Journal of Molecular Liquids 336 (2021) 116329



Contents lists available at ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

Ionic liquids containing plant derived benzoate as anions, exhibiting supramolecular polymeric aggregation: Impact of the aggregation on organic catalysis in aqueous medium



Muhammad Naveed Javed ^a, Imran Ali Hashmi ^a, Shoaib Muhammad ^a, Ahmed Bari ^b, Syed Ghulam Musharraf ^c, Syed Junaid Mahmood ^d, Saima Javed ^a, Firdous Imran Ali ^{a,*}, Faisal Rafique ^e, Muhammad Amjad Ilyas ^e, Waqas Ahmed Waseem ^a

^a Department of Chemistry, University of Karachi, Main University Road, Karachi - 75270, Sindh, Pakistan

^b Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia

^c H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences (ICCBS), Main University Road, Karachi - 75270, Sindh, Pakistan

^d PCSIR Labs Complex, Karachi 75280, Pakistan

^e Department of Applied Physics, University of Karachi, Main University Road, Karachi - 75270, Sindh, Pakistan

ARTICLE INFO

Article history: Received 29 September 2020 Revised 26 March 2021 Accepted 24 April 2021 Available online 28 April 2021

Keywords: Ionic liquids Supramolecular polymeric aggregation Tetrahydrobenzo[b]pyran Benzoates Catalytic activity

ABSTRACT

Naturally occurring benzoic acid (BA) derived anions have been used to prepare halogen free hydrophilic ionic liquids (ILs **1–4**). The supramolecular polymeric aggregation behaviour of these ILs has been studied through high-resolution electron spray ionization mass spectrometry (HR-ESI-MS). Furthermore, these ILs were applied as catalyst/phase transfer catalyst in the synthesis of tetrahydrobenzo[b]pyran and its derivatives. These reactions were conducted in aqueous medium under ultrasound assistance. The results suggested that *1-ethyl-3-methylimidazolium 2-hydroxybenzoate* (**IL-1**) was a highly efficient catalyst yielding 86.9% product in 30 min. In addition, the impact of aggregation behaviour of ILs on their catalytic activity was also investigated.

© 2021 Elsevier B.V. All rights reserved.

1. Introduction

The reaction medium and catalyst both play a significant role in many organic reactions [1]. Selection of suitable reaction media is one of the crucial conditions among the other important variables for organic transformations [2]. Many researchers are involved in modifying the reaction medium to enhance efficiency of organic reactions in terms of time, yield and conditions besides curtailing toxicity levels. The need of environmentally safe and clean procedures for organic synthesis is demanded widely to overcome the diverse effects on the ecosystem [3]. Recently, we employed a variety of ionic liquids (ILs) as effective catalysts in C-C bond forming reactions and as metal extracting agents from water due to their intrinsic properties associated with these unique materials [4–6].

ILs or molten salts exhibit negligible vapor pressure and bulk non-flammability [7]. These features make them green substitutions of volatile organic solvents and applications of ILs as reaction media or as catalyst in the organic reactions is well documented in

* Corresponding author. E-mail address: firdous@uok.edu.pk (F. Imran Ali). literature [7–9]. Since, on one hand above mentioned properties of ILs are responsible to reduce risk towards air pollution but halide containing ILs pose a serious threat of water contamination via accidental spill or waste disposal [10–13]. Studies reveal that imidazolium is the less toxic cation among other nitrogen containing cation like pyridinium, ammonium etc. The studied data further disclose that toxicity of ILs is related to size of alkyl chain appended to cation or anion, longer the alkyl chain greater the toxicity [14]. Hydrophobic ILs with bigger alkyl moiety can release these longer alkyl chains that can penetrate through cell membrane and act as neurotoxin during metabolism. On the other hand, water-soluble ILs containing halogens may release HCl or HF in water due to hydrolysis [11–12]. Boething *et. al.* [15–16] have provided guidelines regarding biodegradability of organic compounds.

In the light of environmental concerns and solubility of ILs, we have prepared halogen free hydrophilic ILs using imidazolium cation with smaller side chains i.e. methyl and ethyl and plant based benzoic acid (BA) anions. These include two phenolic acids and two aromatic amino acids; a) the pant hormone salicylic acid or *ortho*-Hydroxy benzoic acid (SA, oHBA or 2-HBA) naturally found in *Filipendula ulmaria* and many food items i.e. olive oil, nuts,

tea, meat, fish, eggs, coffee etc.; b) *p*-hydroxybenzoic acid (*p*HBA or 4-HBA) naturally found in *Cocos nucifera*, *Spongiochloris spongiosa* etc.; c) Anthranilic acid or *ortho*-amino benzoic acid (AA, 2-ABA, *o*ABA) naturally occur in all living species ranging from bacteria to homo sapiens and d) *p*-amino benzoic acid (*p*ABA or 4-ABA), a significant component of folic acid and naturally occur in a wide range of food items including eggs, meat, grains etc [17–20]. Another reason for picking substituted benzoates, as anions are evidence of cluster formation by these anion in gaseous state [5–6,21–22].

