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Review Article

IONIC LIQUIDS AS SOLVENTS AND CATALYSTS FOR THE GREEN SYNTHESIS OF COUMARINS

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ABSTRACT

Coumarins have a wide variety of applications in the fields of pharmaceuticals, cosmetics and food additives. Therefore, the development of mild, efficient, and eco-friendly benign synthetic methodology is necessary. Ionic liquids (ILs) are environmentally friendly with green chemistry credentials and can be regarded as greener alternatives for conventional organic solvents. The present review focuses on the synthetic approaches toward coumarin analogues that use ILs as a solvent and/or as a catalyst. The review includes the literature after 2005, with the exception of some important historical articles on coumarin derivatives.

Keywords: Coumarins, Ionic liquids, Pechmann reaction, Knoevenagel reaction, Microwave irradiation, Green synthesis

INTRODUCTION

Coumarins are a well-known family of natural organic products [1] which possess a remarkable variety of pharmacological and biological activities, including antioxidant, [2, 3] anti-inflammatory, [2-4] anticancer, [5] antiviral, [6] antibacterial, [7] and anticonvulsant [8]. Coumarin derivatives are presented as additives in food, perfumes, agrochemicals, cosmetics, pharmaceuticals [9], optical brightening agents, dispersed fluorescent and tunable dye lasers [10].

Characteristic examples of coumarin derivatives are Novobiocin (fig. 1), a 3-benzamidocoumarin derivative which possesses strong antibiotic activity by inhibiting DNA gyrase, and has also shown potential as an anticancer agent [11-13] Warfarin (fig. 1) is a natural compound containing the 4-hydroxy-coumarin moiety. It has been isolated from plants such as lavender and is shown that prevents clotting of blood in the veins and heart [14, 15]. Esculetin (fig. 1) is a natural coumarin analogue that presents antiproliferative, antioxidant and anti-inflammatory activities [16]. 7-hydroxycoumarin or Umbelliferone (fig. 1) is a natural coumarin encountered in many plants with remarkable activities such as anti-mycobacterial [17] and anticancer [18].

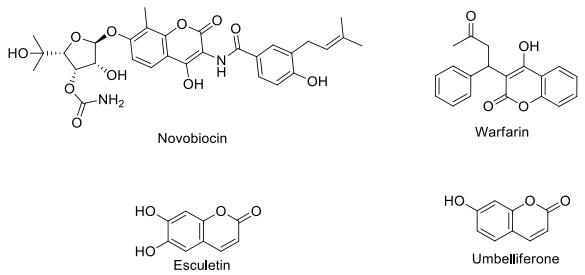


Fig. 1: Different coumarins with significant pharmacological properties

The synthesis of coumarins and their derivatives has attracted considerable attention from organic and medicinal chemists, therefore, several strategies have been developed. Coumarins can be synthesized by various methods such as Pechmann, [19] Perkin, [20] Knoevenagel, [21] Reformatsky [22] and Wittig [23] reactions. Pechmann condensation is one of the most common procedures for the preparation of coumarin derivatives and involves the reactions between a phenol and a-keto ester in the presence of an acidic catalyst. The Knoevenagel reaction is a well-established route to produce coumarins and involves the condensation of aldehydes or ketones with active methylene compounds to form a C=C double bond. The synthesis of simple coumarins has been reported via the Wittig reaction between salicylaldehydes and phosphorus ylides using a variety of acid catalysts [24].

The routes developed so far may possess various disadvantages such as the use of strongly acidic catalysts, long reaction times and, in some cases, low yields. The current trend towards greener synthetic methodologies leads to the development of new, eco-friendly routes towards coumarin derivatives.

Green chemistry possesses the spirit of sustainable development and is attracting increasing interest in the 21st century. In the chemical world, strategies for increasing sustainability often require the redesign of reactions and modifications of existing chemical processes aiming, among other things, at the reduction of chemicals used as solvents in a wide range of industrial applications. In this context, ionic liquids (ILs) have recently emerged as a potential replacement for toxic, hazardous, flammable, and highly volatile organic solvents (VOCs) and as a catalyst under solvent-free conditions. ILs have received a great deal of attention in the synthetic organic chemistry field because of some of their unique properties (thermal and chemical stability, low vapor pressure, the selective solubility of water and organics, recyclability, the ability to be tailored for specific chemical, etc.). In addition, ILs can be recycled and reused while they present remarkable biodegradability potential in a short time period. Thus, ILs are considered to be a safer alternative to original organic solvents as they are cleaner and safer to use and reuse [25-27].

ILs have been increasingly exploited in the pharmaceutical industry in various applications such as drug formulations, solvents for the solubilization of drugs, and both as a catalyst, solvent, and reagents for the synthesis of active pharmaceutical ingredients. Therefore, many types of research included the possibility of using task-specific ILs for developing green methodologies toward novel bioactive compounds have been presented. Owing to green credentials, ionic liquids (ILs) have attracted considerable interest for the synthesis of coumarin derivatives [27].

Driven by our current research in ionic liquids and synthesis of novel bioactive coumarin analogues, [2, 3, 27-29] herein we present a review of recent research reports concerning the green synthetic approaches toward coumarin derivatives focusing in the use of ionic liquids.

