FULL PAPER



Zinc-containing ionic liquid as a dual solvent-catalyst in base-free condensations under ultrasonic irradiation

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Hossein Ghafuri, Catalysts and Organic Synthesis Research Laboratory, Department of Chemistry, Iran University of Science and Technology, PO Box 16846-13114 Tehran, I. R. Iran. Email: ghafuri@iust.ac.ir In this study, natural-based ionic liquid (IL) using caffeine (Caff), trietahnolamine (TEA) and ZnBr₂, [Caff-TEA]⁺[ZnBr₃]⁻, which features high catalytic activity and environmentally-friendly nature was synthesized with melting point of 76 °C by a facile method. The synthesized [Caff-TEA] $^+$ [ZnBr₃]⁻ has high catalytic activity as both of catalyst and solvent in condensation reactions for the synthesis of benzylidenes, bis-hydroxyenones and xanthenes. Synthesized IL was characterized by proton nuclear magnetic resonance (¹HNMR), Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD) and Energy-dispersive X-ray spectroscopy (EDX) analysis. Also synthesized heterocycles were characterized by FT-IR, proton nuclear magnetic resonance (¹HNMR) and carbon nuclear magnetic resonance (¹CNMR).

KEYWORDS

condensation, ionic liquid, ultrasonic irradiation, zinc

1 | INTRODUCTION

The first ionic liquid (IL), non-coordinating salts consist of organic/inorganic anions and bulky organic cations, was reported by Paul Walden in 1914.^[1] Since then this field opened new horizons in science and also increasingly attracted researcher's attentions so that thousands of articles were published about ILs until now.^[1] ILs are considered as environmentally friendly compounds due to their non-volatile and non-flammable character which cause noticeably decrease in pollution of environment.^[2] Their vapor pressure make it possible to use them instead of volatile organic com-pounds VOCs. Also, they have additional properties in compare to neutral fluids which are associated with the Coulomb potential.^[3] ILs can be used as solvents due to their ability in dissolving wide variety of organic/inorganic solutes. One of the earliest report about dissolving materials in ILs is stated in 1934 by Graenacher which dissolved cellulose in benzylpyridinium chloride.^[4] Many applications of ILs were reported till now: ILs showed convenient advantageous

as solvents in bio-transformations in a research which dealt with enzymes,^[5] they exhibited appropriate benefits in membrane science as the separation medium instead of traditional membranes that use unstable solvents under various conditions,^[6] and they have been used for the separation of proteins, DNA fragments, proteins, poly (phenols) and dyes in capillary electrophoresis (CE) as background electrolytes.^[7] Among wide-ranging applications of ILs, catalysis has been known as a favorable application of ILs. Two models of using ILs as catalysis could be named: Liquid-IL biphasic catalysis, and IL both as solvent and catalyst.^[8] Many reports described the catalytic abilities of ILs like in Friedel–Crafts reactions,^[9] in Beckmann rearrangement, in esterification, in carbonylation reactions, and in benzylation of alcohols.^[10] In these cases, the difference of miscibility between IL and the product could lead to simple recycling of catalyst and isolation of products.^[11] In addition, ILs have following applications: as reagents and scavengers, to synthesize energy storage materials, to desulfurize fuel, for energy production, for carbon capture, functional material, and

2 of 8 WILEY-Organometallic Chemistry

in denitrogenating of fuel oils.^[12] In theory, more than a million ILs can be synthesized. It is possible to adjust the properties of ILs by selecting assured components which suited for a precise application.^[13] According to their applications, many kinds of ILs were synthesized till now: acidic ILS, functionalized ILs, covalently and non-covalently supported ILs, ILs transported into metal-organic frame-works (MOFs), superionic liquids, and magnetic ILs, which each of them have their unique proper-ties.^[14]

Imidazolium-based ILs are the most usable ionic liquids which most researches in this field are on the basis of them. One problem of imidazolium based ILs is their synthetic method that cause environmental pollution. To reduce this, natural-based imidazolium structure can be used. Caffeine, a methylxanthine alkaloid, is a natural-based imidazolium compound which extracted from coffee beans. Previously, caffeine was used to synthesize organometallic compounds, used as liquid IL as catalysis in organic compounds, and also used to synthesize solid IL.^[15] So, it could be used instead of synthetic imidazole to synthesized ionic liquid. To enhance the activity of IL, several functional groups can be used. It should be noted that presence of functional groups with active sites, such as free nitrogen and oxygen, make it possible to place various metals in the structure of IL, which cause development in the application of IL. From this kind of compounds, triethanolamine (TEA) with free adjacent hydroxyl groups, can be effective component in the structure of IL to immobilize metals on it.

