, V. Kaplum, D. P. Sangi, T. Ueda-Nakamura, A. G. Corrêa, C. V. Nakamura // Eur. J. Med. Chem. – 2015. – Vol. 90. – P. 107-123.
48. Soto-Sánchez J. Biological activity of esters of quinoxaline-7-carboxylate 1,4-di-N-oxide against *E. histolytica* and their analysis as potential thioredoxin reductase inhibitors / J. Soto-Sánchez, L. A. Caro-Gómez, A. D. Paz-González, L. A. Marchat, G. Rivera, R. Moo-Puc, D. G. Arias, E. Ramírez-Moreno // Parasitol. Res. – 2020. – Vol. 119. – P. 695-711.
49. Chakraborty J. Quinoxaline derivatives disrupt the base stacking of hepatitis C virus-internal ribosome entry site RNA: reduce translation and replication / J. Chakraborty, A. Kanungo, T. Mahata, K. Kumar, G. Sharma, R. Pal, K. S. Ahammed, D. Patra, B. Majhi, S. Chakrabarti, S. Das, S. Dutta, Chem. Commun. – 2019. – Vol. 55. – P. 14027-14030.

50. Shen Q.K. Discovery and evaluation of novel synthetic 5-alkyl-4-oxo-4,5-dihydro-[1,2,4]triazolo[4,3-*a*]quinoxaline-1-carbox-amide derivatives as anti-inflammatory agents / Q. K. Shen, G. H. Gong, G. Li, M. Jin, L. H. Cao, Z. S. Quan // J. Enzyme Inhib. Med. Chem. – 2020. – Vol. 35. – P. 85-95.
51. Montana M.Quinoxaline derivatives as antiviral agents: a systematic review / M. Montana, V. Montero, O. Khoumeri, P. Vanelle // Molecules – 2020. – Vol. 25. – P. 2784.
52. Rashidizadeh A. Graphitic carbon nitride nanosheets covalently functionalized with biocompatible vitamin B1: synthesis, Characterization, and its superior performance for synthesis of quinoxalines / A. Rashidizadeh, H. Ghafuri, H. R. Esmaili Zand, N. Goodarzi // ACS Omega. – 2019. – Vol. 4. – P. 12544-12554.
53. Bajpai S. Rutile phase nano TiO_2 as an effective heterogeneous catalyst for condensation reaction of isatin derivatives with 1,2-di- aminobenzene under solvent free conditions: a greener “NOSE”approach / S. Bajpai, S. Singh, V. Srivastava // Arab. J. Chem. – 2019. – Vol. 12. – P. 1168-1175.
54. Harsha K.B. An easy and efficient method for the synthesis of quinoxalines using recyclable and heterogeneous nanomagnetic-supported acid catalyst under solvent-free condition / K. B. Harsha, S. Rangappa, H. D. Preetham, T. R. Swaroop, M. Gilandoust, K. S. Rakesh, K. S. Rangappa, // ChemistrySelect. – 2018. – Vol. 3. – P. 5228-5232.
55. Peralta-Cruz J. An experimental and theoretical study of intramolecular regioselective oxidations of 6-substituted 2,3-dimethylquinoxaline derivatives / J. Peralta-Cruz, Díaz- M. Fernández, A. Ávila-Castro, D. Ortegón-Reyna, A. Ariza-Castolo // New J. Chem. – 2016. – Vol. 40. – P. 5501-5515.
56. Shamsi-Sani M. Synthesis of benzimidazole and quinoxaline derivatives using reusable sulfonated rice husk ash (RHA-SO_3H) as a green and efficient solid acid catalyst / M. Shamsi-Sani, F. Shirini, M. Abedini, M. Seddighi // Res. Chem. Intermed. – 2016. – Vol. 42. – P. 1091-1099.