ILs display supramolecular polymeric aggregation behavior due to non-covalent interactions especially electrostatic forces and hydrogen bonding [21–22]. Since, the formation of aggregates in the ILs with organic anions is rare. We have previously observed that unlike halogens, phenols do not exhibit cluster formation. But benzoates have significant potential of aggregate formation and is detectable through ESI-MS. Molecular self assemblies resulting into aggregation, influence the effectiveness of catalyst in chemical reactions [21]. But, investigation on relationship between aggregation behaviour and catalytic activity of IL in organic reactions is infrequent. Supramolecular self-assembled cluster formation ability beside unique physio-chemical properties of ILs i.e. thermal stability, non-volatility, non-flammability, ease of handling and recyclability makes them potential candidates for catalysis [7–9].

In continuation of our previous work [4,6], we here report the relationship between the supramolecular aggregation behavior and catalytic activity of four newly synthesized hydrophilic ILs (1–4). The synthesis of tetrahydrobenzo[b]pyran by condensation of aromatic aldehyde, dimedone and malononitrile catalyzed by ILs 1–4 under ultrasonic assistance in aqueous media carried out. Synthesis of tetrahydrobenzo[b]pyran and its analogues involve Knoevenagel condensation and Michael addition reactions, two important base catalysed C-C bond forming reactions. The results indicated that, aggregate formation potential, thermal stability and catalytic activity of ILs depends on the position and nature of substituent on benzoate anion.

2. Methods and materials

2.1. General

For all chemical reactions, oven dried apparatus was used. All commercially available chemicals were used without any additional purification. A rotary evaporator was used for solvent evaporation maintaining water bath temperature 45 °C. Pre-coated aluminium plates, Kieselgel 60, F254, 0.25 mm, e. Merck, Darmstadt, Germany was used for thin layer chromatography (TLC). NMR (¹H & ¹³C) were obtained from AVANCE AV-700 and AVANCE AV-175 BRUKER. An AB SCIEX QSTA R XL LCMSMS Q-Tof was used for high resolution electron spray ionization mass spectrometry (HR-ESI-MS). FSF-020S 220 V/50 Hz was used for ultrasound. Thermogravimetric analysis (TGA) were obtained from a Mettler Toledo (TGA/SDTA 851). TGA of ILs (10 mg \pm 0.1 $\mu g)$ was conducted at isothermal mode (100 °C to 500 °C at heating rate of 5 °C/min, N₂ flow 60 mL/min, platinum pan). pH experiments were recorded using JENCO VisionPlus pH6175 instrument. Moisture content recoreded on Mettler Toledo Karl Fischer titrator Compact V30S serial # B824972927 (version 5.2.0). Stuart Digital Melting Apparatus SMP 10 was used for melting point (M.p.) analysis.

2.2. Synthesis of 1-ethyl-3-methylimidazolium iodide [EMIM]I

Then 0.3 mol ethyl iodide (EtI) in a suitable amount of tetrahydrofuran (THF) was added dropwise in an ice cooled round bottom flask containing 0.3 mol methylimidazole. After complete addition of EtI, the ice bath was removed and reaction mixture was stirred for one hour at room temperature. Reaction was monitored through TLC using pre-coated silica plates. On completion of reaction, the solvent was evaporated on a rotary vacuum. White hygroscopic solid obtain in 97% yield. M.p. 79 °C. The product was identified through comparison of spectral and physical data with published literature [23], Moisture content = 2.11%.

2.3. General Ion-Exchange metathesis method (GIEMM) for ILs 1-4:

In a two neck round bottomed flask, a mixture of sodium bicarbonate (20 mmol) and respective benzoic acid (20 mmol) in water was taken followed by addition of 1-ethyl-3-methylimidazolium iodide (20 mmol). The reaction was stirred for 30 min at room temperature and then water was evaporated on a rotary evaporator. After removal of water, cold absolute ethanol was added to reaction mixture. Insoluble inorganic salt was removed by filtration/ decantation and ethanolic solution was subjected to evaporation to obtain pure desired product.

2.4. Synthesis of 1-ethyl-3-methylimidazolium 2-hydroxybenzoate (IL-1):

The IL-1 was prepared as described in section 2.3. A white coloured highly hygroscopic product was obtained. The product was immediately stored in a desiccator to protect from moisture. Yield: 95.2%, Moisture content = 10.28%.

