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Efficient method for Knoevenagel condensation in aqueous solution of amino acid ionic liquids (AAILs)

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This work reports on the use of the amino acid ionic liquids (AAILs) which have been used as catalysts in Knoevenagel condensation of various aldehydes with malononitrile. For research we use tetrabutylammonium ionic liquids based on eight natural amino acids. The reaction was carried out in an aqueous medium. Using water as solvent provided efficient and simple method of isolation of pure product with high yield. Moreover, amino acid ionic liquid dissolved in water could be reused many times without any loss of its catalytic activity. The influence of the anion was studied. Moreover the effect of technological parameters such as: the temperature, the catalyst content, and the reaction time on yield of reaction were investigated.

Keywords: recycling, catalysis in water, amino acid ionic liquids, Knoevenagel reaction.

INTRODUCTION

Knoevenagel condensation is an important organic reaction. It occurs between carbonyl compounds (aldehydes or ketones) and active methylene compounds, with carbon-carbon bond formation[1]. It has been a subject of interest for the production of highly processed chemicals, such as coumarin derivatives[2–3] fragrances[4] and UV filters in cosmetics[5]. Moreover, synthetic routes to many drugs and therapeutic substances involve production of a key intermediary via Knoevenagel condensation[6–8].

In the early 90's, the development of a new trend in chemistry has forced many changes in the approach to organic synthesis, and among others to the Knoevenagel condensation[9]. Green Chemistry approach to the synthesis of chemicals defined and described by Paul Anastas and John C. Warner in 1998 made it necessary to design technologies safer both for the environment as well as for people[10–11]. Thus, there are great efforts to make relevant changes in the processes used in chemical and related industries.

The basic principle in designing new technologies are the reduction and elimination of the use of hazardous substances. In this context the use of organic, harmful and volatile solvents should be limited. Moreover, the catalytic processes in the presence of active and selective catalysts, which allow the reactants to be better utilized, are preferred.

The Knoevenagel reaction, as majority of organic reactions was commonly carried out in organic solvents. New approach to this reaction was to use water as an environmentally inert solvent[11–15] and also to apply solvent-free processes[13, 16].

Ionic liquids can serve well as substitutes to volatile organic solvents because of their unique properties desirable as ideal solvents, such as low volatility, nonflamability, good thermal stability and recyclability. Additionally they can act as catalysts.

Some studies report utilization of ionic liquids only as reaction medium of the Knoevenagel reaction in which addition of catalyst is involved. For example reaction of various aldehydes with Meldrum's acid was conducted in a very popular imidazolium ionic liquid, $BMIMBF_4$, in the presence of catalytic amounts of piperidine[17]. The same catalyst was used in BMIMOH and BMIMBr, in the condensation of 1H-pyrrole-2-carbaldehyde with a range of phenyl acetonitriles[18]. Ionic liquid $HexMIMPF_6$ was used in the reaction of benzaldehyde with malononitrile, in the presence of glycine as the catalyst[19].

On the other hand, many reports reveal catalytic properties of ionic liquids in the Knoevenagel reaction[20–27]. Ionic liquids used as catalysts have various structures of anions and cations. Among them there are 1,3-dialkylimidazolium ionic liquids with different organic and inorganic anions, such as acetate, trifluoroacetate[27], methanesulfonate, *para*-toluenesulfonate, and dimethyl phosphate[28]. There are known ionic liquids with imidazolium cation functionalized with acetic acid, which act as Broensted acids[21].

There are many other examples of ionic liquids with diverse structures that have beneficial effect on the Knoevenagel condensation of various reactants. Ammonium ionic liquids with 2-hydroxyethylammonium cation and organic acids anions were also successfully used as catalysts in condensation of aldehydes with 2,4-thiazolidinedione[22]. Moreover, protic ammonium ionic liquids (cations: Et_3NH or Me_3NH) with HSO_4^-, HPO_4^{2-} or acetate anion were catalysts and solvents in condensation of 2-chloro-3-formylquinoline with different active methylene compounds[26]. Protic ionic liquid formed from urotropine and acetic acid was used in the Knoevenagel condensation of aromatic aldehydes with ethyl 2-cyanoacetate[24].