Synthesis of coumarins using ionic liquids

In 2005 Gu *et al.* disclosed the non-chloroaluminate acidic ionic liquid [MBsIm][CF_3SO_3] as the best catalyst among the four tested ionic liquids for the synthesis of eight coumarin derivatives *via* Pechmann reactions between phenols and methyl acetoacetate under solvent-free conditions (fig. 2). In addition, they also tested the acidities of the four ionic liquids with Hammett method in dichloromethane as a factor that affects the reaction mechanism. The non-chloroaluminate acidic ionic liquids have an advantage over the chloroaluminate acidic ionic liquid because of their ability to be stable at air and moisture. The ionic liquid that catalyzed the reactions could be reused up to three times and replaced the toxic catalysts and the conventional solvents [30].

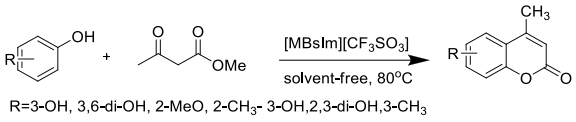


Fig. 2: Pechmann reaction performed in ionic liquid [MBsIm][CF_3SO_3]

Potdar *et al.* reported two methods for the synthesis of coumarin derivatives via Pechmann condensation in the presence of neutral ionic liquids using an additional catalyst or not. In the first method, two ionic liquids 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF_6) and 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) were tested in the role of solvent with a catalytic amount of phosphorus oxychloride ($POCl_3$) in order to study the reaction of activated phenols with ethyl acetoacetate. The reaction was performed at room temperature for 45 min and led to the final coumarins in very high yield (91%-95%). On the other hand, [bmim]PF_6 was used in the same reaction without any catalyst at 100 °C for 1 hour producing notable yields. Both ionic liquids that were used in combination with catalyst could be recycled and reused for four times with effective activity whereas [bmim]PF_6, which was used without the catalyst in the synthesis of coumarins, could be reused for three cycles (fig. 3) [31].

Fig. 3: Synthesis of 4-methyl-coumarin analogues in the presence of the neutral ionic liquid [Bmim]PF_6

In an effort to develop a green synthesis of coumarins, Ranu and Jana report the synthesis of five substituted coumarins *via* Knoevenagel condensation between o-hydroxy benzaldehydes and diethyl malonate or ethyl acetoacetate in the presence of the basic ionic liquid, 1-butyl-3-methylimidazolium hydroxide ([Bmim]OH), in the role both of catalyst and of reaction medium. The reaction was completed in room temperature in a short time (15-25 min) with high products' yield (82%-92%) (fig. 4) while the ionic liquid could be recycled for five cycles without any significant loss in activity. After the five cycles of use, it was necessary to mix the recycled ionic liquid with 50% of fresh [32].

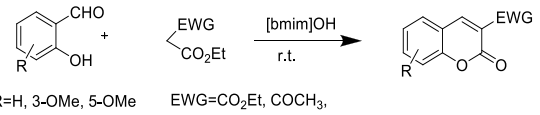


Fig. 4: Synthesis of coumarins via knoevenagel condensation using [Bmim]OH both as a catalyst and medium reaction

Dong *et al.* have developed a facile, efficient, environmentally friendly and high-yielding synthesis of a series of coumarin derivatives. The reaction was performed between phenols and ethyl acetoacetate using as a catalyst N, N, N-trimethyl-N-propane sulfonic acid ammonium hydrogen sulfate ([TMPSA][HSO_4]) in water and the yields were extremely high (fig. 5). [TMPSA][HSO_4] had the best catalytic activity from the other four tested ionic liquids. In addition, this ionic liquid is cheap, air and moisture stable and can be reused five times while the product yields remained at a comparable level [33].

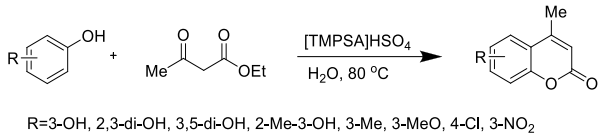


Fig. 5: Pechmann reaction catalyzed by [TMPSA][HSO_4]

Xiu-hong *et al.* used L-proline as a promoter for the reaction between salicylaldehyde analogues and ethyl acetoacetate in the neutral 1-ethyl-3-methylimidazolium tetrafluoroborate ([emim]BF_4) (fig. 6). The method had the advantages of easy procedure, mild reaction conditions as it is performed in room temperature, high yields varying from 81% to 95% and the recyclability of ionic liquids for five times. Remarkably, L-proline proved to be inactive in the presence of organic solvents such as acetonitrile CH_3CN, tetrahydrofuran (THF), and dichloromethane (CH_2Cl_2) while L-proline and [emim]BF_4 do not act separately but seem to operate as a system [34].

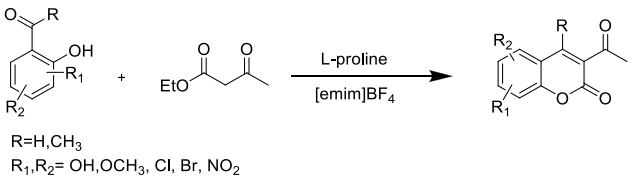


Fig. 6: Synthesis of substituted coumarins using the system L-proline-[Emim]BF_4

Darvatkar and coworkers studied the influence of different ionic liquids both on reaction times and yields for the Knoevenagel condensation between Meldrum's acid and substituted salicylaldehydes. They showed that the ionic liquid with the best activity was the 1-Methylimidazolium trifluoroacetate [Hmim]TFA. The synthetic route, which they developed, was followed for the synthesis of six coumarin-3-carboxylic acids. The reaction was performed at room temperature for 45 min except for one compound (60 min), and significantly high yields (fig. 7). The ionic liquid could be recycled for four cycles without lowering its catalytic activity [35].