Heterocyclic Building Blocks have key role in synthesizing complicated chemical and biological compounds and serving wide range of applications in immense scientific fields. Of these kind of heterocyclic building blocks, thiazoles, hydrazones, pyrrolidines and bis-cyclohexenones can be men-tioned. Bis-hydroxyenones, from biscyclohexenones family, and benzilidenemalono-nitriles/ benzilidene cyclohexenones are of these group of heterocyclic building blocks. Benzilidenemalononitriles can be synthesized from the reaction of one moiety of diketone with one ben-zaldehyde and bis-hydroxyenones can be synthesized from the reaction of two moiety of diketones with one benzaldehyde and formed more complicated heterocyclic compounds such as pyridines, chromenes, acridines and xanthanes.^[16] Various method for the synthesis of these compound have been reports such as using Al_2O_3 , [bmim]OH, Taurine, L-Histidine, SiO₂-Cu, CoFe₂O₄, HClO4-SiO₂ and ZrOCl₂/NaNH₂.^[17] but still better methods should be provide to synthesize it.

In this contribution, a facile procedure for the synthesis of novel natural-based IL using caffeine, 1,3-dibromine, triethanolamine (TEA) and $ZnBr_2$ [Caff-TEA]⁺[ZnBr₃]⁻ was used and lead to dual solvent-

catalyst IL with great catalytic activity in condensation reactions (scheme 1). Three kind of heterocycles were synthesized by this dual solvent-catalyst including the synthesis of benzylidenes, bis-hydroxyenones and xanthenes and characterized by FT-IR, 1HNMR and ¹³CNMR spectroscopy. Also synthesized [Caff-TEA]⁺[ZnBr₃]⁻ was characterized by Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD) and Energy-dispersive X-ray spectroscopy (EDX) analysis.

2 | EXPERIMENTAL

2.1 | Materials

All chemicals and solvents were purchased from Merck and Sigma companies and used without any further purification. The ultrasonic reactions were carried out in an Elmasonic S 60 H (220–240 V) sonicator, the FT-IR spectra were recorded by Shimadzu 800 IR 100 FT-IR spectrometer in KBr, EDX spectra were recorded by Numerix DXP-X10P, the powder X-ray diffraction patterns were recorded by PANalytical X-PERT-PRO MPD diffractometer with Cu K α (λ = 1.5406 Å) irradiation, and NMR spectra were recorded by Burker DRX-500 Avance spectrometer (500 MHz/¹HNMR and 125 MHz/¹³CNMR).

2.2 | Typical procedure for the synthesis of [Caff-TEA]⁺[ZnBr₃]⁻ IL

A mixture of caffeine (1.0 mmol) and 1,3dibromopropane (1.0 mmol) was added to a 50 ml flask in DMF and stirred for 48 hr at 90 °C under N₂ atmosphere. To this mixture, TEA was added and stirred for 24 hr at 80 °C. After completion the reaction, DMF was separated by rotary and obtained product, [Caff-TEA] +[ZnBr₃]⁻, washed with EtOAc and dried under air atmosphere at r.t for 24 hr. Melting point of resulted IL was 176 °C. To this synthesized IL, ZnBr₂ (2.0 mmol) was added in H₂O and stirred for 24 hr at r.t. Resulted IL was separated and washed at r.t. for 24 hr. Melting point of synthesized IL was surprisingly decreased to 76 °C.