The aim of our study was combination of water as reaction medium and ionic liquid as co-solvent and catalyst in the Knoevenagel reaction.

Our interest was focused on the application of amino acid ionic liquids (AAILs), which have an important advantage over other ionic liquid classes. They are produced from renewable raw materials – amino acids and are biocompatible and well biodegradable.

Our interest was focused on the application of amino acid ionic liquids (AAILs), which were a combination of tetrabutylammonium cation with amino acid anions ([TBA][AA]).

There are two examples of AAILs application in the Knoevenagel reaction[29–30].

EXPERIMENTAL

Material

Tetrabutylammonium hydroxide (40% wt. in water), tetrabutylammonium hydrogensulfate (97%), tetrabutylammonium chloride (≥97%), malononitrile (≥99%), aldehydes (benzaldehyde, salicylaldehyde, 3-hydroxybenzaldehyde, 4-chlorobenzaldehyde, 5-chlorosalicylaldehyde, 3-methoxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde, 3,4-dimethoxybenzaldehyde, 2-furalaldehyde, 2-hydroxy-1-naphthaldehyde), amino acids (L-leucine, L-valine, L-isoleucine, L-threonine, L-histidine, L-methionine, L-tyrosine, L-tryptophan) were purchased from Sigma-Aldrich. 4-(Dimethylamino)benzaldehyde and absolute ethanol were purchased from Avantor Performance Materials. All materials were used as received.

Analytical methods

^{1}H-NMR spectra were recorded using Bruker DPX--400 spectrometer. The chemical shifts were referred to tetramethylsilane as internal standard.

Synthetic procedures

General procedures for synthesis of [TBA][AA]

Tetrabutylammonium salts of amino acids were synthesized from tetrabutylammonium hydroxide and amino acids by procedure similar to previously described[31–32].

Amino acid (1.2 equivalents) was dissolved in the aqueous solution of tetrabutylammonium hydroxide (1 equivalent). The mixture was stirred at room temperature for 24 h. Then, the water was evaporated at 60°C under vacuum by using rotary evaporator. The excess of amino acid was precipitated from residue with absolute ethanol and filtered. Then, ethanol was distilled off from filtrate under vacuum. The target tetrabutylammonium salt of amino acids [TBA][AA] was dried in vacuum oven at 60°C.

Structures of tetrabutylammonium salts of amino acids were confirmed by ^{1}H-NMR with d_6-DMSO as solvent.

General procedure for the Knoevenagel condensation

In a typical experiment the appropriate amount of catalyst (0.63, 1.25, 2.5 or 5.0 mol%) was put into a round-bottomed flask (25 mL) equipped with a magnetic stirring bar and dissolved in water at fixed temperature (25°C or 50°C). Then malononitrile (5 mmol) and appropriate aldehyde (5 mmol) were added, the flask was closed with a rubber stopper and the mixture was stirred vigorously for at least 0.5 h. Next, the reaction mixture was cooled in an ice bath and the precipitated product was filtered and washed with cold water on a filter. Then, the product was dried and weighed. In general, no further purification was needed. Purity and structure of the products were confirmed by ^{1}H NMR spectra, in $CDCl_3$ as solvent. Melting points of the products were also determined.

Recycling experiments

In the first experiment of the cycle, 46.6 mg (0.125 mmol) of [TBA][Leu] was dissolved in 15 mL of water at 25°C. Then, 330 mg (5 mmol) of malononitrile and 531 mg (5 mmol) of benzaldehyde were added and the mixture was stirred vigorously for 0.5 h. Next, the reaction mixture was cooled in an ice bath and the precipitated product was filtered. The obtained filtrate was collected, placed in a reaction flask and used in the next cycle. The filtered product was washed with cold water, dried and weighed to determine the yield.