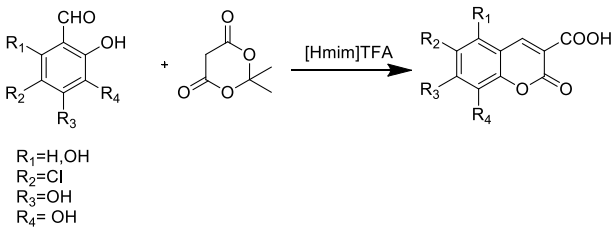
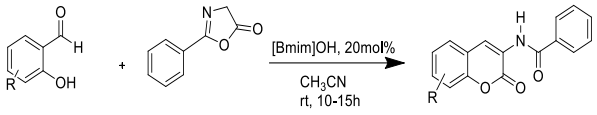


Fig. 7: Synthesis of coumarin-3-carboxylic acids

Kumar and coworkers studied the synthesis of coumarin derivatives *via* Pechmann condensation in the presence of anhydrous $FeCl_3$, in the role of Lewis acid catalyst, and an ionic liquid as the medium of the reaction. They used the reaction between resorcinol and ethyl acetoacetate as a model reaction and five different ionic liquids. The

most effective ionic liquids were 1-methoxyethyl-3-methylimidazolium bis(triflic)-imide [MoeMIm][Tf_2N] and 1-butyl-3-methylimidazolium bis(triflic)-imide [BMIm][Tf_2N] with similar yields (~80%) and reaction times (10-14hours) [MeoMIM][Tf_2N] and [BMIM][Tf_2N] could be recycled and reused four times. The scope of the reaction was tested using four different phenol analogues [36].

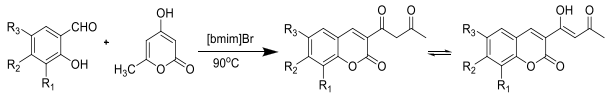
Yadav and his group developed a route to synthesize 3-benzamidocoumarins using 1-butyl-3-methyl imidazolium hydroxide ([Bmim]OH) as a promoter. Their research indicates that [Bmim]OH as a strong base had better catalytic activity than [Bmim]Br and led to products with high yields when acetonitrile was used as a solvent. Thus, twelve coumarin derivatives were synthesized at room temperature in reaction time ranging from 10-15 h (fig. 8). The green catalyst [Bmim]OH could be reused for several times with significant activity [37].



R=H, 3-Br, 3,5-Br, 5-Cl, 3-OMe, 3,5-di-OMe, 3-OEt, 3-OH, 3,5-di-NO_2, 5-NO_2, 3-Cl, 3,5-di-Cl

Fig. 8: The first example of ionic liquid as a promoter in the synthesis of 3-benzamidocoumarins

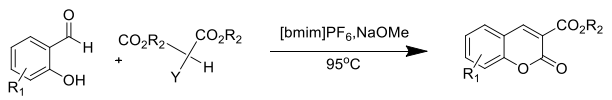
Butyl-methyl imidazole bromide ([bmim]Br) was used as a solvent for the synthesis of 3-acetoacetylcoumarin derivatives in the absence of a catalyst. At first, the condensation of 2-hydroxybenzaldehyde and 4-hydroxy-6-methyl-2H-pyran-2-one was chosen as a model reaction. Variable temperatures, ionic liquids as well as conventional solvents were used, and the most effective reaction conditions were 90 °C, in [bmim]Br for 4 h with 98% yield (fig. 9). In these reaction conditions, ten 3-acetoacetylcoumarin derivatives were synthesized with high yields [38].



R_1,R_2,R_3= H, Br, Cl, CH_3O, $(CH_3)_3C$, CH_3

Fig. 9: [Bmim]Br as a solvent in the synthesis of 3-acetoacetylcoumarin analogues

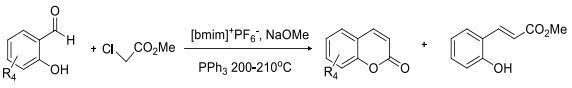
Valizadeh and Vaghefi presented the synthesis of 3-substituted coumarins *via* Knoevenagel reaction between the appropriate 2-hydroxybenzaldehyde and dimethyl or diethyl malonate in the presence of NaOMe as a catalyst and ionic liquid as a reaction medium. The optimum ionic liquid among the butyl methyl imidazolium salts, [bmim]X that was tested, was the 1-Butyl-3-methylimidazolium hexafluorophosphate [bmim]PF_6. After optimization of reaction conditions, eleven coumarin compounds were synthesized in good yields and reaction time approximately 4 h (fig. 10). Moreover, it was shown that in the presence of triphenylphosphine (PPh_3) the same coumarin derivatives were produced *via* Wittig reaction although in lower yields than those that were synthesized *via* Knoevenagel reaction.



R_1= OH, OMe, Et_2N Y=H,Cl R_2=Me, Et

Fig. 10: Synthesis of 3-alkoxycarbonyl-coumarins using [Bmim]PF_6

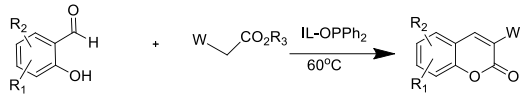
In order to further investigate the potential application of the Wittig reaction to the synthesis of 3,4-unsubstituted coumarins, the authors studied the reaction of 2-hydroxybenzaldehyde, methyl chloroacetate and PPh_3 in the presence of NaOMe as a catalyst and [Bmim]PF6 as the solvent. In ambient temperature the reaction did not proceed to the desired coumarin, therefore, the reactions had to be conducted at 200-210°C (fig. 11) [39].