57. Bakthadoss M. An efficient protocol for the synthesis of benzoheterocyclic compounds via solid-state melt reaction (SSMR) / M. Bakthadoss, R. Selvakumar, J. Srinivasan // Tetrahedron Lett. – 2014. – Vol. 55. – P. 5808-5812.
58. Roy B. Graphene oxide (GO) or reduced graphene oxide (rGO): efficient catalysts for one-pot metal-free synthesis of quinoxalines from 2-nitroaniline / B. Roy, S. Ghosh, P. Ghosh, B. Basu // Tetrahedron Lett. – 2015. – Vol. 56. – P. 6762-6767.
59. Mohammadi H. (3-Oxo-[1,2,4]triazolidin-1-yl)bis (butane-1-sulfonic acid) functionalized magnetic γ-Fe_2O_3 nanoparticles: a novel and heterogeneous nanocatalyst for one-pot and efficient four-component synthesis of novel spiroindeno[1,2-b]quinoxaline derivatives / H. Mohammadi, H. R. Shaterian // Appl. Organomet. Chem. – 2019. – Vol. 33. – P. e4901.
60. Jafarpour M. A novel protocol for selective synthesis of monoclinic zirconia nanoparticles as a heterogeneous catalyst for condensation of 1,2-diamines with 1,2-dicarbonyl compounds / M. Jafarpour, E. Rezapour, M. Ghahramaninezhad, A. Rezaeifard // New J. Chem. – 2014. – Vol. 38. – P. 676-682.
61. Arde S.M. Synthesis of quinoxaline, benzimidazole and pyrazole derivatives under the catalytic influence of biosurfactant-stabilized iron nanoparticles in water / S. M. Arde, A. D. Patil, A. H. Mane, P. R. Salokhe, R. S. Salunkhe // Res. Chem. Intermed. – 2020. – Vol. 46. – P. 5069-5086.
62. Sharma A. Efficient and sustainable Co_3O_4 nanocages based nickel catalyst: a suitable platform for the synthesis of quinoxaline derivatives / A. Sharma, R. Dixit, S. Sharma, S. Dutta, S. Yadav, B. Arora, M. B. Gawande, R. K. Sharma // Mol. Catal. – 2021. – Vol. 504. – P. 111454.
63. Arunachalapandi M. Ultrasound/visible light-mediated synthesis of N -heterocycles using g-C_3N_4/Cu_3TiO_4 as sonophotocatalyst / M. Arunachalapandi, S. M. Roopan // Res. Chem. Intermed. – 2021. – Vol. 47. – P. 3363-3378.

64. Gu P.Y. Synthesis, characterization, and nonvolatile ternary memory behavior of a larger heteroacene with nine linearly fused rings and two different heteroatoms / P. Y. Gu, F. Zhou, J. K. Gao, G. Li, C. Y. Wang, Q. F. Xu, Q. C. Zhang, J. M. Lu // J. Am. Chem. Soc. – 2013. – Vol. 135. – P. 14086-14089.
65. Andrade-Neto V.F. Antimalarial activity of phenazines from lapachol, β-lapachone and its derivatives against *Plasmodium falciparum* in vitro and *Plasmodium berghei* in vivo / V. F. Andrade-Neto, M. O. F. Goulart, J. F. da Silva Filho, M. J. da Silva, F. R. do Carmo, M. Pinto, A. V. Pinto, M. G. Zalis, L. H. Carvalho, A. U. Krettli // Bioorg. Med. Chem. Lett. – 2004. – Vol. 14. – P. 1145-1149.
66. Krishnaiah M. Synthesis, biological evaluation, and metabolic stability of phenazine derivatives as antibacterial agents / M. Krishnaiah, N. R. Almeida, V. Udumula, Z. Song, Y. S. Chhonker, M. M.Abdelmoaty, V. A. Nascimento, D. J. Murry, C. M. Sheridan // Eur. J. Med. Chem. – 2018. – Vol. 143. – P. 936-947.
67. Yang L. Colorimetric and ratiometric near-infrared fluorescent cyanide chemodosimeter based on phenazine derivatives / L. Yang, X. Li, J. B. Yang, Y. Qu, J. L. Hua // ACS Appl. Mater. Interfaces – 2013. – Vol. 5. – P. 1317-1326.
68. Soni N. Absorption and emission of light in red emissive carbon nanodots / N. Soni, S. Singh, S. Sharma, G. Batra, K. Kaushik, C. Rao, N. C. Verma, B. Mondal, A. Yadav, C. K. Nandi // Chem. Sci. – 2021. – Vol. 12. – P. 3615-3626.
69. Laursen J.B. Phenazine natural products: biosynthesis, synthetic analogues, and biological activity / J. B. Laursen, J. Nielsen // Chem. Rev. – 2004. – Vol. 104. – P. 1663-1686.
70. Okazaki M. Thermally activated delayed fluorescent phenothiazine–dibenzo[*a*,*j*]phenazine–phenothiazine triads exhibiting tricolor-changing mechanochromic luminescence / M. Okazaki, Y. Takeda, P. Data, P. Pander,