RESULTS AND DISCUSSION

In our studies tetrabutylammonium salts of eight amino acids ([TBA][AA]) were tested as catalysts of the Knoevenagel reaction between malononitrile and aldehydes (Fig. 1).

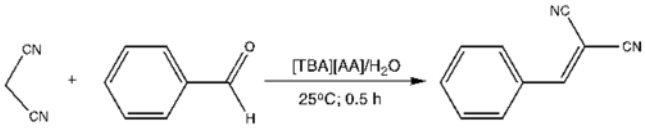


Figure 1. Model Knoevenagel reaction of malononitrile with benzaldehyde

In contrast to the earlier studies[29–30], we conducted the reaction in water as medium and we isolated pure product without the use of chlorinated solvents. AAILs are soluble in water and are stable in the aqueous solution. The product of the Knoevenagel reaction precipitated from the reaction mixture and could be easily separated by filtration.

In the first step of our studies, the effect of tetrabutylammonium salts on the yield of the product was determined. The model reaction of malononitrile and benzaldehyde was carried out in 30 minutes with vigorous mixing, at room temperature. Preparative yields of 2-benzylidenemalononitrile were between 74% and 89%. The highest yields were noted for tetrabutylammonium L-valinate and L-leucinate (Table 1).

Table 1. Effect of the amino acid anion in AAILs on the yield of 2-benzylidenemalononitrile

Catalyst	Yield [%][b]
[TBA][Leu]	89
[TBA][Val]	89
[TBA][Ile]	81
[TBA][Thr]	74
[TBA][His]	81
[TBA][Met]	85
[TBA][Tyr]	80
[TBA][Trp]	79
without	0
L-Leu	9
[TBA][Cl]	55
[TBA][HSO_4]	47

[a] Reaction conditions: 5 mmol of malononitrile; 5 mmol of benzaldehyde; 15mL of water; 0.125 mmol of catalyst; 25°C; 30 minutes; [b] Preparative yield.

Apart from the tetrabutylammonium salts of amino acids we also used different tetrabutylammonium salts, for comparative purposes. It was found, that the addition of tetrabutylammonium chloride (TBACl) or

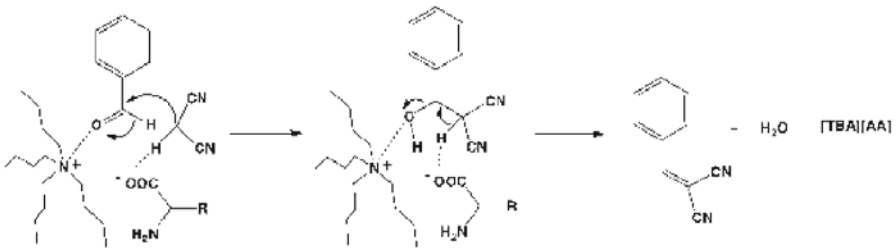


Figure 2. Mechanism of the Knoevenagel reaction catalyzed by [TBA][AA] in aqueous solution

hydrogensulfate ($TBAHSO_4$) gave lower yields, 55% and 47% respectively.

In the reaction conducted under the same conditions, but without TBA salts, we didn't observe the formation of the product.

These results showed that tetrabutylammonium salts are catalysts of the Knoevenagel reaction. Combinations of tetrabutylammonium cation with amino acid anions proved to be the most preferred. Low yield (9%) obtained in the presence of L-leucine instead of its TBA salt, indicated the substantial role of the amino acid anion for the reaction mechanism (Fig. 2).

Anion (amino acid, Cl^- or HSO_4^-) combined with TBA cation participates in this reaction. It affects the malononitrile and facilitates deprotonation of methylene group. Proton acceptor abilities of anions are dependent on their basicity. Amino acid anions are stronger bases/proton acceptors than chloride or hydrogensulfate anions, so AA salts make deprotonation of malononitrile easier. Therefore, we observed higher yields of the Knoevenagel reaction in the presence of [TBA][AA] than either [TBA][Cl] or [TBA][HSO_4]. Additionally, tetrabutylammonium cation can interact with carbonyl oxygen atom of aldehyde, and the electron withdrawing effect causes carbon atom of carbonyl group to become more susceptible to the nucleophilic attack (Fig. 2).

