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Rapid Access Synthesis of Quinoline, Chromene, Thiochromene Benzimidazol-Ylideneamines and Benzimidazolones via Traceless Tandem Transformation Under Microwave Irradiation on Ionic Liquid Support

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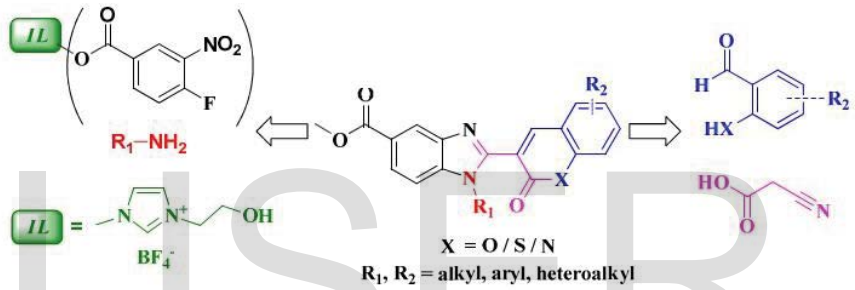
Abstract

A fast and efficient protocol have explored to access the various benzimidazole constituted quinoline, chromene, thiochromenyldenamines and ones under microwave irradiation on ionic liquid support. Ionic liquid supported 4-floro3-nitrobenzoicacid has been used as a structural building block to generate these structural frameworks. After subsequent transformation the benzimidazole constituted cyanoacetic acid has been used as a molecular scaffold to generate various structural motifs. By taking the benzimidazole constituted cyanoacetic acid treated with various 2-substituted hydroxyl, amino and thiobanzaldehydes in order to get the described decorated structural scaffolds in the presence of organic base such as triethylamine. Under the same reaction conditions by leave the product and the cleavage of product from the support occurred sequence of transformations in traceless tandem manner. The same reaction under the hydrous conditions the imine hydrolysis leads to formation of quinoline, chromene, thiochromene benzimidazolones was described. The final compounds have been obtained high yield and purity making this procedure facile, practical, and rapid to execute.



Keywords: Benzimidazole; Chromene; Quinolone; Thiochromene; Microwave assisted synthesis; Ionic liquid support; Traceless synthesis; Synergistic approach; Rapid tandem transformations

Introduction

Benzimidazole fused or benzimidazoles constituted molecules have been a major source of new drugs to explore, and many successful drugs were originally synthesized to mimic the action of benzimidazole molecules found in nature [1-9]. The numerous benzimidazole embracing coumarin derivatives structural scaffolds containing compounds are highly diverse and often provide highly specific biological activities [10-12]. To this end the proposition that essentially all benzimidazole structural frameworks have some receptor binding capacity [13]. The benzimidazoles in combination with various quinazolines [14], chromen [15], and thiochromen [16-20] structures have attracted considerable attention. These heterocyclic ring-systems due to their presence in many naturally and synthetically derived molecules, which possess a wide range of biological properties and frequently, hold promising pharmaceutical potential [21]. 4-amino-3-benzimidazol-2-ylhydro quinolin-2-ones are a class of potent RTK inhibitors involved in important signal transduction pathways within the cell with attractive physicochemical and pharmacokinetic properties and significant efficacy in murine and human xenograft tumor models [22]. Compounds possessing coumarin, imidazole, benzothienopyrimidine or thiophene, benzopyran moieties represented basic structures screened for inhibitory activity against EGF, PDGF receptor tyrosine kinases and their inhibitory effects on tyrosine kinase pp6O$^{c\text{-}src}$ and p56^{lck} were evaluated [23-26]. Molecular scaffolds based on 3-benzimidazol-2-ylhydroquinolin-2-one analogues as inhibitors of VEGF, PDGF, and fibroblast growth factor (FGF) receptor tyrosine kinases [27]. These compounds were also found to possess attractive pharmacokinetic characteristics and efficacy in several human tumor xenograft models [28,29]. The biological activities having the structural template coumarin derivatives shown as anticoagulant and antithrombotic activity of certain natural and Synthetic coumarin derivatives are known [30]. Certain coumarin derivatives are also reported as triplet sensitizers, anti-HIV agents; Lipid lowering agents antioxidents, inhibitors of lipid peroxidation and vasorelaxant agents, anti-inflammatory agents and free radical Scavengers [31-37]. In addition, two naturally occurring coumarins have been found to exhibit cytotoxicity across a selection of mammalian cancer cell lines [38]. Certain coumarin-3-carboxamides have been reported as inhibitors of protease, including A-chymotrypsin and human leukocyte elastase [39-44].