¹*H NMR* (DMSO *d*₆, 700 MHz) *δ* ppm: 16.02 (s, 1H), 9.18 (s, 1H), 7.79 (s, 1H), 7.71 (s, 1H), 7.68 (d, *J* = 7.35, 1H), 7.15 (t, *J* = 7.63, 1H), 6.63 (d, *J* = 8.33, 1H), 6.60 (d, *J* = 7.21 Hz, 1H), 4.19 (q, *J* = 7.21, 2H), 3.85 (s, 3H), 1.41 (t, *J* = 7.21, 3H).

¹³C NMR (DMSO *d*₆, **700** MHz) δ ppm: 172.38, 163.09, 136.74, 131.94, 130.47, 124.01, 122.42, 120.73, 116.58, 44.59, 36.19, 15.59.

HR-ESI-MS + ve: m/z 111.0915 [calcd. m/z 111.0922 for C₆H₁₁N²₂]; m/z 359.2079 [calcd. m/z 359.2083 for C₁₉H₂₇N₄O³₃].

HR-ESI-MS -ve: m/z 137.0242 [calcd. m/z 137.0238 for $C_7H_5O_3$]; m/z 275.0560 [calcd. m/z 275.0555 for $(C_{14}H_{10}O_6 + H)^-$]; m/z 297.0380 [calcd. m/z 297.0375 for $(C_{14}H_{10}O_6 + Na)^-$]; m/z 385.1404 [calcd. m/z 385.1399 for $C_{20}H_{21}N_2O_6^-$].

FTIR: 3421.72 (phenolic OH), 2976.16 (C-H stretch), 1639.49 (C = O), 1577.77 (C = N imidazole ring), 1489.05 (C = C imidazole ring), 1386.82 (C-O), 1163.08 (C-C).

2.5. Synthesis of 1-ethyl-3-methylimidazolium 4-hydroxybenzoate (IL-2):

The IL-2 was prepared as described in section 2.3. The pure IL is white coloured hygroscopic solid product was obtained. The product was stored in a desiccator to protect from moisture. Yield: 97.6%, Moisture content = 19.46%

¹*H NMR* (DMSO *d*₆, 700 MHz) δ ppm: 9.25 (s, 1H), 7.78 (s, 1H), 7.74 (d, *J* = 8.12, 2H), 7.69 (s, 1H), 6.69 (d, *J* = 8.19 Hz, 2H), 4.17 (q, *J* = 7.21, 2H), 3.83 (s, 3H), 1.37 (t, *J* = 7.28, 3H).

¹³C NMR (DMSO *d*₆, 700 MHz) δ ppm: 171.46, 159.67, 136.82, 131.23, 123.97, 122.38, 114.42, 44.58, 36.20, 15.61.

HR-ESI-MS + ve: m/z 111.0925 [calcd. m/z 111.0922 for C₆H₁₁N²₂]; m/z 359.2085 [calcd. m/z 359.2083 for C₁₉H₂₇N₄O³₃].

HR-ESI-MS -ve: m/z 137.0244 [calcd. m/z 137.0238 for $C_7H_5O_3$]; m/z 275.0548 [calcd. m/z 275.0555 for $(C_{14}H_{10}O_6 + H)^-$]; m/z 385.1391 [calcd. m/z 385.1399 for $C_{20}H_{21}N_2O_6^-$]; m/z 633.2552 [calcd. m/z 633.2560 for $C_{33}H_{37}N_4O_9^-$].

FTIR: 3431.36 (phenolic OH), 2970.00 (C-H stretch), 1639.49 (C = O), 1462.04 (C = C imidazole ring), 1381.03 (C-O), 1134.14 (C-C).

2.6. Synthesis of 1-ethyl-3-methylimidazolium 2-aminobenzoate (IL-3):

The IL-3 was prepared as described in section 2.3. The pure IL is light reddish brown coloured hygroscopic solid substance was obtained. The product was stored in a desiccator to protect from moisture. Yield is 93.4%, Moisture content = 8.62%

¹*H NMR* (DMSO *d*₆, 700 MHz) δ ppm: 9.26 (s, 1H), 7.79 (s, 1H), 7.74 (s, 1H), 7.71 (s, 1H), 6.942 (s, 1H), 6.72 (s, 2H), 6.51 (s, 1H), 6.36 (d, *J* = 5.39 Hz, 1H), 4.20 (s, 2H), 3.85 (s, 3H), 1.41 (d, broad, 3H).