In the next step, the effect of concentration of tetrabutylammonium L-leucinate, as exemplary AAIL, on the yield of 2-benzylidenemalononitrile was tested. Moreover, the amount of water as the medium was also changed to indicate the optimal synthesis conditions and product isolation (Table 2).

Table 2. Effect of [TBA][Leu] concentration and amount of water on the yield of 2-benzylidenemalononitrile (Reaction conditions: 5 mmol of malononitrile; 5 mmol of benzaldehyde; 25°C; 30 minutes)

Entry	[TBA][Leu] concentration [%mol][b]	Water [mL]	Yield [%][c]
1	0.63	15	64
2	1.25	15	82
3	2.5	15	89
4	5.0	15	87
5	2.5	5	85
6	2.5	10	84
7	2.5	20	78
8	2.5	25	74

[a] Reaction conditions: 5 mmol of malononitrile; 5 mmol of benzaldehyde; 25°C; 30 minutes; [b] vs. malononitrile; [c] preparative yield.

The yield of product increased when [TBA][Leu] concentration was changed from 0.63% to 2.5% (Table 2). The increase in AAIL concentration above 2.5% had no effect on the further improvement of the yield. Moreover, we observed that the amount of water should be maintained on the level of 1–3 mL per 1 mmol of reactant to achieve the high yield of pure 2-benzylidenemalononitrile. Water was necessary to prevent a competitive reaction of aldehyde with amine group of AAIL. As we described earlier, in anhydrous medium AAILs react with aldehyde with formation of amino acid ionic liquid supported Schiff bases (AAIL-SB)[33]. So the utilization of pure AAIL in the Knoevenagel reaction instead of its aqueous solution resulted in solidification of the reaction mixture and production of 2-benzylidenemalononitrile contaminated with reactants and AAIL-SB.

The effectiveness of [TBA][Leu] aqueous solution was also checked in the Knoevenagel condensation between malononitrile and structurally diverse aromatic aldehydes. Benzene ring of aldehyde contained halogens atoms, alkyl, hydroxy and methoxy groups as substituents (Table 3). All products were identified by NMR analysis that gave evidence of obtaining pure product without the need of additional purification. The appropriate condensation product was produced with moderate to high (13÷98%) yield for the majority of the used aldehydes at 25°C in 30 minutes reaction time. We observed that the yield was depended on both the type of substituent and its position in the ring. For example, the product from 2-hydroxybenzaldehyde and malononitrile was obtained with 86% yield, from 3-hydroxybenzaldehyde - 29% and from 3-methoxybenzaldehyde – 91%.

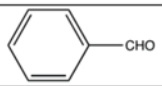
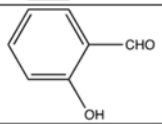
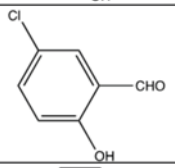
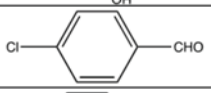
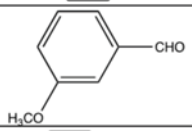
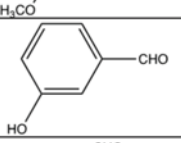
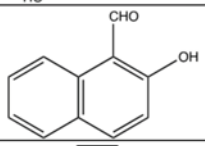
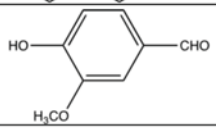
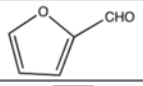
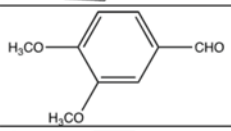
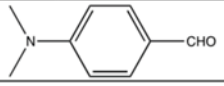
Aldehydes, which formed the product with malononitrile at 25°C with low or moderate yield reacted more effectively at a higher temperature of 50°C and in longer reaction time (Table 3). For example 2-(2-hydroxynaphthalen-1-ylmethylene)malononitrile reached 86% yield after 24 h at 50°C, while at 25°C it was formed with only 13% yield.