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The current acceleration of expensive and time-consuming process drug discovery is a result of the combinatorial chemistry to generate large libraries of high structural diversity molecules, which are subsequently used in the high-throughput screening (HTS) process [45,46]. The use of solid phase and soluble polymer supported synthesis of combinatorial libraries; dramatically extended the structural diversity of the compounds tested in the drug discovery process and demonstrated that this approach is able to identify biologically active molecules far more rapidly than with the conventional solution phase synthetic approaches [47-49]. However the very effective, solid-supported synthesis suffers from a certain number of problems linked to the heterogeneous nature of the reaction conditions. In fact, the non-linear kinetic behavior, the unequal distributions, the sites which are non-accessible to reagents [50-52]. This limits the flexibility of the process to generate large compound libraries in shorter periods via different reactions [53]. The drawbacks of solid supports have led to the exploration of alternatives in order to find homogeneous reaction conditions [54,55]. In fact, the use of soluble polymers bypasses the difficulties of synthesis on solid supports whilst retaining a large number of its positive features [56]. This synthetic methodology has received considerable attention in various synthetic aspects [57,58]. However, the use of soluble polymer supports suffer from the drawback of low loading capacity, difficulties in the selective precipitation of the oligosaccharide-attached polymer, limited solubility during the synthesis of longer peptides, low aqueous solubility, the lack of solubility in ether solvents and energy intensive cooling required for purification [59,60]. In order to meet multi-faced drug discovery endeavor and overcome the debilitating, limiting factor for molecule submission to an assay, led researchers to develop ionic liquid supported synthetic methodologies by which large numbers of molecules possessing diverse chemical structures can be rapidly and efficiently synthesized [61-68]. The ionic liquid supported synthesis stands to benefit greatly from proper utilization of microwave energy due to their efficient microwave absorbance [69,70]. The synergetic synthetic chemistry has emerged as one of the most promising approaches to chemical library synthesis for the purpose of drug discovery [71,72].

With the aim of develop more efficient synthetic methodologies and in continuation of our interest in developing combinatorial approaches to the synthesis of highly functionalized rapid access synthesis of quinoline, chromene, thiochromene benzimidazol-ylideneamines and benzimidazolones via traceless tandem transformation under microwave irradiation on Ionic Liquid support. Herein we describe a practical and rapid microwave-assisted method for the synthesis of highly functionalized quinoline, chromene, thiochromene benzimidazol-ylideneamines and benzimidazolones have been synthesized (Figures 1 and 2).

Experimental Section

General remarks

Melting points were determined on a Kofler melting point apparatus and were uncorrected. Thin-layer chromatography (TLC) was accomplished on 0.2-nm precoated plates of silica gel 60 F-254 (Merck) or Neutral alumina oxide gel 60 F 254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm) or with a fluorescence indicator. For preparative column chromatography, silica gel 60F 254 Merck (230-240 Mesh ASTM) and neutral alumina oxide gel 90 (Merck) were used. IR spectra were recorded on a BIORAD FTS 175°C spectrometer. ^{1}H NMR spectra were recorded on BRUKER AC 300 P (300 MHz), ^{13}C NMR spectra on BRUKER AC 300 P (75 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Data are given in the following order: δ value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons, coupling constants J is given in Hertz. The mass spectra (HRMS) were taken respectively on a MS/MS ZABSpec TOF MIcromass (EBE TOF geometry) at an ionizing potential of 8 eV for the ILPs and on a VARIAN MAT 311 at an ionizing potential of 70 eV for the other compounds in the centre Regional de Mesures Physiques de 1'Ouest (CRMPO, Rennes). Reactions under microwave irradiations were realized in the synthewave 402 apparatus (Merck Eurolab, Div. Prolabo, France) in quartz open reactor vessel fitted with a condenser or in the Discover apparatus (CEM, France). The