R_4= H, OH, MeO, Br, NO_2

Fig. 11: Wittig reaction for the synthesis of 3-4-unsubstituted coumarins

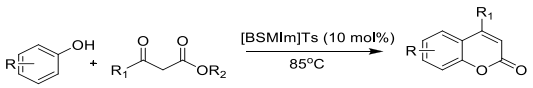
Valizadeh and Gholipour in their studies focused on finding the appropriate amount of the task–specific ionic liquid imidazolium-based phosphinite (IL-$OPPh_2$) to be used both as a catalyst and a solvent in the Knoevenagel reaction between salicylaldehydes and active methylene compounds (fig. 12). The optimum amount of IL was determined to be 1 mmol. The advantages of the method are the high yields (77%-87%) and the ability to reuse the ionic liquid for five cycles without loss of activity [40].



R_1, R_2, R_3= H,OH,OMe, Et_2N, Br

Fig. 12: IL-OPPh2 as a catalyst and solvent for the synthesis of coumarin derivatives

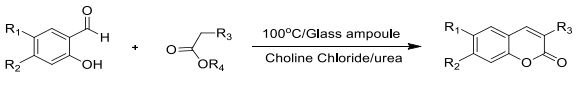
S. Das and his group reported the synthesis of nine coumarin derivatives using the task-specific ionic liquid, 1-Butanesulfonic acid-3-methylimidazolium tosylate ([BSMIm]Ts) as a catalyst in Pechmann condensation of the appropriate phenols with β-ketoester (fig. 13). As a result, coumarin analogues were produced in 1,5-4 h in good yield (70%-86%). The Ionic liquid can be recycled and reused for 6 times without reduction of its catalytic activity. The methodology is advantageous regarding the simple solvent-free experimental procedure and the reusability of the IL [41].



R= OH,EtO, AcO, TsO
R_1= CH_3, Ph
R_2= OEt, OMe

Fig. 13: Synthesis of coumarins in the presence of the acidic ionic liquid ([BSMIm]Ts

Choline chloride/urea is the first ionic liquid that belongs to the family of deep eutectic solvents (DES). Hosanagara *et al.* showed that choline chloride/urea can be effectively used as a solvent and catalyst for the synthesis of 3-substituted coumarins via Knoevenagel condensation between substituted salicylaldehydes and active methylene compounds (fig. 14). Coumarin analogues were obtained in very high yield over 93% within 1-4 h.



R_1= H, Cl, Br, CH_3
R_2= H, Et_2N, OH, Morpholine, $CH(CH_3)_2$, OCH_3, F
R_3=H R_4=H, OCH_3

Fig. 14: Synthesis of various 3-substituted coumarins via Knoevenagel condensation in choline chloride/urea

The developed synthetic approach produces better results than conventional methods both in regards of reaction times and yields. Moreover, choline chloride/urea is soluble in the water helping the isolation of the products [42].

Valizadeh and his group, studied the appropriate conditions to synthesize 3-cyanocoumarins *via* Knoevenagel condensation of malononitrile with salicylaldehyde derivatives in the presence of the appropriate amount of catalyst $ZrCl_4$ in the ionic liquid. They observed that 15 mol% of catalyst $ZrCl_4$ in combination with 1-(n-butyl)-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) in room temperature and variable reaction time up to 40 min leads to the final products in good yields (42%-83%) (fig. 15). The advantages of this synthetic route is the eco-friendly character resulting from the ability to reuse the ionic liquid and conducting the reaction at room temperature [43].

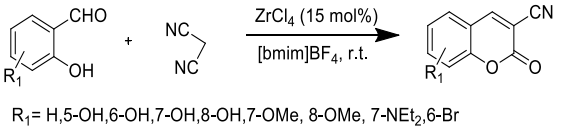


Fig. 15: Synthesis of 3-cyanocoumarins using [bmim]BF_4

The research of Nader *et al.* focused initially on finding the appropriate task-specific ionic liquid for the synthesis of coumarin derivatives *via* Pechmann condensation. They identified that among the tested ionic liquids, halogen-free acidic ionic liquid 3-methyl-1-sulfonic acid imidazolium hydrogen sulfate [Msim]HSO_4 was the most effective catalyst for the synthesis of 7-hydroxy-4-methylcoumarin. After that, they presented the synthesis of a series of appropriately substituted coumarins under solvent-free conditions in good to high yields (75% to 98%) and reaction times varying from 22 to 45 min (fig. 16). The ionic liquid [Msim]HSO_4 could be reused five times without significantly reducing its catalytic activity [44].