The advantage of the used method was the simplicity at which the product can be separated by filtration after cooling the reaction mixture. The remaining aqueous solution of AAIL was used again to determine its activity in the reaction. A sequence of experiments were conducted using filtrates obtained from the previous synthesis (Fig. 3).

In six consecutive experiments no significant loss of catalytic activity was noticed (Table 4). Even in ninth cycle the yield of 2-benzylidenemalononitrile was high (68%). The little decrease could be the effect of mass loss of the recycled aqueous solution of AAILs.

We have also tested utility of our methodology for another compounds with active methylene group, such as methyl cyanoacetate and dimethyl malonate (Table 5). We obtained moderate results for the reaction with various aldehydes and observed like other authors[29], a decrease in reactivity of active methylene compounds

Table 3. Knoevenagel condensation of malononitrile with various aldehydes catalyzed by aqueous solution of [TBA][Leu][a]

Entry	Aldehyde	Temperature; reaction time	Yield [%]
1.		25°C; 0.5 h	89
2.		25°C; 0.5 h	86
3.		25°C; 0.5 h	98
4.		25°C; 0.5 h 50°C, 1 h	46 97
5.		25°C; 0.5 h	91
6.		25°C; 0.5 h 50°C, 1 h	29 79
7.		25°C; 0.5 h 50°C, 1 h	13 86
8.		25°C; 0.5 h 50°C, 1h	67 97
9.		25°C; 0.5 h	81
10.		25°C; 0.5 h	90
11.		25°C; 0.5 h 50°C, 24 h	43 84

[a] Reaction conditions: 5 mmol of malononitrile; 5 mmol of benzaldehyde; 15 mL of water.

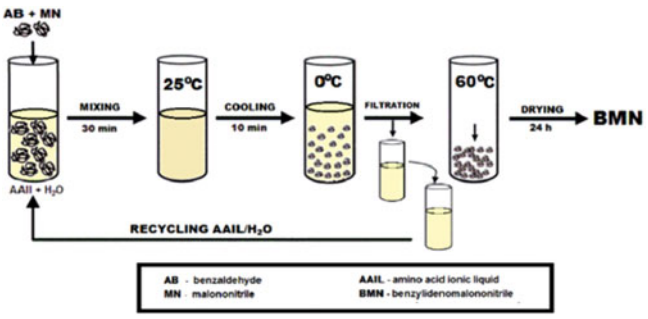


Figure 3. Scheme of the recycling experiment

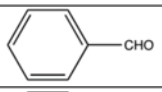
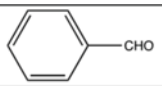
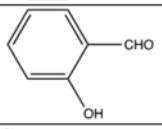
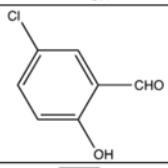
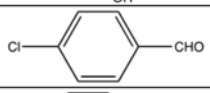
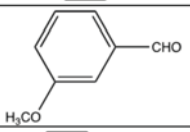
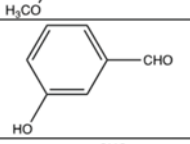
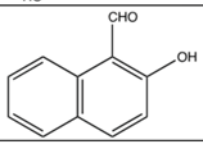
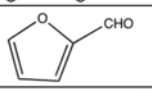
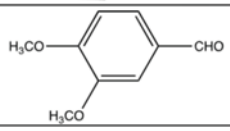
with replacement of cyano group to ester group. Ester group is weaker electron-acceptor than cyano group, so it decreases acidity of the methylene active compound. The modification of the method and extending the range of used amino acid ionic liquids are in a progress of our research.