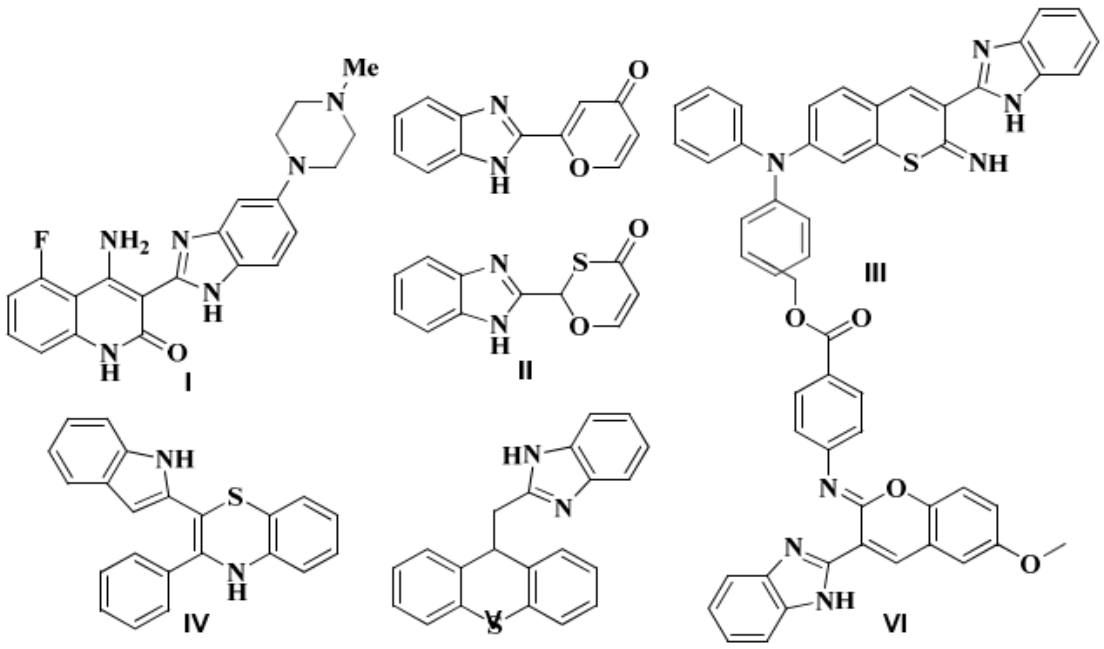

Figure 1: Biologically active substances.

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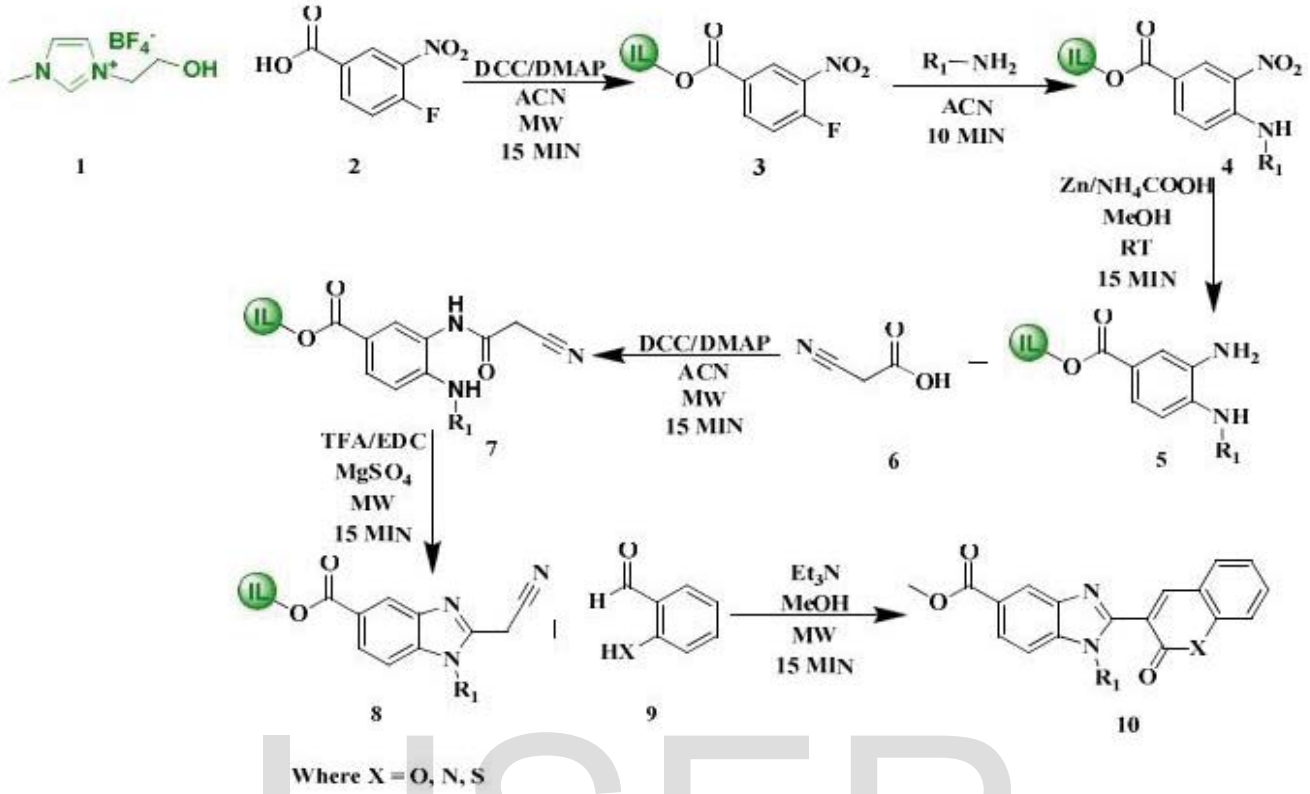