2.3 | Typical procedure for benzylidene synthesis

A mixture of benzaldehyde (1.0 mmol), dimedone/cyclohexandione (1.0 mmol) and IL [Caff-TEA]⁺[ZnBr₃]⁻ (0.5 mL) was added to a 50 ml flask and sonicated for 15 min h at 80 °C under air atmosphere. After completion the reaction, which was followed by



SCHEME 1 Synthesis of benzylidenes (3), bis-hydroxyenones (4) and xanthenes (5) using synthesized IL

TLC, IL was separated from the reaction by $EtOAc/H_2O$ combination and remaining product in organic layer recrystallized.

2.4 | Typical procedure for the synthesis of bis-hydroxyenones/xanthenes under sonochemical conditions

A mixture of benzaldehyde (1.0 mmol), dimedone/ cyclohexandione (2.0 mmol) and IL (0.5 mL) was added to a 50 ml flask and sonicated for 40 min at 80 °C under air atmosphere. After com-pletion the reaction, which was followed by TLC, IL was separated from the reaction by EtOAc/H₂O combination and remaining product in organic layer recrystallized.

2.5 | Selected spectral data

2.5.1 | 2-(4-hydroxybenzylidene)-5,5dimethylcyclohexane-1,3-dione (3D)

¹HNMR (500 MHz, DMSO) $\delta_{\rm H}$ (ppm) = 0.97 (3H, s, Me), 1.03 (3H, s, Me), 2.73–2.89 (4H, doublet, CH₂), 7.01–7.47 (3H, m, Ar), 7.96 (1H, s, CH), 10.28 (1H, OH_{Ar}). ¹³CNMR (125 MHz, DMSO) $\delta_{\rm C}$ (ppm) = 25.68, 27.67, 35.35, 49.72, 52.08, 108.21, 125.36, 127.29, 130.15, 131.83, 139.67, 161.87, 167.14, 195.05, 204.39.

2.5.2 | 2,2'-[(4-Hydroxyphenyl)methylene] bis(3-hydroxy-5,5-dimethylcyclohex-2enone) (4D)

¹HNMR (500 MHz, DMSO) $\delta_{\rm H}$ (ppm) = 0.84 (3H, s, Me), 0.94 (3H, s, Me), 0.96 (3H, s, Me), 1.09 (3H, s, Me), 2.20–2.43 (8H, m, CH₂), 5.78 (1H, s, CH), 6.52–6.95 (3H, m, Ar), 8.94–8.98 (s, 2OH), 10.5–12.5 (broad, OH_{Ar}). ¹³CNMR (125 MHz, DMSO) $\delta_{\rm C}$ (ppm) = 28.35 (2CH), 30.68, 31.73 (2CH), 46.98 (2CH), 115.17 (2CH), 115.35 (2CH), 127.78, (2CH), 129.17, 130.83, 156.28 (2C), 187.77 (2C).

2.5.3 | 3,4,6,7-tetrahydro-9-(2,4dichlorophenyl)-2H-xanthene-1,8(5H,9H)dione (5 l)

1HNMR (500 MHz, DMSO) $\delta_{\rm H}$ (ppm) = 0.93 (3H, s, Me), 0.99 (3H, s, Me), 1.03 (3H, s, Me), 1.09 (3H, singlet, Me),

4 of 8 WILEY Organometalli Chemistry

2.03–2.38 (8H, m, CH₂), 4.52 (1H, s, CH), 7.02–7.19 (3H, m, Ar). $^{13}\text{CNMR}$ (125 MHz, DMSO) δ_{C} (ppm) = 26.67, 26.76, 28.21, 29.05, 29.55, 32.63, 33.14, 100.02, 101.64, 126.41, 128.37, 131.02, 132.83, 133.33, 140.54, 168.36, 186.06, 196.07, 205.40.

3 | **RESULTS AND DISCUSSION**

3.1 | Characterization of [Caff-TEA] ⁺[ZnBr₃]⁻

Proton nuclear magnetic resonance (¹HNMR) analysis has taken to prove the covalent bond between caffeine and 1,3-dibromo propane to form imidazolium ionic liquid. In ¹HNMR, peaks at 1.47–1.63 ppm, 3.36–3.48 ppm and 3.87–3.91 ppm indicate six aliphatic CH groups, two sharp peaks at 2.73 and 2.89 ppm indicate three methyl groups and single peak at 7.95 ppm indicate single proton of imidazole (Figure 1).