Fig. 16: Synthesis of different coumarins in the presence of [Msim]HSO_4

Zhang and coworkers identified the ionic liquid N,N'-dimethylaminoethanol hydrosulfate ([N_{112}OH][HSO_4]) as a nontoxic catalyst for the synthesis of coumarin analogs under solvent free conditions. After assays with a model system they concluded that [N_{112}OH][HSO_4] had the best catalytic activity among eleven ionic liquids in short reaction time (2h) and 87% yield. In addition, they identified the amount of catalyst and temperature that led to a very high yield of the desired compound and synthesized twelve coumarin derivatives (fig. 17) in notable yields. Moreover, they studied the acidity of three ionic liquids possessing different cations and HSO_4-as the common anion and concluded that [N_{112}OH][HSO_4] with strong acidity and a hydroxyl group on the cation, shifts the keto-enol equilibrium of ethyl acetoacetate to the keto-form. In addition, the OH group forms a hydrogen bond with the carbonyl oxygen thus rendering the carbonyl group more susceptible to the subsequent nucleophilic attacks by resorcinol. [N_{112}OH][HSO_4] is a cheap cholinium ionic liquid and can be reused for 6 cycles without loss its activity creating an environmentally friendly character [45].

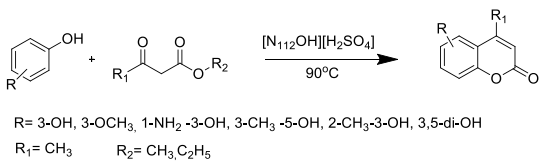


Fig. 17: Synthesis of coumarin analogs in the presence of [N_{112}OH][HSO_4]

In 2015 Shirini *et al.* presented the synthesis of coumarin derivatives *via* Pechmann condensation in the presence of 1,3-Disulfonic acid imidazolium hydrogen sulfate (DSIMHS) as an inexpensive catalyst under solvent-free conditions. The optimum conditions of the reaction between phenol analogs and ethyl acetoacetate or methyl acetoacetate were determined by a model reaction that was performed in different temperatures and concentrations of the ionic liquid. As a result, twenty-two substituted coumarins were synthesized at 75°C under solvent-free conditions in high yields (80% to 96%) and short reaction times varying from 2 to 27 min (fig. 18). In addition, they observed that DSIMHS was the most effective catalyst among five ionic liquids and could be reused up to four times without any loss of its efficiency [46].

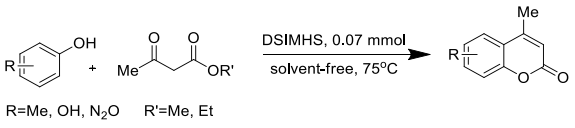


Fig. 18: DSIMHS as a catalyst in the synthesis of coumarin derivatives

Synthesis of coumarins using ionic liquids and microwave irradiation

The acidic nature of the ionic liquid 1-hexyl-3-methyl-imidazolium hydrogen sulphate ([hmim][HSO_4]) enables it to catalyze Pechmann condensation of appropriate phenols and β-ketoesters. Therefore, Singh and his group investigated the parameters of the reaction and reported the synthesis of five coumarin derivatives using [hmim][HSO_4], under heating conditions and microwave irradiation (fig. 19). The advantages which occur by the microwave heating are the very high yield (65%-96%) of the products, in comparison with thermal heating (45%-75%) and additionally the remarkable short times required [47].

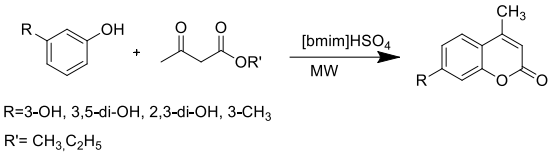


Fig. 19: Synthesis of coumarins under microwave irradiation in [hmim]HSO_4

In order to synthesize 3-substituted coumarins from aryl aldehydes with acidic methylene compounds *via* Knoevenagel condensation, Valizadeh *et al.* used potassium carbonate K_2CO_3 as an inexpensive catalyst in 1-*n*-Butyl-3-methylimidazolium bromide ([bmim]Br) under solvent free conditions and microwave irradiation (fig. 20). The results indicate very good yield, short reaction time and a reduced amount of waste [48].

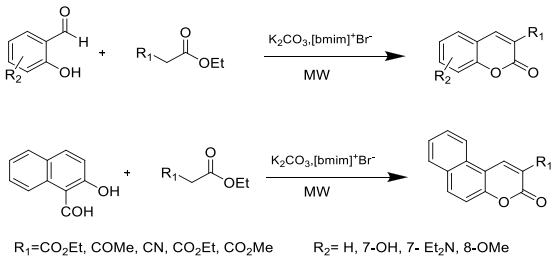


Fig. 20: Synthesis of coumarins in ionic liquid under microwave irradiation and solvent-free conditions

Shaabani *et al.* presented the use of 1,1,3,3-N,N,N',N'-tetramethylguanidine trifluoroacetate (TMGT) as a promoter for the synthesis of either coumarin-3-carboxylic acids or their ester derivatives under heating conditions or microwave irradiation. In Knoevenagel condensation the starting materials are the appropriate *ortho*-hydroxyaryl aldehyde and dialkyl malonate or

Meldrum's acid (fig. 21). The reaction was performed under solvent-free conditions by conventional heating at 120 °C in reaction time varying from 30 min-40 min and yield approximately 75%. The same reaction under microwave irradiation was completed in remarkably reduced reaction time 1-4 min with improved yields. As presented, ionic liquid could be reused four times without loss of activity. The combination of short reaction times under microwave irradiation with the recyclability of ionic liquid renders the developed methodology sufficiently environmentally friendly [49].