Table 4. The yield of 2-benzylidenemalononitrile in the reaction of benzaldehyde and malononitrile in the consecutive experiments with the recycled [TBA][Leu] aqueous solution[a]

Cycle	Yield [%]
1	88
2	94
3	81
4	83
5	85
6	84
7	72
8	78
9	68

[a] Reaction conditions: 5 mmol of malononitrile; 5 mmol of benzaldehyde; 25°C; 30 minutes; 15 mL of water and 0.125 mmol of [TBA][Leu] were added in the first cycle.

Table 5. Knoevenagel condensation of methyl cyanoacetate (A) and dimethyl malonate (B) with various aldehydes catalyzed by aqueous solution of [TBA][Leu][a]

Entry	Aldehyde	Methylene active compound	Yield [%]
1.		A	17
2.		B	8
3.		A	<1
4.		A	39
5.		A	19
6.		A	4
7.		A	57
8.		A	30
9.		A	86
10.		A	33

[a] Reaction conditions: 5 mmol of A or B; 5 mmol of aldehyde; 15 mL of water; 0.125 mmol of [TBA][Leu]; reaction temperature: 25°C; reaction time: 0.5.

CONCLUSIONS

We provided methodology for eco-friendly, very simple, clean synthesis of Knoevenagel reaction product from diverse aldehydes and malononitrile in aqueous solution of amino acid ionic liquids (AAILs). AAILs can be used in catalytic amount providing good yields under mild conditions. The product was separated in pure form by filtration and the remaining amino acid ionic liquid solution was successfully reused without decrease in the product yield even after 6 cycles. Our studies established that amino acid in anionic form is needed to the catalytic process. The role of amino acid anion is to cause deprotonation and increasing nucleophilicity of malononitrile. Moreover, TBA cation activates the aldehyde to nucleophilic attack.

LITERATURE CITED

1. March, J. (1992). Advanced Organic Chemistry: Reactions, Mechanisms, and Structure (7th ed.). New York, USA: John Wiley & Sons.

2. Song, A., Wang, X. & Lam, K.S. (2003). A convenient synthesis of coumarin-3-carboxylic acids via Knoevenagel condensation of Meldrum's acid with ortho-hydroxyaryl aldehydes or ketones. Tetrahedron Lett. 44(9), 1755–1758. DOI:10.1016/S0040-4039(03)00108-4.

3. Bigi, F., Chesini, L., Maggi, R. & Sartori, G.J. (1999). Montmorillonite KSF as an Inorganic, Water Stable, and Reusable Catalyst for the Knoevenagel Synthesis of Coumarin-3-carboxylic Acids. J. Org. Chem. 64(3), 1033–1035. DOI: 10.1021/jo981794r.

4. Flachsmann, F. (2013). Fragrance compounds. U.S. Patent No. 8575386B2. Duebendorf C.H.: United States Patent Application.

5. Hoshino, M., Sugiyama, M., Kawamata, A., Joukura, H. & Imokawa, G. 1994. Naphtalenmethylenemalonic diesters and UV absorbers and cosmetic compositions containing the diesters. EU Pat. EP 663206A1.

6. Beutler, U., Fuenfschilling, P.C. & Steinkemper, A. (2007). An Improved Manufacturing Process for the Antimalaria Drug Coartem. Part II. Org. Process Res. Dev. 11(3), 341–343. DOI: 10.1021/op060244p.

7. Martinez, C.A., Hu, S., Dumond, Y., Tao, J., Kelleher, P. & Tully, L. (2008). Development of a chemoenzymatic manufacturing process for pregabalin. Org. Process Res. Dev. 12(3), 392–398. DOI: 10.1021/op7002248.

8. Walker, S.D., Borths, C.J., DiVirgilio, E., Huang, L., Liu, P., Morrison, H., Sugi, K., Tanaka, M., Woo, J.C.S. & Faul, M.M. (2011). Development of a scalable synthesis of a GPR40 receptor agonist. Org. Process Res. Dev. 15(3), 570–580. DOI: 10.1021/op1003055.