3H).
 ¹³C NMR (DMSO d₆, 700 MHz) δ ppm: 173.04,150.59, 136.87, 132.21, 130.10, 124.02, 122.42, 121.16, 115.52, 114.12, 44.57, 36.16, 15.61.

HR-ESI-MS + ve: m/z 111.0929 [calcd. m/z 111.0922 for C₆H₁₁N⁺₂]; m/z 358.2251 [calcd. m/z 358.2242for C₁₉H₂₈N₅O⁺₂].

HR-ESI-MS -ve: m/z 136.0400 [calcd. m/z 136.0398 for $C_7H_6NO_2^-$]; m/z 273.0883 [calcd. m/z 273.0875for ($C_{14}H_{12}N_2-O_4 + H_1^-$]; m/z 295.0703 [calcd. m/z 295.0694 for ($C_{14}H_{12}N_2-O_4 + Na_1^-$]; m/z 454.1000 [calcd. m/z 454.0991 for ($C_{21}H_{18}N_3O_6 + Na_2^-$]; m/z 613.1294 [calcd. m/z 613.1287 for ($C_{28}H_{24}N_4O_8 + Na_3^-$]; m/z 772.1585 [calcd. m/z 772.1583 for ($C_{35}H_{30}N_5O_{10} + Na_4^-$].

FTIR: 3441.01 (H₂O masked NH₂), 1622.13 (Conjugated C = O), 1523.76 (C = N), 1379.10 (C = C), 1136.07 (C-O).

2.7. Synthesis of 1-ethyl-3-methylimidazolium 4-aminobenzoate (IL-4):

The IL-4 was prepared as described in section 2.3. The pure IL is light greenish brown coloured hygroscopic solid was obtained. The product was stored immediately in a desiccator to protect from moisture, Yield: 98.2%, Moisture content = 15.61%

¹*H NMR* (DMSO d_6 , 700 MHz) δ ppm: 9.26 (s, 1H), 7.79 (s, 1H), 7.70 (s, 1H), 7.59 (d, J = 8.05, 2H), 6.42 (d, J = 8.33 Hz, 2H), 5.13 (s, 2H), 4.19 (q, J = 7.28, 2H), 3.85 (s, 3H), 1.40 (t, J = 7.28, 3H).

¹³*C* NMR (DMSO *d*₆, **700** MHz) *δ* ppm: 171.67, 149.96, 136.87, 130.94, 124.01, 122.41, 112.63, 44.57, 36.17, 15.62.

HR-ESI-MS + ve: m/z 111.0913 [calcd. m/z 111.0922 for C₆H₁₁N⁺₂]; m/z 358.2235 [calcd. m/z 358.2242for C₁₉H₂₈N₅O⁺₂].

HR-ESI-MS -ve: m/z 136.0391 [calcd. m/z 136.0398 for $C_7H_6NO_2^-$]; m/z 273.0870 [calcd. m/z 273.0875for ($C_{14}H_{12}N_2-O_4 + H^-$]; m/z 295.0689 [calcd. m/z 295.0694 for ($C_{14}H_{12}N_2-O_4 + Na^-$]; m/z 383.1725 [calcd. m/z 383.1719 for $C_{20}H_{23}N_4O_4^-$].

FTIR: 3462.22 (H₂O masked NH₂), 1639.49 (Conjugated C = O), 1386.82 (C = C), 1136.07 (C-O).

2.8. General method (GM) for tetrahydrobenzo[b]pyrans:

In a round bottomed flask an aromatic aldehyde (9 mmol), malononitrile (9 mmol) and dimedone (9 mmol) were mixed in 10–20 mL of water and IL-1 (4 mol %) was added. The reaction mixture was then subjected to irradiation under ultrasound (Table 2). The solid insoluble product was started to appear within minutes. Completion of reaction was confirmed through TLC. After completion of reaction as indicated by TLC, the solid product was filtered, washed with deionized water and dried. Recrystallization of products was carried out with 95% ethanol. Comparisons of pure product with publish literature and TLC with authentic sample confirmed the formation.

3. Results & discussion

3.1. Synthesis and characterization of ILs (1-4)

The most commonly investigated type of cations in ILs are N,N'dialkylimidazolium and 1-alkyl-3-methylimidazolium. Quaternization of methylimidazole using equimolar amount of ethyl iodide in THF yielded 1-ethyl-3-methylimidazolium iodide [EMIM][I] as a white hygroscopic solid in excellent yield under mild condition [23]. The ¹H NMR spectrum of [EMIM][I] exhibited a downfield signal at δ 9.2 ppm, suggesting the formation of imidazolium moiety. In addition, ¹³C NMR spectra showing signal at δ 136 ppm confirms synthesis of imidazolium ion. As our strategy, to prepare halogen free, environmentally benign anion with a diffused or delocalized negative charge, Group-I metal salts of substituted benzoates were prepared by reacting corresponding naturally occurring benzoic acids (o-HBA, p-HBA, o-ABA and p-ABA) with sodium bicarbonate in situ during ion exchange metathesis (Scheme 1). Sodium bicarbonate (instead of sodium hydroxide) was used to avoid N-heterocyclic carbene (NHC) formation. Sodium salts were used to provide strong preference to counter ion i.e. iodide for optimum ion exchange.