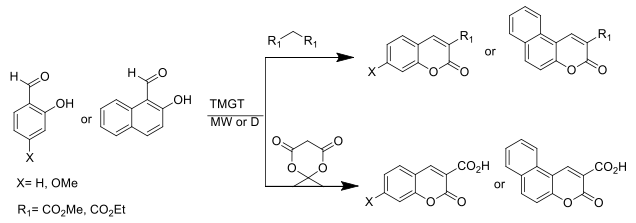


Fig. 21: Knoevenagel synthesis of different coumarin analogues in the presence of TMGT under microwave irradiation

Valizadeh and Shockravi disclosed a task-specific imidazolium-based phosphinite ionic liquid (IL-OPPh$_2$) as a solvent and reagent for the synthesis of substituted coumarins *via* one-pot Horner–Wadsworth–Emmons–type reaction. Investigation of the reaction parameters using a model reaction showed that the use of sodium methoxide as the base, under microwave irradiation, provided the desired products with satisfactory yield (79%-83%) in significant short reaction time (12 min) (fig. 22) in comparison with the heating method, that required 16 h with about 69% yield.[49] The use of microwave irradiation conditions significantly improved the methodology developed earlier by the same research group [50].

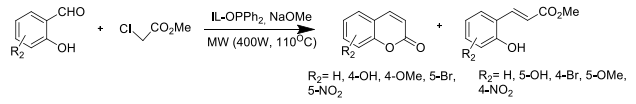


Fig. 22: Synthesis of coumarin derivatives under microwave irradiation using IL-OPPh$_2$

Furthermore, the group of Valizadeh and Shockravi used the task specific phosphinite ionic liquid (IL-OPPh$_2$) as a catalyst and reagent in the synthesis of 4-substituted coumarins under solvent-free conditions and microwave irradiation. They demonstrated the conditions required for the reaction between phenolic compounds and di (methyl or ethyl) acetylene dicarboxylate to lead to products with good yields in short reaction times 1.5-5 min (fig. 23). The conventional route required 3.5 h (yield about 60%). In addition, they report the recyclability of the ionic liquid, which could be used for 3 times [51].

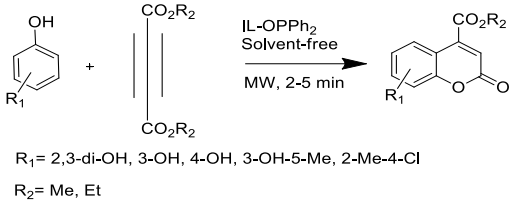


Fig. 23: IL-OPPh2 as a catalyst in solvent-free synthesis of coumarins using microwave irradiation

CONCLUSION

In conclusion, the importance of coumarin derivatives is undeniable. Therefore the development of mild, efficient, and environmentally benign synthetic approaches is crucial. Ionic liquids that act as alternative solvents and catalysts are rapidly and easily prepared, satisfactory biodegradable, recyclable, and not harmful to the environment compared to conventional solvents. We have made here efforts to compile the methods that use ionic liquids for the synthesis of coumarin analogues and have been reported in the literature. The majority of the literature involves both Pechmann or Knoevenagel reactions and the use of imidazole-based ILs, with few examples using choline chloride/urea or ammonium-based ILs. As presented, the final coumarin products were obtained in high purity and in satisfactory yields, comparable or better than the corresponding yields produced by heating in conventional solvents. In addition to the purity of the products, the short reaction times and ease of workup make the methods described advantageously. The developed methodologies benefit from several green aspects such as no use of toxic catalysts and solvents, simple experimental procedure, recovery and utilization of the catalyst, high chemoselectivity and elimination of production of acidic waste streams generated with the conventional acid catalyst.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Borges F, Roleira F, Milhazes N, Santana L, Uriarte E. Simple coumarins and analogues in medicinal chemistry: occurrence, synthesis and biological activity. Curr Med Chem 2005;12:887.
2. Roussaki M, Zelianaios K, Kavetsou E, Hamilakis S, Hadjipavlou-Litina D, Kontogiorgis C, *et al*. Structural modifications of coumarin derivatives: determination of antioxidant and lipoxygenase (LOX) inhibitory activity. Bioorg Med Chem 2014;22:6586–94.
3. Roussaki M, Kontogiorgis CA, Hadjipavlou-Litina D, Hamilakis S, Detsi A. A novel synthesis of 3-aryl coumarins and evaluation of their antioxidant and lipoxygenase inhibitory activity. Bioorg Med Chem Lett 2010;20:3889-92.
4. Huang GJ, Deng JS, Liao JC, Hou WC, Wang SY, Sung PJ, *et al.* Inducible nitric oxide synthase and cyclooxygenase-2 participate in the anti-inflammatory activity of imperatorin from Glehnia littoralis. J Agric Food Chem 2012;60:1673–81.
5. Khaghanzadeh N, Mojtahedi Z, Ramezani M, Erfani N, Ghader A. Umbelliprenin is cytotoxic against QU-DB large cell lung cancer cell line but anti-proliferative against A549 adenocarcinoma cells daru. J Pharm Sci 2012;20:69-75.
6. Shikishima Y, Takaishi Y, Honda G, Ito M, Takfda Y, Kodzhimatov OK, *et al*. Chemical constituents of prangos tschiniganica, structure elucidation and absolute configuration of coumarin and furanocoumarin derivatives with anti-HIV activity. Chem Pharm Bull 2001;49:877-80.
7. Rosselli S, Maggio AM, Faraone N, Spadaro V, Morris-Natschke SL, Bastow KF, *et al*. The cytotoxic properties of natural coumarins isolated from roots of Ferulago campestris (Apiaceae) and of synthetic ester derivatives of aegelinol. Nat Prod Commun 2009;4:1701–6.
8. Luszczki JJ, Wojda E, Andres-Mach M, Cisowski W, Glensk M, Glowniak K, *et al*. Anticonvulsant and acute neurotoxic effects of imperatorin, osthole and valproate in the maximal electroshock seizure and chimney tests in mice: a comparative study. Epilepsy Res 2009;85:293–9.
9. Kennedy RO, Thornes RD, Coumarins: biology, applications, and mode of action, John Wiley and Sons, Chichester; 1997.
10. Maeda M, Laser Dyes. Academic Press: New York; 1984.
11. Raad I, Darouiche R, Hachem R, Sacilowski M, Bodey GP. Antibiotics and prevention of microbial colonization of catheters. Antimicrob Agents Chemother 1995;39:2397–400. (b) Raad II, Hachem RY, Abi-Said D, Rolston KVI, Whimbey E, Buzaid AC, *et al.* A prospective crossover randomized trial of novobiocin and rifampin prophylaxis for the prevention of intravascular catheter infections in cancer patients treated with interleukin-2. Cancer 1998;82:403–11. (c) Walsh TJ, Standiford HC, Reboli AC, John JF, Mulligan ME, Ribner BS, *et al.* Randomized double-blinded trial of rifampin with either novobiocin or trimethoprim-sulfamethoxazole against methicillin-resistant staphylococcus aureus coloni-