9. Menegatti, R. (2012). Designing highly efficient solvents for the Knoevenagel condensation: two novel dicationic dimethyl phosphate ionic liquids. In: M. Kidwai & N.K. Mishra (Eds.), Green Chemistry – Environmentally Benign Approaches (pp. 13–32). Intech, Rijeka.

10. Anastas, P.T. & Warner, J.C. (1998). Green Chemistry: Theory and Practice (1st ed.). Oxford University Press, New York.

11. Anastas, P.T. & Kirchhoff, M.M. (2002). Origins, current status, and future challenges of green chemistry. Acc. Chem. Res. 35(9), 686–694. DOI: 10.1021/ar010065m.

12. Reddy, T.I. & Verma, R.S. (1997). Rare earth-exchanged NaY zeolite-promoted Knoevenagel condensation. Tetrahedron Lett. 38(10), 1721–1724. DOI: 10.1016/S0040-4039(97)00180-9.

13. McCluskey, A., Robinson, P.J., Hill, T., Scott, J.L. & Edwards, J.K. (2002). Green chemistry approaches to the Knoevenagel condensation: comparison of ethanol, water and solvent free (dry grind) approaches. Tetrahedron Lett. 43(17), 3117–3120. DOI: 10.1016/S0040-4039(02)00480-X.

14. Bigi, F., Conforti, M.L., Maggi, R., Piccinno, A. & Sartori, G. (2000). Clean Synthesis in Water: Uncatalysed Preparation of Ylidenemalononitriles. Green Chem. 2, 101–103. DOI: 10.1039/B001246G.

15. Gomes, M.N., de Oliveira, C.M.A., Garrote, C.F.D., de Oliveira, V. & Menegatti, R. (2011). Condensation of ethyl cyanoacetate with aromatic aldehydes in water, catalyzed by morpholine. Synth. Commun. 41(1), 52–57. DOI: 10.1080/00397910903531771.

16. Mallouk, S., Bougrin, K., Laghzizil, A. & Benhida, R. (2010). Microwave-Assisted and Efficient Solvent-free Knoevenagel Condensation. A Sustainable Protocol Using Porous Calcium Hydroxyapatite as Catalyst. Molecules 15(2), 813–823. DOI: 10.3390/molecules15020813.

17. Tahmassebi, D., Wilson, L.J.A. & Kieser, J.M. (2009). Knoevenagel Condensation of Aldehydes with Meldrum's Acid in Ionic Liquids. Synth. Commun. 39(14), 2605–2613. DOI: 10.1080/00397910802663345.

18. Otaibi, A.A., Gordon, C.P., Gilbert, J., Sakoff, J.A. & McCluskey, A. (2014), The influence of ionic liquids on the Knoevenagel condensation of 1H-pyrrole-2-carbaldehyde with phenyl acetonitriles – cytotoxic 3-substituted-(1H-pyrrol-2-yl)acrylonitriles. RSC Adv. 4, 19806–19813. DOI: 10.1039/c3ra47418f.

19. Morrison, D.W., Forbes, D.C. & Davis, Jr J.H. (2001). Base-promoted reactions in ionic liquid solvents. The Knoevenagel and Robinson annulation reactions. Tetrahedron Lett. 42(35), 6053–6055. DOI: 10.1016/S0040-4039(01)01228-X.

20. Suresh, J. & Sandhu, J. (2013). Ultrasound-assisted synthesis of 2,4-thiazolidinedione and rhodanine derivatives catalyzed by task-specific ionic liquid: [TMG][Lac]. Org. Med. Chem. Lett. 3:(2), 1–6. DOI: 10.1186/2191-2858-3-2.

21. Moosavi-Zare, A.R., Zolfigol, M.A., Khaledian, O., Khakyzadeh, V., Farahani, M.D. & Kruger, H.G. (2014). Tandem Knoevenagel-Michael-cyclocondensation reactions of malononitrile, various aldehydes and dimedone using acetic acid functionalized ionic liquid. New J. Chem. 38, 2342–2347. DOI: 10.1039/C3NJ01509B.