Figure 2: Synthetic scheme for the preparation of the targeted library [10].

microwave instrument consists of a continuous focused microwave power output from 0 to 300W. All the experiments were performed using stirring option. The target temperature was reached with a ramp of 3 minutes and the chosen microwave power stay constant to hold the mixture at this temperature. The reaction temperature is monitored using calibrated infrared sensor and the reaction time includes the ramp period. Acetonitrile was distilled over calcium chloride after standing overnight and stored over molecular sieves (3A°). Solvents were evaporated with a BUCHI rotary evaporator. All reagents were purchased from Acros, Aldrich Chimie, Fluka France and used without further purification. The starting [HOC_2mim] [X] ionic liquid phases 1a and 1b were synthesized according to our previous method for 1-(2-hydroxy-ethyl)-3-methyl- imidazolium haxafluorophosphate [HOC_2mim] [PF_6] 1a and 1-(2-hydroxy-ethyl)-3- methyl-imidazolium tetrafluoroborate [HOC_2mim] [BF_4] 1b.

Preparation of ionic liquid supported 3-(2-((4-fluoro-3-nitrobenzoyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium as BF_4 salt

By taking the appropriate amounts of ionic liquid and the 4-fluoro-3-nitrobenzoicacid and the coupling reagent DCC and the cat, Amount of DMAP in a microwave vessel as DCM/CAN is the solvent. The reaction mixture further submitted to the microwave irradiation for about 20 min of reaction time at 100°C of reaction temperature. Then the reaction mixture has been filtered off and the precipitated DCU and the reaction mixture submitted to the rotavapour in order to reduce the solvent. The reaction mixture has been washed several times with the chilled ether then it has been dried to carry out the further steps. The formation of the product has been confirmed by the ^{1}H NMR spectroscopy (Scheme 1).

Preparation of 1-methyl-3-(2-((4-(substitutedamino)-3-nitrobenzoyl)oxy)ethyl)-1H-imidazol-3-ium as BF_4 salt

By taking the appropriate amount of ionic liquid substituted 4-fluoro-3-nitrobenzoic acid and the 5.0 eq of aliphatic or the aromatic primary amines in a microwave reaction vessel as the solvent of acetonitrile and then the reaction mixture has been irradiated for about 15 min of reaction time at 80°C of the reaction temperature. After the completion of the reaction the reaction mixture has been submitted to the rotavapour and then the reaction crude washed several times with the chilled ether. The formation of the product has been confirmed by the proton NMR spectroscopy (Scheme 2).

Preparation of the 3-(2-((3-amino-4-(substitutedamino) benzoyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium as BF_4 salt

By taking the appropriate amount of the above compound and then the reaction mixture treated with the reducing agent 7.0 eq of Zn and 15.0 eq of ammonium formate to reduce the nitrofunctional group. The reaction mixture was placed in a microwave vessel and irradiated for about 5 min of reaction time at 80°C of reaction temperature. Then the crude reaction mixture washed several times with the chilled ether. Then it has been dried and confirmed by the proton NMR spectroscopy (Scheme 3).

Preparation of 3-(2-((3-(2-cyanoacetamido)-4-(methylamino) benzoyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium as BF_4 salt

By taking the appropriate amounts of ionic liquid supported diamine and then the cyanoaceticacid in the microwave reaction vessel and the coupling reagent DCC and the catalytic amount of DMAP allowed to stir at room temperature; and then subjected to the microwave irradiation for about 15 min of reaction time at 120°C of reaction temperature. Then the reaction mixture subjected to the rota

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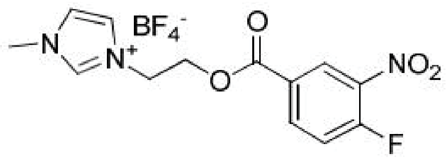
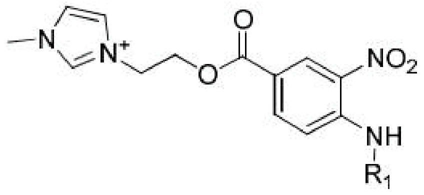
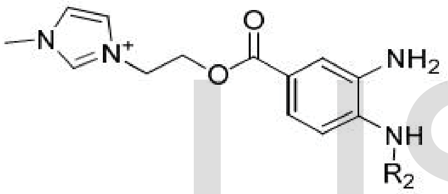


Scheme 1: 3-(2-((4-fluoro-3-nitrobenzoyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium.