Post synthetic purification of ILs, especially for hydrophilic ILs, is very challenging due to their inherent properties. For removal of alkali metal and halide salt, we have used cold absolute ethanol (vide experimental). For the removal of water, neither chemical drying agents nor molecular sieves or sorbents were used, as these are the main sources of particulate contaminations of ILs. Synthesis of ILs (1-4) at room temperature via ion exchange of metathesis in water fulfilled principles of green and sustainable chemistry. For characterization of synthesized ILs, ¹H NMR, ¹³C NMR and HR-ESI-MS techniques were employed. IL-1 displayed a downfield singlet at δ 16.17, indicating intermolecular/intramolecular Hbonding. In addition, ¹³C NMR spectra of ILs (1-4) displayed carboxylate carbon around δ 171–173 ppm (vide Supplementary Infor*mation* Figure-S1). FTIR spectra of ILs **1–4** displayed a broad signal in the range of 3440-3460 cm⁻¹, indicative of H-bonded OH (Figure S14-S17). In addition, a signal with medium intensity around 1620-1640 affirms presence of conjugated carbonyl of benzoate.

3.2. Thermal properties of ILs:

The high onset decomposition temperature (T_{onset}) defines the thermal stability of ILs [24]. The thermal stability of ILs mostly were depended on the structure of ions, the cations and anions. Literature shows that, there is a close relationship between thermal stability and anion type because by varying the anions, the decomposition temperature of ILs was changed from 200 to 400 °C [24-25]. The thermal stabilities of newly synthesized ILs (1-4) were investigated via thermogravimetric analyser. Thermogravimetric analysis (TGA) was performed at temperature ranging from 100 °C to 500 °C at heating rate of 5 °C/min under N_2 gas flow. The thermogram (Figure-1) shows start of weight lose at 100 ^{0}C due to water content, indicated by Karl Fischer titration (section). Literature revealed that, imidazolium cations were more stable as compared to tetraalkyl ammonium cations [26–27]. Herein, we evaluated the impact of ortho/para hydroxy and ortho/para amino substituted benzoate-based anions on thermal stability of ILs 1-4. It was evident from data that the thermal stability increases in the order of IL-3 > IL-4 > IL-2 > IL-1 showing Tonset at 305 °C, 290 °C, 245 °C and 238 °C, respectively. These results were suggestive of comparatively higher thermal stability of amino benzoates. This was because the size, and molar mass of amino benzoates were also increased. Hydrogen bonding can be another contributing

Catalyst evaluations for tetrahydrobenzo[b]pyrans synthesis^a.

	Catalyst (mol%)	Conditions	Time (min)	Yield (%) ^b
1	None	H ₂ O, 50 °C	180	Traces [35]
2	None	H ₂ O, Reflux	360	[36]
3	None	Ethanol, Reflux	360	[37]
4	None))) ^c , H ₂ O	20	[36]
5	None))), Ethanol	150	[37]
6	2 mol %))), H ₂ O, 45 °C	30	
6a	IL-1			84.67
6b	IL-2			84.55
6c	IL-3			78.96
6d	IL-4			82.56
7	IL-1))), H ₂ O, 45 °C	30	
7a	4 mol %			86.13
7b	6 mol %			86.41
7c	8 mol %			86.74
7d	10 mol %			87.10

^a Reaction Conditions: Benzaldehyde (9 mmol); Dimedone (9 mmol); Malononitrile (9 mmol); ILs (mol %); H₂O; 45 °C. ^bIsolated yield. ^c))) = Ultrasound irradiation.

Table 2 Preparation of tetrahydrobenzo[b]pyrans analogues using IL-1 (4 mol %)^a.