H. Higgbotham, A. P. Monkman, S. Minakata // Chem. Sci. – 2017. – Vol. 8. – P. 2677-2686.

71. Kour H. A mild and simple method for the synthesis of substituted phenazines / H. Kour, S. Paul, P. P. Singh, R. Gupta // Synlett. – 2014. – Vol. 25. – P. 495-500.

72. Tandon V.K. Micelles catalyzed one pot regio-and chemoselective synthesis of benzo[*a*]phenazines and naphtho[2, 3-*d*]imidazoles 'in H_2O' / V. K.Tandon, M. K. Verma, H. K.Maurya, S. Kumar // Tetrahedron Lett. – 2014. – Vol. 55. – P. 6331-6334.

73. Chen J.W. Modulated emission from dark triplet excitons in aza-acene compounds: Fluorescence versus phosphorescence / J. W. Chen, Y. Chen, Y. S. Wu, X. D. Wang, Z. Y. Yu, L. Xiao, Y. P. Liu, H. Tian, J. N. Yao, H. B. Fu // New J. Chem. – 2017. – Vol. 41. – P. 1864-1871.

74. Walsh C.T. Biological formation of pyrroles: nature's logic and enzymatic machinery / C. T. Walsh, S. Garneau-Tsodikova, A. R. Howard-Jones // Nat. Prod. Rep. – 2006. – Vol. 23. – P. 517-531.

75. Joshi S.D. Synthesis of new 4-pyrrol-1-yl benzoic acid hydrazide analogs and some derived oxadiazole, triazole and pyrrole ring systems: A novel class of potential antibacterial and antitubercular agents / S. D. Joshi, H. M. Vagdevi, V. P. Vaidya, G. S. Gadaginamath // Eur. J. Med. Chem. – 2008. – Vol. 43. – P. 1989-1996.

76. Shinde V.V. p-Toluenesulfonic acid doped polystyrene (PS-PTSA): solvent-free microwave assisted cross-coupling-cyclization–oxidation to build one-pot diversely functionalized pyrrole from aldehyde, amine, active methylene, and nitroalkane / V. V. Shinde, S. D. Lee, Y. S. Jeong, Y. T. Jeong // Tetrahedron Lett. – 2015. – Vol. 56. – P. 859-865.

77. Mondal P. Creation of DABCO-based amphoteric ionic liquid supported TiO_2 nanoparticles: Execution of amplified catalytic properties on microwave-assisted synthesis of N-substituted pyrroles / P. Mondal, S. Chatterjee, A.

Bhaumik, S. Maity, P. Ghosh, C. Mukhopadhyay // ChemistrySelect. – 2019. – Vol. 4. – P. 3140-3150.

78. Estevez V. Three-component access to pyrroles promoted by the CAN–silver nitrate system under high-speed vibration milling conditions: a generalization of the Hantzsch pyrrole synthesis / V. Estevez, M. Villacampa, J. C. Menendez // Chem. Commun. – 2013. – Vol. 49. – P. 591-593.
79. Estevez V. Concise synthesis of atorvastatin lactone under high-speed vibration milling conditions / V. Estevez, M. Villacampa, J. C. Menendez // Org. Chem. Front. – 2014. – Vol. 1. – P. 458-463.
80. Xu H. One-pot multicomponent mechanosynthesis of polysubstituted *trans*-2,3-dihydropyrroles and pyrroles from amines, alkyne esters, and chalcones / H. Xu, H. W. Liu, K. Chen, G. W. Wang // J. Org. Chem. – 2018. – Vol. 83. – P. 6035-6049.
81. Babaei S.E. Fe_3O_4 nanoparticles as an efficient and reusable catalyst for the solvent-free synthesis of 1*H*-indole and 1*H*-pyrrole derivatives / S. E. Babaei, Z. Hossaini, R. R. Besheli, V. Tavakkoli // Chem. Heterocycl. Compd. – 2016. – Vol. 52. – P. 294-298.
82. Shahvelayati A.S. Sonochemically assisted synthesis of N-substituted pyrroles catalyzed by ZnO nanoparticles under solvent-free conditions / A. S. Shahvelayati, M. Sabbaghan, S. Banihashem // Monatsh. Chem. – 2017. – Vol. 148. – P. 1-7.
83. Seebach D. β-Peptides: a surprise at every turn / D. Seebach, J. L. Matthews // Chem. Commun. – 1997. – Vol. 1997. – P. 2015-2022.
84. Knapp S. Synthesis of complex nucleoside antibiotics / S. Knapp // Chem. Rev. – 1995. – Vol. 95. – P. 1859-1876.
85. Damodiran M. Synthesis of highly functionalized oxazines by Vilsmeier cyclization of amidoalkyl naphthols / M. Damodiran, N. P. Selvam, P. T. Perumal // Tetrahedron Lett. – 2009. – Vol. 50. – P. 5474-5478.