22. Zhang, J., Zhang, Y. & Zhou, Z. (2014). Hydroxyl ammonium ionic liquid-catalyzed simple and efficient synthesis of 5-arylidene-2,4-thiazolidinediones under solvent-free conditions. Green Chem. Lett. Rev. 7(1), 90–94. DOI: 10.1080/17518253.2014.895866.

23. Ying, A., Ni, Y., Xu, S., Liu, S., Yang, J. & Li, R. (2014). Novel DABCO Based Ionic Liquids: Green and Efficient Catalysts with Dual Catalytic Roles for Aqueous Knoevenagel Condensation. Ind. Eng. Chem. Res. 53(14), 5678–5682. DOI: 10.1021/ie500440w.

24. Zhao, S., Wang, X. & Zhang, L. (2013). Rapid and efficient Knoevenagel condensation catalyzed by a novel protic ionic liquid under ultrasonic irradiation. RSC Adv. 3, 11691–11696. DOI: 10.1039/C3RA40809D.

25. Tzani, A., Douka, A., Papadopoulos, A., Pavlatou, E.A., Voutsas, E. & Detsi, A. (2013). Synthesis of Biscoumarins Using Recyclable and Biodegradable Task-Specific Ionic Liquids. ACS Sustainable Chem. Eng. 1(9), 1180–1185. DOI: 10.1021/sc4001093.

26. Siddiqui, Z.N. & Khan, K. (2014). [Et3NH][HSO4]--Catalyzed Efficient, Eco-Friendly, and Sustainable Synthesis of Quinoline Derivatives via Knoevenagel Condensation. ACS Sustainable Chem. Eng. 2(5), 1187–1194. DOI: 10.1021/sc500023q.

27. Hu, X., Zhang, B., Gao, Y. & Dong, S. (2014). Knoevenagel reactions catalyzed by ionic liquids. J. Chem. Pharm. Res. 6, 864–868. CODEN:JCPRC5 ISSN:0975-7384.

28. Zicmanis, A. & Anteina, L. (2014). Dialkylimidazolium dimethyl phosphates as solvents and catalysts for the Knoevenagel condensation reaction. Tetrahedron Lett. 55(12), 2027–2028. DOI: 10.1016/j.tetlet.2014.02.035.

29. Moriel, P., Garcia-Suarez, E.J., Martinez, M., Garcia, A.B., Montes-Moran, M.A., Calvino-Casilda, V. & Banares, M.A. (2010). Synthesis, characterization, and catalytic activity of ionic liquids based on biosources. Tetrahedron Lett. 51(37) 4877–4881. DOI: 10.1016/j.tetlet.2010.07.060.

30. Ouyang, F., Zhou, Y., Li, Z.M., Hu, N. & Tao, D.J. (2014). Tetrabutylphosphonium amino acid ionic liquids as efficient catalysts for solvent-free Knoevenagel condensation reactions. Korean J. Chem. Eng. 31(8), 1377–1383. DOI: 10.1007/s11814-014-0077-4.

31. Fukumoto, K., Yoshizawa, M. & Ohno, H. (2005). Room Temperature Ionic Liquids from 20 Natural Amino Acids. J. Am. Chem. Soc. 127(8), 2398–2399. DOI: 10.1021/ja043451i.

32. Allen, C.R., Richard, P.L., Ward, A.J., Van de Water, L.G.A., Masters, A.F. & Maschmeyer, T. (2006). Facile synthesis of ionic liquids possessing chiral carboxylates. Tetrahedron Lett. 47(41), 7367–7373. DOI: 10.1016/j.tetlet.2006.08.007.

33. Ossowicz, P., Janus, E., Schroeder, G. & Rozwadowski, Z. (2013). Spectroscopic studies of amino acid ionic liquid-supported Schiff bases. Molecules 18(5), 4986–5004. DOI: 10.3390/molecules18054986 18, 4986–5004.