Sr No.	R ₁	R ₂	Time (min)	Yield (%) ^[b]	M.p. °C (lit.)
1	Н	Н	30	86.93	231 (233–234) [38]
2	OH	Н	25	84.23	235 (230–232) [39]
3	Н	OH	30	85.97	226 (220–222) [40]
4	OCH ₃	Н	15	85.76	187 (188–190) [41]
5	OH	OCH ₃	20	86.90	228 (230–232) [42]
6	OCH ₃	OH	20	86.44	240 (238–239) [43]
7	Н	Cl	30	86.13	215 (214–215) [40]
8	Н	Br	30	83.68	204 (202–203) [40]
9	Н	F	15	83.12	191 (191–193) [39]
10	Cl	Н	20	87.19	232 (230–231) [38]
11	Br	Н	25	87.25	290 (289–291) [41]
12	Н	$N(CH_3)_2$	35	84.14	208–210 (212–213) [44]

^a Reaction Conditions: Benzaldehyde (9 mmol); Dimedone (9 mmol); Malononitrile (9 mmol); IL-01 (4 mol %); H₂O; 45 °C. ^bIsolated yield.



Scheme 1. Synthesis of ILs (1-4).

factor. After decomposition, the residual amounts of 3-ethyl-1methylimidazolium aminobenzoates were also higher than those of 1-ethyl-3-methylimidazolium hydroxybenzoates, as shown in Fig. 1.

3.3. Aggregation behavior of ILs:

ILs exhibit supramolecular polymeric aggregation behaviour [28]. Therefore, ILs **1–4** were subjected to HR-ESI-MS to investigate cluster formation. Previously, through ESI-MS, we observed that ILs containing phenolate anions [4] did not show self-assembly to form clusters/aggregates while benzoates containing ILs did [6]. The results are in agreement with the previous results i.e. anionanion aggregates support it (Table-4). Figures (S9-S12) in SI displayed

that ILs (1–4) exhibited peaks around m/z 111 corresponding to C⁺ (C₆H₁₁N₂⁺). Furthermore, it also showed singly positive charge aggregation around m/z 359 which were attributed to C₂A⁺. However, HR-ESI-MS (negative) of IL-1 exhibited a peak at m/z 137.0242, which represents to A⁻ (C₇H₅O₃), along with singly negative charged aggregates, which corresponds to CA₂. In addition to this, anion-anion cluster formation with additional proton [A₂ + H]⁻ or sodium [A₂ + Na]⁻, observed at m/z 275.0560 and m/z 297.0380 respectively (as shown in Fig. 2). Similar behaviour was witnessed in ILs **2–4** (Figs. 3–5).

The overall HR-ESI-MS results were suggestive of two different types of supramolecular polymeric aggregates i.e. usual cationsanions aggregates and anion-anion aggregates. Presence of remaining sodium ion (inorganic salt) in ILs was also obvious. Thus, additional purification (*vide experimental*) was carried out and impurity



Fig. 1. Thermal behavior of benzoates based ILs.



Fig. 2. HR-ESI-MS of IL-1 in negative mode exhibited singly charged negative aggregates.

free ILs were obtained and verified through ¹H NMR spectra (SI). This behavior of ILs was correlated with catalytic activity in the synthesis of tetrahydrobenzo[b]pyran derivatives.

3.4. Catalytic activity of ILs towards the synthesis of tetrahydrobenzo [b]Pyrans:

Application of ILs in the chemical reactions has been undertaken in different ways including as a reaction medium, as a phase transfer catalyst, as a co-catalyst / catalyst activator and many more [29–30]. ILs with modified anions exhibiting potential for H-bonding can serve as conjugate bases and phase transfer catalyst in organic synthesis. Furthermore, the use of IL catalyst in combination of solvent is reported to be more effective [31–32]. Due to the high cost of ILs, water was selected as solvent and ILs were investigated only for their catalytic activity. For model reaction, benzaldehyde, dimedone and malononitrile were reacted to prepare tetrahydrobenzo[b]pyran, using different ILs (Scheme 2).

Literature shows that, ultrasound can break the hydrogen bond, depending on counter anion and accelerates ILs catalysed reaction. Fusion of ultrasound with ILs has proved to be ideal combination in the organic synthesis especially multicomponent reactions [33–34]. The results of reactions under ultrasonic conditions are depicted in Table 1. The results presented in table-1 clearly indicate **IL-1** as the best catalyst for these reactions at 45 °C under ultrasonic irradiation.

The ILs 1 – 4 contains different acidic and basic functional groups in anions. Moreover, the catalytic reactions are carried



Fig. 3. HR-ESI-MS of IL-2 in negative mode exhibited series of singly charged negative aggregates.



Fig. 4. HR-ESI-MS of IL-3 in negative mode exhibited series of singly charged anion aggregates.

out in water, therefore, the activity of the catalyst could be related to the pH. Hence, we check the pH of the reaction medium before (pH = 6.59) and after addition of IL-4 (pH = 6.44) but no significant change in pH observed.



Fig. 5. HR-ESI-MS of IL-4 in negative mode exhibited singly charged negative aggregates.



Scheme 2. Preparation of tetrahydrobenzo[b]pyran using IL under ultrasound.