86. Shen A.Y. Synthesis and cardiovascular evaluation of N-substituted 1-aminomethyl-2-naphthols / A. Y. Shen, C. T. Tsai, C. -L. Chen // Eur. J. Med. Chem. – 1999. – Vol. 34. – P. 877-882.
87. Kusakabe Y. Minimycin, a new antibiotic / Y. Kusakabe, J. Nagatsu, M. Shibuya, O. Kawaguchi, C. Hirose, S. Shirato // J. Antibiot. – 1972. – Vol. 25. – P. 44-47.
88. Lesher G.Y. A new method for the preparation of 3-substituted-2-oxazolidones / G. Y. Lesher, A. R. Surrey // J. Am. Chem. Soc. – 1955. – Vol. 77. – P. 636-641.
89. Mosher H.S. Heterocyclic diphenylmethane derivatives / H. S. Mosher, M. B. Frankel, M. Gregory // J. Am. Chem. Soc. – 1953. – Vol. 75. – P. 5326–5328.
90. Remillard S. Antimitotic activity of the potent tumor inhibitor maytansine / S. Remillard, L. I. Rebhun, G. A. Howie, S. M. Kupchan // Science. – 1975. – Vol. 189. – P. 1002-1005.
91. Benedini F. New antianginal nitro esters with reduced hypotensive activity. Synthesis and pharmacological evaluation of 3-[(nitrooxy) alkyl]-2*H*-1,3-benzoxazin-4(3*H*)-ones / F. Benedini G., Bertolini, R. Cereda, G. Dona, G. Gromo, S. Levi, J. Mizrahi, A. Sala // J. Med. Chem. – 1995. – Vol. 38. – P. 130-136.
92. Ren H. Design, synthesis, and biological evaluation of a series of simple and novel potential antimalarial compounds / S. Grady, D. Gamenara, H. Heinzen, P. Moyna, S. L. Croft, H. Kendrick, V. Yardley, G. Moyna // Bioorg. Med. Chem. Lett. – 2001. – Vol. 11. – P. 1851-1854.
93. Peglion J.-L. Tetracyclic analogues of [+]-S 14297: Synthesis and determination of affinity and selectivity at cloned human dopamine D3 vs D2 receptors / J. -L. Peglion, J. Vian, B. Goument, N. Despaux, V. Audinot, M. J. Millan // Bioorg. Med. Chem. Lett. – 1997. – Vol. 7. – P. 881-886.
94. Matsuoka H. Antirheumatic agents: Novel methotrexate derivatives bearing a benzoxazine or benzothiazine moiety / H. Matsuoka, N. Ohi, M. Mihara, H.

Suzuki, K. Miyamoto, N. Maruyama, K. Tsuji, N. Kato, T. Akimoto, Y. Takeda, J. Med. Chem. – 1997. – Vol. 40. – P. 105-111.