zation: prevention of antimicrobial resistance and effect of host factors on outcome. Antimicrob Agents Chemother 1993;37:1334–42.
12. Anderle C, Stieger M, Burrell M, Reinelt S, Maxwell A, Page M, et al. Biological activities of novel gyrase inhibitors of the aminocoumarin class. Antimicrob Agents Chemother 2008;52:1982–90.
13. Janin YL. Heat shock protein 90 inhibitors. a textbook example of medicinal chemistry? J Med Chem 2005;48:7503–12. (b) Burlison JA, Neckers L, Smith AB, Maxwell A, Blagg BSJ. Novobiocin: Redesigning a DNA gyrase inhibitor for selective inhibition of Hsp90. J Am Chem Soc 2006;128:15529–36.
14. Heide L. The aminocoumarins: biosynthesis and biology. Nat Prod Rep 2009;26:1241-50.
15. Bansal Y, Silakari O. Multifunctional compounds smart molecules for multifactorial diseases. Eur J Med Chem 2014;76:31-42.
16. Witaicenis A, Seito LN, Di Stasi LC. The intestinal anti-inflammatory activity of esculetin and 4-methylesculetin in the trinitrobenzene sulphonic acid model of rat colitis. Chem Biol Interact 2010;186:211–8.
17. Chiang CC, Cheng MJ, Peng CF, Huang HY, Chen IS. A novel dimeric coumarin analog and antimycobacterial constituents from *Fatoua pilosa*. Chem Biodiversity 2010;7:1728–36.
18. Ramalingam R, Vaiyapuri M. Effects of umbelliferone on lipid peroxidation and antioxidant status in diethylnitrosamine-induced hepatocellular carcinoma. J Acute Med 2013;3:73-82.
19. Valizadeh H, Shockravi A. An efficient procedure for the synthesis of coumarin derivatives using $TiCl_4$ as catalyst under solvent-free conditions. Tetrahedron Lett 2005;46:3501–3.
20. Donnelly BJ, Donnelly DMX, Sullivan AMO. Dalbergia species—VI: The occurrence of melannein in the genus dalbergia. Tetrahedron 1968;24:2617–22.
21. Bigi F, Chesini L, Maggi R, Sartori G. Montmorillonite KSF as an inorganic, water stable, and reusable catalyst for the Knoevenagel synthesis of coumarin-3-carboxylic acids. J Org Chem 1999;64:1033–5.
22. Shirner RL. The reformat sky reaction. Org React 1942;1:1-35.
23. Yavari I, Hekmat-shoar R, Zonuzi A. A new and efficient route to 4-carboxymethylcoumarins mediated by vinyl triphenylphosphonium salt. Tetrahedron Lett 1998;39:2391–92.
24. Shockravi A, Valizadeh H, Heravi MM. A one-pot and convenient synthesis of coumarins in the solventless system. Phosphorus Sulfur Silicon Relat Elem 2003;178:501–4.
25. Wasserscheid P, Welton T. Eds. Ionic Liquids in Synthesis. Wiley-VCH, Verlag GmbH and Co.: Weinheim; 2002.
26. Yue C, Fang D, Liu L, Yi TF. Synthesis and application of task-specific ionic liquids used as catalysts and/or solvents in organic unit reactions. J Mol Liq 2011;163:99–121.
27. Tzani A, Douka A, Papadopoulos A, Pavlatou EA, Voutsas E, Detsi A. Synthesis of bis coumarins using recyclable and biodegradable task-specific ionic liquids. ACS Sustainable Chem Eng 2013;1:1180-5.
28. Tsanas C, Tzani A, Papadopoulos A, Detsi A, Voutsas E. Ionic liquids as entrainers for the separation of the ethanol/water system. Fluid Phase Equilib 2014;379:148–56.
29. Gjineci N, Boli E, Tzani A, Detsi A, Voutsas E. Separation of the ethanol/water azeotropic mixture using ionic liquids and deep eutectic solvents. Fluid Phase Equilibria 2015. Doi:10.1016/j. fluid.2015.07.048. [Article in Press]
30. Gu Y, Zhang J, Duan Z, Deng Y. Pechmann reaction in non-chloroaluminate acidic ionic liquids under solvent-free conditions. Adv Synth Catal 2005;347:512–6.
31. Potdar MK, Rasalkar MS, Mohile SS, Salunkhe MM. Convenient and efficient protocols for coumarin synthesis via Pechmann condensation in neutral ionic liquids. J Mol Catal A: Chem 2005;235:249–52.
32. Ranu BC, Jana R. Ionic liquid as catalyst and reaction medium–a simple, efficient and green procedure for knoevenagel condensation of aliphatic and aromatic carbonyl compounds using a task-specific basic ionic liquid. Eur J Org Chem 2006;16:3767–70.