The scope of methodology was examined using IL-1 (4%) with 12 different aromatic aldehydes resulting in excellent yields (Table 2). Halogenated aldehydes at meta position (entry 10 and 11) furnish excellent yields suggesting presence of electron with-drawing group at meta position may enhance the yield of product.



There are different approaches reported in literature for tetrahydrobenzo[b]pyrans synthesis using different materials as catalyst and reaction medium with or without solvent. All previously reported procedures exhibit harsh reaction conditions (Table 3). However, in this study recycled and reusable greener catalyst was used under ultrasonic irradiation with high selectivity, mild reaction conditions, and short reaction time with simple and effortless work-up procedures. Table 3 shows the assessment and comparison of our study with previously reported work.

3.5. Recyclability of the Catalyst:

A greater advantage of ILs is their recyclability. Although, recyclability of water miscible ILs is challenging, especially for the removal of inorganic by-products. After every run, the IL-1 was recycled. Solid product was removed through filtration and filtrate containing IL was evaporated and washed with cold ethanol and repeatedly used further for four times and no considerable loss of its efficiency and activity was observed (Fig. 6). Recycling of 4 mol % of water miscible IL is quite difficult. Therefore, we conducted higher concentration experiments to investigate recyclability of the catalyst.

Table 3

Evaluation of existing work with previously reported methodologies for the model reaction among malononitrile, dimedone and benzaldehyde.

Sr No.	Catalyst (mol/g)	Condition	Time (min)	Yield (%) ^[a]	Ref
1	MgFe ₂ O ₄ nanoparticles	EtOH,))) ^[c] , 65 °C	12	74	[45]
2	$MNPs-PhSO_3H$ (0.01 g)	H ₂ O/ EtOH (1:1), 100 °C	10	91	[46]
3	[Py-SO ₃ H]Cl (10%)	Solvent free, 95 °C	8	91	[47]
4	$PPA-SiO_2$ (0.1 g)	H ₂ O, Reflux	13	80	[48]
5	$Fe_3O_4@SiO_2@TiO_2 (0.01 g)$	Solvent free, 100 °C	20	93	[44]
6	[ADPPY][OH] (10 mol%)	H ₂ O, rt	10	95	[52]
7	IL-1 (4 mol %)	H ₂ O,))), 45 °C	30	86.13	_ [b]

^aIsolated Yield. ^bOur Work. ^c))) = Ultrasound irradiation.



Fig. 6. Recycling of IL-1 in the model reaction of tetrahydrobenzo[b]pyran.

3.6. Conductivity of ILs:

To further ascertain the formation of aggregates in IL 1–4 electrical conductivities of these ILs along with parent cation [EMIM][I] were recorded at different concentrations of ILs in water. Critical aggregation concentration (CAC) and degree of ionization (α) were determined using method reported by Wang et. al. [54]. The results are presented in Fig. 7 and Table S13.

The concentration at point of interaction of two linear fragments corresponds to CAC while α is the ratio of slope of linear lines above and below CAC. The higher CAC value (1100 mmol. dm⁻³) in IL-3 indicates that negative ion is loosely bonded to cation. However, lowest α value (0.241) in IL-3 supports presence of anion-anion [A₂ + H]⁻ aggregation. These finding fully support the HR-ESI-MS observation showing highest relative intensity of [A₂ + H]⁻ Fig. 3.

3.7. Relationship of thermal stability, Conductivity, and aggregation behavior with catalytic activity of ILs:

The effect of anions on catalytic behavior of ILs was investigated. ILs 1-2 (hydroxy benzoates) furnished excellent result in the model reaction. On the other hand, ILs **3–4** (amino benzoates) offered moderate yield in tetrahydrobenzo[b]pyrans synthesis. The results also revealed that, there is a close relationship between thermal stability and catalytic activity of ILs as shown in Table 4. Moreover, IL-**1** that showed intermolecular/intramolecular hydrogen bonding (*Supplementary Information* Figure S1) exhibited comparatively lower thermal stability and enhanced catalytic activity. This was attributed to strong ion packing between cation and anion. The overall results suggested that, anion-anion interactions occur in hydroxyl/amino benzoates influence catalytic activity. Furthermore, it was also realized that greater the anion-anion interaction, weaker the cation–anion packing and reduced catalytic activity of ILs.

3.8. Proposed Mechanism:

In 2009, Chakraborti *et. al.* [49] reported a dual role (electrophilic and nucleophilic) of imidazolium based ILs as catalyst in the organic reactions [49]. On the other hand, Gauchot *et. al.* [50] showed that anion of the ILs involves in the aldol condensation by activating aldehydes through hydrogen bonding. While Tao *et. al.* [51] demonstrated that deprotonation of C-2 proton of imidazolium moiety induces electrophilic activation to anhydride in the presence of DMF or DMSO [51]. In the light of these observations, results obtained from present study (especially that of IL-1) we have proposed a mechanism demonstrated in Scheme 3.