95. Clark R.D. Synthesis and antihypertensive activity of 4'-substituted spiro [4*H*-3,1-benzoxazine-4, 4'-piperidin]-2(1*H*)-ones / R. D. Clark, J. M. Caroon, A. F. Kluge, D. B. Repke, A. P. Roszkowski, A. M. Strosberg, S. Baker, S. M. Bitter, M. D. Okada, J. Med. Chem. – 1983. – Vol. 26. – P. 657-661.
96. Karimi-Jaberi Z. Efficient synthesis of 1-amidoalkyl-2-naphthols by one-pot, three-component reaction under solvent-free conditions / Z. Karimi-Jaberi, M. Jokar, S. Z. Abbasi // J. Chem. – 2013. – Vol. 2013 – P. 341649.
97. Taghrir H. Preparation of 1-amidoalkyl-2-naphthol derivatives using barium phosphate nano-powders / H. Taghrir, M. Ghashang, M. N. Biregan // Chin. Chem. Lett. – 2016. – Vol. 27. – P. 119-126.
98. Mansoor S.S. $ZrOCl_2 \cdot 8H_2O$: an efficient and recyclable catalyst for the three-component synthesis of amidoalkyl naphthols under solvent-free conditions / S. S. Mansoor, K. Aswin, K. Logaiya, S. P. N. Sudhan // J. Saudi Chem. Soc. – 2016. – Vol. 20. – P. 138-150.
99. Madankumar N. β-Cyclodextrin-Monosulphonic Acid Catalyzed Efficient Synthesis of 1-Amidoalkyl-2-naphthols/ N. Madankumar, K. Pitchumani // ChemistrySelect. – 2017. – Vol. 2. – P. 10798-10803.
100. Singh R.K. Environment-friendly green chemistry approaches for an efficient synthesis of 1-amidoalkyl-2-naphthols catalyzed by tannic acid / R. K. Singh, R. Duvedi // Arab. J. Chem. – 2018. – Vol. 11. – P. 91-98.
101. Nguyen V.T. One-pot three-component synthesis of 1-amidoalkyl naphthols and polyhydroquinolines using a deep eutectic solvent: A green method and mechanistic insight / V. T. Nguyen, H. T. Nguyen, P. H. Tran // New J. Chem. – 2021. – Vol. 45. – P. 2053-2059.
102. Haneishi T. Oxazinomycin, a new carbon-linked nucleoside antibiotic / T. Haneishi, T. Okazaki, T. Hata, C. Tamura, M. Nomura // J. Antibiot. – 1971. – Vol. 24. – P. 797-799.

103. Renullard S. Antimitotic activity of the potent tumor inhibitor maytansine / S. Renullard, L. I. Rebhun, G. A. Havic, S. M. Kupchan // Science. – 1975. – Vol. 189. – P. 1002-1005.
104. Lesher G.Y. A new method for the preparation of 3-substituted-2-oxazolidones / G. Y. Lesher, A. R. Surrey // J. Am. Chem. Soc. – 1955. – Vol. 77. – P. 636-641.
105. Mosher H.S. Heterocyclic diphenylmethane derivatives / Mosher H.S., Frankel M.B., Gregory M. // J. Am. Chem. Soc. – 1953. - Vol 75. – P. 5326-5328.
106. Peglion J.L. Tetracyclic analogues of [+]-S 14297: Synthesis and determination of affinity and selectivity at cloned human dopamine D3 vs D2 receptors / J. L. Peglion, J. Vian, B. Gourment, N. Despaux, V. Audinot, M. Millan // Bioorg. Med. Chem. Lett. – 1997. – Vol. 7. – P. 881-886.
107. Ren H. Design, synthesis, and biological evaluation of a series of simple and novel potential antimalarial compounds / H. Ren, S. Grady, D. Gamenara, H. Heinzen, P. Moyna, S. Croft, H. Kendrick, V. Yardley, G. Moyna // Bioorg. Med. Chem. Lett. – 2001. – Vol. 11. – P. 1851-1854.
108. Benedini F. New antianginal nitro esters with reduced hypotensive activity. Synthesis and pharmacological evaluation of 3-[(nitrooxy) alkyl]-2*H*-1, 3-benzoxazin-4(3*H*)-ones / F. Benedini, G. Bertolini, R. Cereda, G. Doná, G. Gromo, S. Levi, J. Mizrahi, A. Sala // J. Med. Chem. – 1995. – Vol. 38. – P. 130-136.
109. Clark R.D. Synthesis and antihypertensive activity of 4'-substituted spiro[4H-3,1-benzoxazine-4,4'-piperidin]-2(1*H*)-ones / R. D. Clark, J. M. Caroon, A. F. Kluge, D. B. Repke, A. P. Roszkowski, A. M. Strosberg, S. Baker, S. M. Bitter, M. D. Okada // J. Med. Chem. – 1983. – Vol. 26. – P. 657-661.
110. Matsuoka H. Antirheumatic agents: Novel methotrexate derivatives bearing a benzoxazine or benzothiazine moiety / H. Matsuoka, N. Ohi, M. Mihara, H. Suzuki, K. Miyamoto N., Maruyama, K. Tsuji, N. Kato, T. Akimoto, Y. Takeda, K. Yano, T. Kuroki // J. Med. Chem. – 1997. – Vol. 40. – P. 105-111.