33. Dong F, Jian C, Kai G, Qunrong S, Zuliang L. Synthesis of coumarins *via* pechmann reaction in water catalyzed by acyclic acidic ionic liquids. Catal Lett 2008;121:255–9.
34. Liu XH, Fan JC, Liu Y, Shang ZC. L-Proline as an efficient and reusable promoter for the synthesis of coumarins in the ionic liquid. J Zhejiang Univ Sci B 2008;9:990-5.
35. Darvatkar NB, Deorukhkar AR, Bhilare SV, Raut DG, Salunkhe MM. Ionic liquid–mediated synthesis of coumarin-3-carboxylic acids via knoevenagel condensation of meldrum's acid with ortho-hydroxyaryl aldehydes. Synth Commun 2008;38:3508-13.
36. Kumar V, Tomar S, Patel R, Yousaf A, Parmar VS, Malhotra SV. $FeCl_3$-catalyzed pechmann synthesis of coumarins in ionic liquids. Synth Commun 2008;38:2646-54.
37. Yadav LDS, Singh S, Rai VK. A one-pot [Bmim]OH-mediated synthesis of 3-benzamidocoumarins. Tetrahedron Lett 2009;50:2208–12.
38. Shi DQ, Zhou Y, Rong SF. Ionic liquid, [bmim]Br, as an efficient promoting medium for synthesis of 3-acetoacetylcoumarin derivatives without the use of any catalyst. Synth Commun 2009;39:3500-8.
39. Valizadeh H, Vaghefi S. One-pot wittig and knoevenagel reactions in ionic liquid as convenient methods for the synthesis of coumarin derivatives. Synth Commun 2009;39:1666-78.
40. Valizadeh H, Gholipour H. Imidazolium-based phosphinite ionic liquid (IL-$OPPh_2$) as reusable catalyst and solvent for the knoevenagel condensation reaction. Synth Commun 2010;40:1477-85.
41. Das S, Majee A, Hajra A. A convenient synthesis of coumarins using the reusable ionic liquid as a catalyst. Green Chem Lett Rev 2011;4:349-53.
42. Harishkumar HN, Mahadevan KM, Kumar HCK, Satyanarayan ND. A facile, choline chloride/urea catalyzed solid phase synthesis of coumarins *via* knoevenagel condensation. Org Commun 2011;4:26-32.
43. Valizadeh H, Mahmoodian M, Gholipour H. $ZrCl_4$/[bmim]BF_4-catalyzed condensation of salicylaldehydes and malononitrile: single-step synthesis of 3-cyanocoumarin derivatives. J Heterocycl Chem 2011;48:799-802.
44. Khaligh NG. Synthesis of coumarins via Pechmann reaction catalyzed by 3-methyl-1-sulfonic acid imidazolium hydrogen sulfate as an efficient, halogen-free and reusable acidic ionic liquid. Catal Sci Technol 2012;2:1633–6.
45. Zhang Y, Zhu A, Li Q, Li L, Zhao Y, Wang J. Cholinium ionic liquids as cheap and reusable catalysts for the synthesis of coumarins via Pechmann reaction under solvent-free conditions. RSC Adv 2014;4:22946-50.
46. Shirini F, Yahyazadeh A, Mohammadi K. A solvent-free synthesis of coumarins using 1,3-disulfonic acid imidazolium hydrogen sulfate as a reusable and effective ionic liquid catalyst. Res Chem Intermed 2015;41:6207-18.
47. Singh V, Kaur S, Sapehiyia V, Singh J, Kad GL. Microwave accelerated the preparation of [bmim][HSO_4] ionic liquid: an acid catalyst for improved synthesis of coumarins. Catal Commun 2005;6:57–60.
48. Valizadeh H, Shockravi A, Gholipur H. Microwave assisted synthesis of coumarins *via* potassium carbonate catalyzed knoevenagel condensation in 1-n-butyl-3-methylimidazolium bromide ionic liquid. J Heterocycl Chem 2007;44:867-70.
49. Shaabani A, Ghadari R, Rahmati A, Rezayan AH. Coumarin synthesis *via* knoevenagel condensation reaction in 1,1,3,3-*N,N,N',N'*-tetramethylguanidine trifluoroacetate ionic liquid. J Iran Chem Soc 2009;6:710-4.
50. Valizadeh H, Shockravi A. Task-specific ionic liquid as reagent and reaction medium for the one-pot horner–wadsworth–emmons–type reaction under microwave irradiation. Synth Commun 2009;39:4341–9.
51. Valizadeh H, Gholipour H, Mahmoudian M. Phosphinite ionic liquid (IL-$OPPh_2$) as a recyclable reagent for the efficient synthesis of coumarins under microwave irradiation conditions. J Iran Chem Soc 2011;8:862-71.

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