FT-IR spectra of final IL can be seen in Figure 2. Characterization peaks about stretching vibrations of hydroxyl group (for TEA) was found at 3490 cm⁻¹, stretching vibrations of aromatic CH group observed at 3116 cm⁻¹, stretching vibrations of aliphatic CH group observed at 2954 cm⁻¹, C=O stretching vibrations (2 C=O for caffeine) observed at 1697 and 1652 cm⁻¹, C=N stretching



2000

1000

FIGURE 2 FT-IR spectra of [Caff-TEA] + [ZnBr3]- IL

3000

5000

4000

observed at 1454 and 1386 cm⁻¹, C-N stretching observed at 1191 cm⁻¹, C-O stretching observed at 1043 cm⁻¹, and stretching peaks of Zn-Br and Zn-O can be seen at 495 and 435 cm⁻¹, respectively.

XRD analyses is indicated the crystalline structure of synthesized IL (Figure 3). In XRD patterns of synthesized IL, each part of IL can be seen separately with their characterization peaks. As can be seen in Figure, these peaks proved the presence of caffeine and $\text{ZnBr}_{2/3}$ in the structure of IL. For caffeine, characterization peaks present at $2\theta = 13.7$, 20.8, 23.3, 26.4 and 27.4°. For ZnBr_{2/3}, characterization peaks present at $2\theta = 13.6$ (overlapped with caffeine peak), 22.1, 24.2, 31.2, 32.3, 38.4, 44.3, 48.7, 49.9 and 55.5°.



FIGURE 1 1HNMR spectra for the condensation of caffeine and 1,3-dibromopropane

0

n



FIGURE 3 XRD patterns of [Caff-TEA+][ZnBr3-] IL

EDX analyses of synthesized IL can be seen in Figure 4. All elements which from IL are presented in this analyses. As a result, from figure, presence of C, N, O, Zn, Br, and therefore, successful synthesis of IL were proved.

3.2 | Optimizing the reactions conditions

To optimize benzylidenes, bis-hydroxyenones and xanthenes synthesis, various temperatures, solvents, amount of catalysts and conditions were used. According to results, it can be concluded that all above reactions have the same optimized condition. Briefly, following results were gained after optimization reactions: a) Increasing the amount of IL have no positive effect in the yield of products. b) Reactions have higher yields with lower reaction times under ultrasonic reactions compared to stirring conditions. c) Four solvent systems were used to understand the best solvent including: H_2O , EtOH, CH_3CN and $[Caff-TEA]^+[ZnBr_3]^-$. After the experiments were performed on the above solvents and at different



FIGURE 4 EDX result of [Caff-TEA] + [ZnBr3]- IL

6 of 8 WILEY Organometallic Chemistry

temperatures, the best result was obtained at 80°C under ultrasonic sonication with $[Caff-TEA]^+[ZnBr_3]^-$. d) Hence melting point of $[Caff-TEA]^+[ZnBr_3]^-$ is 76 °C and also in the presence of $[Caff-TEA]^+[ZnBr_3]^-$ as both of catalyst and solvents reactions have better results, so temperature of the reactions should be at 80 °C. e) Extending the reaction time to 25 and 45 have no positive effects on the yield of final products, also minimum time of the reactions are 15 and 35 for the synthesis of benzylidene (3A) and both of Bis-hydroxyenone (4E) and xanthene (5E), respectively (Table 1).

This catalytic system also have better times and yield compared to studied literatures (Table 2).