Scheme 2: 1-methyl-3-(2-((4-(substitutedamino)-3-nitrobenzoyl)oxy)ethyl)-1H-imidazol-3-ium.



Scheme 3: 3-(2-((3-amino-4-(substitutedamino)benzoyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium.

evaporator and then crude reaction mixture washed several times with the chilled ether. Then the reaction product has been confirmed by the [1]H NMR spectroscopy (Scheme 4).

Preparation of 3-(2-((2-(cyanomethyl)-1-methyl-1H-benzo[d] imidazole-5-carbonyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium as BF_4 salt

The above obtained above compound has been placed in a microwave reaction vessel and then it has been added by the solution of 10% TFA in EDC solution, subjected to microwave irradiation for 15 min of reaction time. Then the reaction mixture has been washed several times with the chilled ether and dried for the further scaffold preparation (Scheme 5).

Preparation of methyl 1-methyl-2-(2-oxo-2H-chromen-3-yl)-1H- benzo[d]imidazole-5-carboxylate

By taking the benzimidazole tathered cyanoaceticacid in the microwave vessel and it has been added the ortho hydroxyl benzaldehyde and the appropriate amounts of triethylamine and the reaction mixture allowed microwaving irradiation for about 15 min of reaction time at 120°C reaction temperature methanol as a solvent. The presence of methanol solvent under organic base condition the ionic liquid will be removed from the scaffold compound. After completion of the reaction the reaction solution has been washed several times with the chilled ether. And then the crude sample subjected to the column chromatography in order to isolate the final scaffolds. Further the same reaction under NaOMe reaction conditions given the better traceless reaction yields (Scheme 6).

Methyl 1-isobutyl-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d] imidazole-5- carboxylate

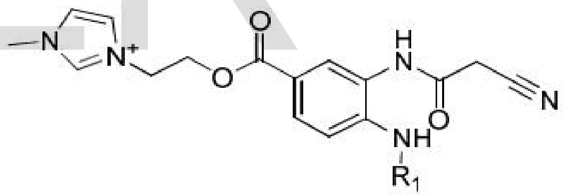
[1]H NMR (300 MHz, CDCl3) δ 8.52 (d, J=0.7 Hz, 1H), 8.36 (s, 1H), 8.06 (dd, J=8.6, 1.35 Hz, 1H), 7.70-7.63 (m, 1H), 7.47-7.35 (m, 1H), 4.09 (d, J=7.7 Hz, 2H), 3.92 (s, 3H), 2.12 (p, J=6.8 Hz, 1H), 0.78 (d, J=6.6 Hz, 6H); [13]C NMR (75 MHz, $CDCl_3$) δ 167.4, 158.8, 154.4, 147.4, 142.0, 133.4, 129.0, 125.1, 124.8, 122.3, 118.5, 116.9, 110.4, 52.7, 52.2, 33.8, 28.9, 24.9, 20.0. MS (ESI): m/z 377.0 $(M+H)^+$; HRMS (ESI): calculated for $C_{22}H_{20}N_2O_4$: m/z 376.4052; Found 377.0 $(M+1)^+$; IR(neat): 2958, 1718, 1608 cm^{-1} (Scheme 7). Yield 75%.

Methyl 1-butyl-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d]imidazole-5- carboxylate