111. Damodiran M. Synthesis of highly functionalized oxazines by Vilsmeier cyclization of amidoalkyl naphthols / M. Damodiran, N. P. Selvam, P. T. Perumal // Tetrahedron Lett. – 2009. – Vol. 50. – P. 5474-5478.
112. Ghomi J.S. AgI nanoparticles as a remarkable catalyst in the synthesis of (amidoalkyl) naphthol and oxazine derivatives: an eco-friendly approach / J. S. Ghomi, S. Zahedi, M. A. Ghasemzadeh // Monatsh. Chem. – 2014. – Vol. 145. – P. 1191-1199.
113. Salaklang J. Telescoped continuous flow synthesis of phenyl acrylamide / J. Salaklang, E. Mertens, V. Maes, R. Dams, W. Dermaut, T. Junkers // J. Flow Chem. – 2020. – Vol. 10. – P. 673–679.
114. Rulev A.Y. Aza-Michael reaction: Achievements and prospects. Aza-Michael reaction: achievements and prospects / A. Y. Rulev // Russ. Chem. Rev. – 2011. – Vol. 80. – P. 197-218.
115. Azizi N. Silicon tetrachloride catalyzed aza-Michael addition of amines to conjugated alkenes under solvent-free conditions / N. Azizi, R. Baghi, H. Ghafuri, M. Bolourtchian, M. Hashemi // Synlett. – 2010. – Vol. 2010. – P. 379-382.
116. Yao R.-S. Synthesis and characterization of N-substitutional ethylenediamine derivatives / R. -S. Yao, L. -E. Jiang, S. -H. Wu, S.-S. Deng, Y. Yang // Asian J. Chem. – 2011. – Vol. 23. – P. 3792-3794.
117. Gupta A. Rapid and convenient microwave-assisted synthesis of aza-Michael type addition of substituted aniline to α, β-unsaturated ester / A. Gupta, O. S. Yadav, R. Kumar, G. Singh // Heterocycl. Lett. – 2015. – Vol. 5. – P. 169-172.
118. Zhang T. Design, synthesis and biological activity evaluation of novel methyl substituted benzimidazole derivatives / T. Zhang, Q. Liu, Y. Ren // Tetrahedron. – 2020. – Vol. 76. – P. 131027.
119. Tang X.-J. Aza-Michael reaction promoted by aqueous sodium carbonate solution / X. -J. Tang, Z. -L. Yan, W. -L. Chen, Y. -R Gao., S. Mao, Y. -L. Zhang, Y. -Q. Wang // Tetrahedron Lett. – 2013. – Vol. 54. – P. 2669-2673.