3.3 | Mechanism of the reactions

Suggested mechanism for the synthesis of benzylidenes (3), bis-hydroxyenones (4) and xanthenes (5) using $[Caff-TEA]^+[ZnBr_3]^-$ IL are illustrated in scheme 2 and scheme 3. To prove this mechanism, NMR analysis of two of reaction's intermediates including ¹HNMR of benzylidene K (intermediate of xanthene **5 K**) and ¹HNMR of benzylidene N (intermediate of bis-hydroxyenone **4 N**) were provided and added to supporting information (Figure 1S, 2S). As can be seen, $[Caff-TEA]^+[ZnBr_3]^-$ as both of solvent and catalyst activated carbonyl parts of aldehyde and dimedone/

			Time (min)		Yield (%)			M.p. °C			
Entry	Aldehyde	Dione	3	4	5	3	4	5	3	4	5
А	C_6H_5	Dimedone	15		30	96		95	185–187 ^[18]		197–198 ^[19]
В	C_6H_5	1,3-Cyclohexanedione			35			95			204-206 ^[20]
С	3-OH C ₆ H ₄	Dimedone		40			84			190-192 ^[20]	
D	$4\text{-OH C}_6\text{H}_4$	Dimedone	15	40		91	95		$177 - 180^{[18]}$	198-200 ^[21]	
Е	$4\text{-OH }C_6H_4$	1,3-Cyclohexanedione		35			92			200-202 ^[20]	
F	4-Me C_6H_4	Dimedone	30			83					
G	2-OMe C_6H_4	Dimedone			40			86			188-189 ^[22]
Н	2-NO2 C_6H_4	Dimedone		40			79			194–196 ^[23]	
Ι	3-NO2 C ₆ H ₄	Dimedone	15		35	88		82	180-182 ^[18]		198–199
J	C4H ₃ S	Dimedone		40			80			195–197 ^[23]	
Κ	$4\text{-Cl }C_6H_4$	Dimedone			35			92			183-185 ^[19]
L	2,4-Cl C ₆ H ₃	Dimedone	15		40	92		91	125-127 ^[18]		205-207 ^[24]
М	2,4-Cl C ₆ H ₃	1,3-Cyclohexanedione			30			84			202-204 ^[20]
Ν	2,6-Cl C ₆ H ₃	Dimedone	20	35			82		126-128	205-207	

TABLE 1	Various	derivatives	of benzylidenes	(3),	bis-hydroxyenones	(4)) and	l xanthenes	(5)) using synthesized	IL
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 TABLE 2
 Comparative studies between different systems for the synthesis of benzylidene (3F), bis-hydroxyenone (4C) and xanthene (5A) using synthesized IL

		Time			Yield (%)					
Entry	Solvent-catalyst	3F	4C	5A	3F	4C	5B			
1	[Caff-TEA] ⁺ [ZnBr ₃] ⁻	30 min	40 min	30 min	83	84	95			
2	No catalyst ^[25]	30 min	-	-	60	-	-			
3	[PEG (mim) ₂][OH]2 ^[25]	3 h	-	-	89	-	-			
4	No catalyst ^[26]	-	30 min	-	-	65	-			
5	Activated silica ^[26]	-	30 min	-	-	70	-			
6	PPA-SiO ₂ ^[27]	-	-	10 h	-	-	52			
7	DBSA ^[27]	-	-	6 h	-	-	90			
8	NaHSO ₄ -SiO ₂ ^[27]	-	-	6.5 h			90			



SCHEME 3 Suggested mechanism for the synthesis of bis-hydroxyenones (4) and xanthenes (5) using synthesized IL

cyclohexanone and from this activation, reactions lead to desired final products.

4 CONCLUSION

In summary, natural-based IL which syndicates activity of ZnBr₂ and caffeine-triethanolamine IL was successfully synthesized using easy and facile method. This IL can be used in wide range of organic reactions. Melting point of initial IL in the absence of ZnBr₂ was about 176 °C which limited the use of IL in temperatures below 100 °C, but after adding ZnBr₂ to initial IL, melting point was decreased to 76 °C, that made it possible to carry out reaction under 100 °C in milder reaction conditions. This procedure is released a new dual solvent-catalyst system which showed effective role in increasing the yield of products, lowering the time of the reactions and with simple procedures in the absence of any organic solvent.

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8 of 8 WILEY Organometallic Chemistry

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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