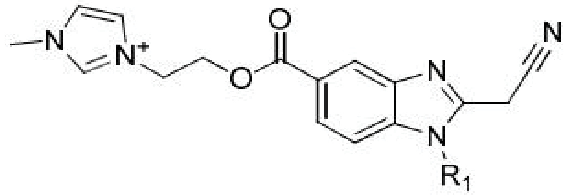
[1]H NMR (300 MHz, CDCl3) δ 8.51 (d, J=1.1 Hz, 1H), 8.33 (s, 1H), 8.06 (dd, J=8.6, 1.56 Hz, 1H), 7.69-7.62 (m, 2H), 7.48-7.36 (m, 2H), 4.26 (d, J=7.5 Hz, 2H), 3.93 (s, 3H), 1.81 (p, J=7.6 Hz, 1H), 1.26 (sex, J=7.7 Hz, 2H), 0.87 (t, J=7.3 Hz, 3H); [13]C NMR (75 MHz, $CDCl_3$) δ 167.9, 159.4, 157.4, 154.8, 150.2, 147.8, 142.9, 139.3, 136.2, 134.8, 133.8, 130.2, 129.4, 125.6, 125.2, 125.1, 123.4, 122.9, 119.5, 118.9, 117.2, 110.6, 52.6, 45.8, 34.3, 32.0, 25.3, 20.5, 13.9; MS (ESI): m/z 377.1 $(M+H)^+$; HRMS (ESI): calculated for $C_{22}H_{20}N_2O_4$: m/z 376.4052; Found 377.1 $(M+1)^+$; IR(neat): 2952, 1718, 1608 cm^{-1} (Scheme 8). Yield 80%.

Methyl 2-(2-oxo-2H-chromen-3-yl)-1-phenethyl-1H-benzo[d] imidazole- 5-carboxylate

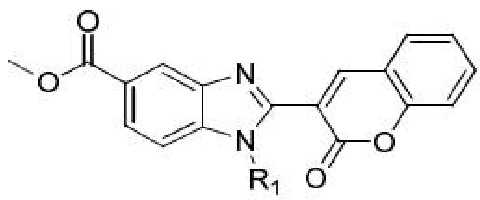
[1]H NMR (300 MHz, CDCl3) δ 8.51 (d, J=0.9 Hz, 1H), 8.11 (dd, J=8.5 Hz, xH), 7.63-7.50 (m, 1H), 7.41-7.29 (m, 2H), 6.95 (t, J=3.5 Hz, 1H), 4.26 (d, J=7.5 Hz, 2H), 3.93 (s, 3H), 1.81 (p, J=7.6 Hz, 1H), 1.26 (six, J=7.7 Hz, 2H), 0.87 (t, J=7.3 Hz, 2H); [13]C NMR (75 MHz, $CDCl_3$) δ



Scheme 4: 3-(2-((3-(2-cyanoacetamido)-4-(methylamino)benzoyl)oxy)ethyl)-1-methyl-1H-imidazol-3-ium.



Scheme 5: 3-(2-((2-(cyanomethyl)-1-methyl-1H-benzo[d]imidazole-5-carbonyl) oxy)ethyl)-1-methyl-1H-imidazol-3-ium.



Scheme 6: methyl 1-methyl-2-(2-oxo-2H-chromen-3-yl)-1H- benzo[d] imidazole-5-carboxylate.

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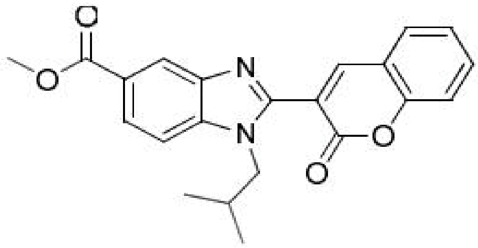
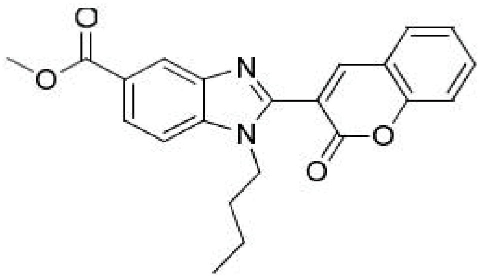


Scheme 7: Methyl 1-isobutyl-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d]imidazole-5-carboxylate.



Scheme 8: Methyl 1-butyl-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d]imidazole-5-carboxylate.

167.4, 166.9, 158.9, 154.1, 150.2, 148.5, 146.6, 142.5, 138.4, 137.8, 133.0, 128.9, 128.8, 128.5, 127.1, 124.9, 122.5, 118.5, 117.9, 116.6, 109.9, 52.2, 47.1, 35.3; MS (ESI): m/z 425.2 $(M+H)^+$; HRMS (ESI): calculated for $C_{26}H_{20}N_2O_4$: m/z 424.4480; Found 425.2 $(M+1)^+$; IR (neat): 2925, 1718, 1608 cm^{-1} (Scheme 9). Yield 85%.