120. Ranu B.C. Significant rate acceleration of the aza-Michael reaction in water / B. C. Ranu, S. Banerjee // Tetrahedron Lett. – 2007. – Vol. 48. – P. 141-143.
121. De K. Solvent-promoted and-controlled aza-Michael reaction with aromatic amines / K. De, J. Legros, B. Crousse, D. Bonnet-Delpon // J. Org. Chem. – 2009. – Vol. 74. – P. 6260-6265.
122. Boruah K. Design of water stable 1,3-dialkyl-2-methyl imidazolium basic ionic liquids as reusable homogeneous catalysts for aza-Michael reaction in neat condition / K. Boruah, R. Borah // ChemistrySelect. – 2019. – Vol. 4. – P. 3479-3485.
123. Dai Z. Michael Addition Reaction Catalyzed by Imidazolium Chloride to Protect Amino Groups and Construct Medium Ring Heterocycles / Z. Dai, Q. Tian, Y. Li, S. Shang, W. Luo, X. Wang, D. Li, Y. Zhang, Z. Li, J. Yuan // Molecules. – 2019. – Vol. 24. – P. 4224.
124. Kumar S. Efficient protocol for aza-Michael addition of *N*-heterocycles to α,β-unsaturated compound using [Ch]OH and [*n*-butyl urotropinium]OH as basic ionic liquids in aqueous/solvent free conditions / S. Kumar, A. Kaur, V. Singh // Synth. Commun. – 2019. – Vol. 49. – P. 193-201.
125. Gu B. Probing the mechanism of CAL-B-catalyzed aza-Michael addition of aniline compounds with acrylates using mutation and molecular docking simulations / B. Gu, Z. -E. Hu, Z. -J. Yang, J. Li, Z. -W. Zhou, N. Wang, X. -Q. Yu // ChemistrySelect. – 2019. – Vol. 4. – P. 3848-3854.
126. Liu X. Aza-Michael reactions in water using functionalized ionic liquids as the recyclable catalysts / X. Liu, M. Lu, G. Gu, T. Lu // J. Iran. Chem. Soc. – 2011. – Vol. 8. – P. 775-781.
127. Liu X.-B. Functionalized ionic liquid promoted aza-Michael addition of aromatic amines / X. -B. Liu, M. Lu, T. -T. Lu, G.-L. Gu // J. Chin. Chem. Soc. – 2010. – Vol. 57. – P. 1221-1226.
128. Ying A. Guanidine-based task-specific ionic liquids as catalysts for aza-Michael addition under solvent-free conditions / A. Ying, M. Zheng, H. Xu, F. Qiu, C. Ge // Res. Chem. Intermed. – 2011. – Vol. 37. – P. 883-890.

129. Mukherjee A. A convenient and sustainable method for the synthesis of 4-substituted coumarins catalyzed by Brønsted acidic ionic liquids / A. Mukherjee, R. Chatterjee, S. Santra, G. V. Zyryanov, O. N. Chupakhin, A. Majee // VI International Conference “Modern synthetic methodologies for the creation of drugs and functional materials” (MOSM2022). Collection of abstracts. – 2022. – II56.
130. Chatterjee R. An expedient solvent-free C-benzylation of 4-hydroxycoumarin with styrenes / R. Chatterjee, A. Mukherjee, S. Santra, Zyryanov G.V., Chupakhin O.N., Majee A. // Mendeleev Commun. – 2021. – Vol. 31. – P. 123-124.
131. Chatterjee R. Metal and solvent free direct C_3-alkylation of 4-hydroxycoumarins with styrene / R. Chatterjee, A. Mukherjee, G. V. Zyryanov, A. Majee // AIP Conf. Proc. – 2020. – Vol. 2280. – P. 040011-1-4.
132. Chatterjee R. Synthesis of quinoxaline derivatives catalyzed by Brønsted acidic ionic liquid under solvent-free conditions /R. Chatterjee, S. Mahato, A. Mukherjee, G. V. Zyryanov, A. Majee // AIP Conf. Proc. – 2020. – Vol. 2280, - P. 050012-1-5.
133. Mahato S. Synthesis of quinoxaline derivatives catalyzed by brønsted acidic ionic liquid under solvent-free conditions / S. Mahato, R. Chatterjee, A. Mukherjee, G. V. Zyryanov, A. Majee // International Conference “Modern synthetic methodologies for the creation of drugs and functional materials” (MOSM2022). Collection of abstracts. – 2019. – DR34.
134. Mukherjee A. Green approach towards synthesis of quinoxaline derivatives / A. Mukherjee, D. Kopchuk, S. Santra, G. V. Zyryanov, O. N. Chupakhin // VI International Conference “Modern synthetic methodologies for the creation of drugs and functional materials” (MOSM2022). Collection of abstracts. – 2022. – II53.
135. Mukherjee, A. New phenazine-based Y-type and T-type push-pull fluorophores: Synthesis and photophysical studies / A. Mukherjee, A. F.

Khasanov, B. S. Al-Ghezi, I. S. Kovalev, D. S. Kopchuk, S. Santra, A. Majee, G. V. Zyryanov, B. C. Ranu // Molecules. – 2023, In press.