Methyl 1-(2-(cyclohex-1-en-1-yl)ethyl)-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d]imidazole-5-carboxylate

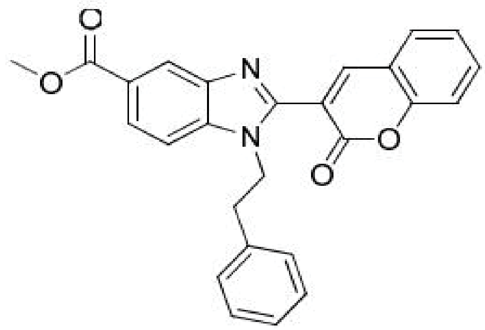
^{1}H NMR (300 MHz, CDCl3) δ 8.50 (d, J=1.0 Hz, 1H), 8.32 (s, 1H), 8.1 (dd, J=1.4, 8.5 Hz, 2H), 7.67-7.59 (m, 1H), 7.48-7.34 (m, 2H), 5.17 (s, 1H), 4.35 (t, J=7.2 Hz, 2H), 3.95 (s, 3H), 2.39 (t, J=7.2 Hz, 2H), 1.92-1.87 (m, 2H), 1.80-1.78 (m, 4H), 1.43-1.33 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 158.9, 154.4, 149.8, 147.4, 142.4, 133.4, 133.3, 128.9, 125.2, 124.8, 124.7, 124.5, 122.4, 119.1, 118.5, 116.8, 110.2, 52.1, 49.1, 44.4, 37.6, 33.8, 32.5, 28.2, 25.5, 25.0, 24.8, 22.5, 21.8; MS (ESI): m/z 429.1 $(M+H)^+$; HRMS (ESI): calculated for $C_{26}H_{24}N_2O_4$: m/z 428.4798; Found 429.1 $(M+1)^+$; IR (neat): 2925, 1718, 1608 cm^{-1}; yield 80% (Scheme 10).

Methyl 1-cyclooctyl-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d]imidazole-5-carboxylate

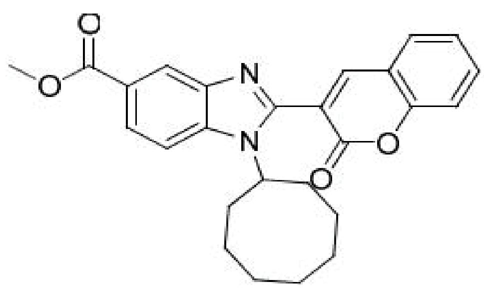
^{1}H NMR (300 MHz, CDCl3) δ 8.50 (s, 1H), 8.28 (s, 1H), 8.02 (dd, J=1.4, 8.6 Hz, xH), 7.66-7.55 (m, 1H), 7.47-7.31 (m, 2H), 4.47-4.46 (m, 1H), 3.95 (s, 3H), 2.45-2.34 (m, 4H), 2.18-2.04 (m, 4H), 1.93-1.79 (m, 4H), 1.70-1.52 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ MS (ESI): m/z 452.2 $(M+Na)^+$; HRMS (ESI): calculated for $C_{26}H_{26}N_2O_4$: m/z 430.4956; Found 452.2 $(M+Na)^+$; IR (neat): 2923, 1716, 1608 cm^{-1}. Yield: 81%.

Results and Discussion

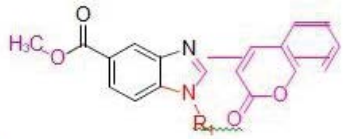
By taking the 3-methylimidazole into the reaction vessel; it has been added by the 1.0 equivalence of bromoethanol in sufficient amount of methanol. This reaction mixture has been allowed to the reflux conditions for about 12 hours and then the reaction mixture cooled down to the room temperature and the solution allowed to stir in the room temperature for about 24 hours and the reaction mixture subjected to the Rota vapor in order to remove the methanol solvent. After the solvent evacuated the crude mixture has been appeared to look like a salt. This salt has been washed several times with diethylether in order to remove the rest of bromoethanol present in the reaction crude; after several times washed with the ether solvent the crude has been subjected to the high pressure vacuum. By taking the sample of the diethyl amine based liquid form ionic liquid and the 2.0 equivalence of 4-Fluoro-3-nitro-benzoicacid and the corresponding amount of coupling reagent DCC and the catalytic amount of DMAP has been taken into the microwave reaction vessel in the acetonitrile as solvent. The reaction mixture has been allowed to stir at room temperature for about 10 hours and then the reaction mixture has been subjected to the microwave irradiation for about 10 min of reaction time at 80°C of temperature. The reaction crude has been filtered through the filter paper in order to remove the undissolved DCU in the reaction mixture. After that the reaction mixture has been subjected to the rotavapor and the solvent residues are removed. The obtained crude product has been washed several times with the diethyl ether until the product has been precipitated. The precipitated product has been dissolved into the acetonitrile soilvent and the various ranges of primary and amine has been added to form the nucleophilic substituted products. This reaction has been done at the room temperature conditions for about one hour. Then the reaction crude residue has been subjected to the rotavapour and the obtained crude washed several times with the ethyl ether until the formation of product in the form of precipitation. Then the obtained product has been taken to reduce the nitro functional group in the presence of the reducing reagent. This reaction has been done in the presence of Zn and the ammoniumformate in methanol as a solvent. After the reaction completion the crude has been filtered and the solvent was evacuated. The ammonimformate was removed by dissolving the crude in the dichloromethane and precipitation. All these subsequent reaction intermediate are taken and submitted to the mass. The mass been matched to the expected value on accurate actual value. There be taking the ionic liquid supported conjugate diamaine and the



Scheme 9: Methyl 1-(2-(cyclohex-1-en-1-yl)ethyl)-2-(2-oxo-2H-chromen-3-yl)-1H- benzo[d]imidazole-5-carboxylate.



Scheme 10: Methyl 1-cyclooctyl-2-(2-oxo-2H-chromen-3-yl)-1H-benzo[d]imidazole-5-carboxylate.



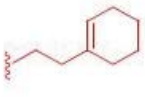
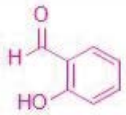
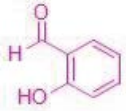
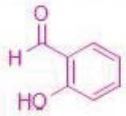
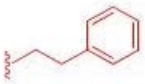
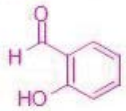
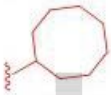
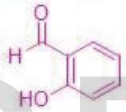
Entry	R_1	R_2	MASS[a]	Yields[b](%)
10a			428	75%
10b			376	80%
10c			376	82%
10d			424	80%
10e			416	75%

Figure 3: Library of synthetic analogues [10,11].

cyanoacetic acid and to couple with the diamine to acid substrate. This reaction has been done in the presence of DCC as the coupling reagent and catalytic amount of DMAP as the reaction catalyst in acetonitrile in room temperature for about 10 hour of reaction of time. The same reaction was done in the microwave irradiation for about of 10 min of reaction time. The reaction mixture was subjected to the rota vapor to evacuate the acetonitrile solvent. There by the reaction crude has been washed several times with diethyl ether. The obtained substrate has been taken for to generate the benzimidazole attached methyl cyanide substance. This reaction has been done in the presence of 10% of TFA in EDC solvent under reflux conditions for about 10 hours of reaction time. The same reaction was completed in 15 min of reaction under microwave irradiation. After the completion of the reaction the reaction crude has been washed with the diethyl ether for several times. The obtained crude product has taken and added the appropriate amounts of various 2-hydroxy benzaldehyde, 2-aminobenzaldehyde and 2-mercaptobenzaldehyde and the triethylamine in methanol for about of 10 hours of reaction time under reflux condition. The obtained reaction crude has been taken tested for the TLC; then concluded the substrate has been detached from the ionic liquid support to leave the product (Figure 3).

Conclusion

In conclusion we described highly automated multistep procedure polymer-assisted solution phase (PASP) protocols for the synthesis of quinoline, chromene, thiochromen benzimidazol-ylideneamines and benzimidazolones via traceless tandem transformation under microwave irradiation on Ionic strategy with a generic protocol of coupling, detachment, and purification. The synergistic ionic liquid microwave assisted synthesis methodology technology offers several advantages in comparison to the other methods used and developed in solid- and liquid-phase organic synthesis. First, the attachment of the 4-fluoro-3-nitrobenzoicacid was rapidly performed under microwave irradiation, and the subsequent transformations led intermediates were easily purified by solvent washings. The quantitative transformation of quinoline, chromene, thiochromen benzimidazol-ylideneamines and benzimidazolones via traceless tandem transformation under microwave irradiation into two-component traceless approach because the loading capacity of the hydroxyl functionalized ionic liquids is very high. This method offers the structure and purity of each intermediate could be verified by routine spectroscopic methods. Furthermore, the cost of the starting ionic liquid is probably lower than the solid and liquid support, and in large scale synthesis, this may be an important economic consideration. Although the reaction was accomplished in the homogeneous model, isolation of the desired products as well as ionic liquids could be achieved via a simple filtration, and the TSIL could be reused. This methodology should be compatible with high-throughput liquid-phase organic synthesis and automation technology in regard to the yield of products and emphasizes the green chemistry aspects by avoiding toxic solvents.

Acknowledgements

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