136. Mukherjee, A. Iron(III) chloride-catalyzed mechanochemical cascade synthesis of highly-substituted pyrrolyl indoles / A. Mukherjee, D. S. Kopchuk, S. Santra, A. Majee, G. V. Zyryanov, O.N. Chupakhin, O.N. // Mendeleev Commun. – 2022. – Vol. 32. – P. 624-626.
137. Mukherjee A. Iron(III)-catalyzed multicomponent synthesis of highly substituted pyrroles under ball-milling conditions / A. Mukherjee, B. S. Al-Ghezi, G. V. Zyryanov, O. N. Chupakhin // V International Conference "Modern synthetic methodologies for the creation of drugs and functional materials" (MOSM2022). Collection of abstracts. – 2021. – PR186.
138. Chatterjee S. A combined spectroscopic and computational study on the mechanism of iron-catalyzed aminofunctionalization of olefins using hydroxylamine derived N–O reagent as the "amino" source and "oxidant" / S. Chatterjee, I. Harden, G. Bistoni, R. G. Castillo, S. Chabbra, M. van Gastel, A. Schnegg, E. Bill, J. A. Birrell, B. Morandi, F. Neese, S. DeBeer // J. Am. Chem. Soc. – 2022. – Vol. 144. – P. 2637-2656.
139. Tomifuji R. $FeCl_3$ as an ion-pairing Lewis acid catalyst. Formation of highly Lewis acidic $FeCl^{2+}$ and thermodynamically Stable $FeCl^{4-}$ to catalyze the aza-Diels-Alder reaction with high turnover frequency / R. Tomifuji, K. Maeda, T. Takahashi, T. Kurahashi, S. Matsubara // Org. Lett. – 2018. – Vol. 20. – P. 7474-7477.
140. Yang L. Highly efficient and expedient synthesis of 5-hydroxy-1*H*-pyrrol-2-(5*H*)-ones from $FeCl_3$-catalyzed tandem intramolecular enaminic addition of tertiary enamides to ketones and 1,3-hydroxy rearrangement / L. Yang, C.-H. Lei, D.-X. Wang, Z.-T. Huang, M.-X. Wang // Org. Lett. – 2010. – Vol. 12. – P. 3918-3921.
141. Chatterjee R. Brønsted acidic ionic liquid promoted synthesis of amidoalkyl naphthols under solvent-free conditions / R. Chatterjee, A. Mukherjee, S. Pal,

S. Santra, G. V. Zyryanov, A. Majee // AIP Conf. Proc. – 2020. – Vol. 2280. – P. 040009-1-5.

142. Mukherjee A. Conjugated addition of amines to electron deficient alkenes: A green approach / A. Mukherjee, R. Chatterjee, A. De, S. Samanta, S. Mahato, N. C. Ghosal, G. V. Zyryanov, A. Majee // Chimica Techno Acta. – 2017. – Vol. 4. – P. 140-147.
143. Mukherjee A. Recent advances on diverse decarboxylative reactions of amino acids / M. Rahman, A. Mukherjee, I. S. Kovalev, D. S. Kopchuk, G. V. Zyryanov, M. V. Tsurkan, A. Majee, B. C. Ranu, V. N. Charushin, O. N. Chupakhin, S. Santra // Adv. Synth. Catal. – 2019. – Vol. 361. – P. 2161-2214.
144. Vuong Q.V. Effects of aqueous brewing solution pH on the extraction of the major green tea constituents / Q. V. Vuong, J. B. Golding, C. E. Stathopoulos, P. D. Roach // Food Res. Int. – 2013. – Vol. 53. – P. 713-719.
145. Du Z. Synthesis and characterization of sulfonyl-functionalized ionic liquids / Z. Du, Z. Li, Y. Deng // Synth. Commun. – 2005. – Vol. 35. – P. 1343-1349.
146. Sainuddin T. Organometallic Ru(II) photosensitizers derived from π-expansive cyclometalating ligands: Surprising theranostic PDT effects / T. Sainuddin, J. McCain, M. Pinto, H. Yin, J. Gibson, M. Hetu, S. A. McFarland // Inorg. Chem. – 2016. – Vol. 55. – P. 83-95.