Here, the role of water cannot be excluded, as water is known to solvate ionic species. Cammarata et. al. carried out experiments on water-IL interaction and suggested the possibility of carboxylate anions binding with water in case of deliberate addition of water. Further, they experimentally proved that ILs, containing 1-butyl-3-methyl imidazolium as cation, capture water from the atmosphere with different types of anion [53].

4. Conclusion

In short, we have synthesized four new ILs **1–4**. Thermally stable and water-soluble hydroxy/amino benzoates anions paired with methyl alkyl imidazolium to furnish environmentally benign ILs as catalyst. In the present studies **IL-1** was found to be excellent catalyst. **IL-1** showed stronger supramolecular aggregation behaviour (possibly due to H-bonding) as exhibited in HR-ESI-MS



Fig. 7. Conductivity of ILs in aqueous medium.

Table 4

Correlation of thermal stabilit	, Conductivity at CAC, an	l relative intensity of ILs	(1-4) with catalytic	activity in tetrah	ydrobenzo[b]pyrans reactions.
---------------------------------	---------------------------	-----------------------------	----------------------	--------------------	-------------------------------

Relative Intensity (10 ⁵)		Conductivity at CAC	CAC	α	Tonset	Catalytic activit	у		
ILs	$[A_2 + H]^-$	[CA ₂] ⁻	$[C_2A_3]^-$	(mS/cm)	(mM)		(°C)	Time (min)	Yield (%)
IL-1	0.5	0.72	0	33	850	0.374	238	30	84.67
IL-2	0.8	0.5	0.21	38	760	0.364	245	30	84.55
IL-4	0.8	0.39	0	21	750	0.391	290	30	82.56
IL-3	1	0	0	30	1100	0.241	305	30	78.96



Scheme 3. Proposed mechanism for the synthesis of tetrahydrobenzo[b]pyran.

(*Supplementary information*; Figure S9) and ¹H NMR (*Supplementary information*; Figure S1), and in consistence with previously

reported results [5-6]. The less intense $[A^2 + H]^+$ signal, exhibiting anion-anion interaction is suggestive of intermolecular H-bonding.

On the basis of these observations, we can conclude that intermolecular H-bonding lowers thermal stability, reduces anionanion interaction and enhance catalytic activity.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors thank Research Centre, College of Pharmacy and Deanship of Scientific Research, King Saud University for supporting this study. The authors also thank Prof. Yanan Gao (Dalian Institute of Chemical Physics, Chinese Academy of Sciences, China) for their valuable comments and suggestions.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.molliq.2021.116329.

References

- [1] P. Liu, J.-W. Hao, L.-P. Mo, Z.-H. Zhang, Recent advances in the application of deep eutectic solvents as sustainable media as well as catalysts in organic reactions, RSC Advances 5 (2015) 48675–48704.
- [2] P.E. Savage, Organic chemical reactions in supercritical water, Chemical reviews 99 (1999) 603–622.
- [3] M.C. Bubalo, K. Radošević, I.R. Redovniković, J. Halambek, V.G. Srček, A brief overview of the potential environmental hazards of ionic liquids, Ecotoxicology and environmental safety 99 (2014) 1–12.
- [4] M.N. Javed, S. Muhammad, I.A. Hashmi, A. Bari, S.G. Musharraf, F.I. Ali, Newly designed pyridine and piperidine based lonic Liquids: Aggregation behavior in ESI-MS and catalytic activity in CC bond formation reactions, Journal of Molecular Liquids 272 (2018) 84–91.
 [5] S. Muhammad, F.I. Ali, A. Aslam, V.U. Ahmad, A.N. Khan, I.A. Hashmi, Synthesis
- [5] S. Muhammad, F.I. Ali, A. Aslam, V.U. Ahmad, A.N. Khan, I.A. Hashmi, Synthesis of Thiosalicylate based Hydrophobic Ionic Liquids and their Applications in Metal Extraction from aqueous solutions, Journal of the Chemical Society of Pakistan 37 (2015).
- [6] S. Muhammad, M.N. Javed, F.I. Ali, A. Bari, I.A. Hashmi, Supramolecular polymeric aggregation behavior and its impact on catalytic properties of imidazolium based hydrophilic ionic liquids, Journal of Molecular Liquids 300 (2020) 112372.
- [7] T. Welton, Room-Temperature Ionic liquids, solvents for synthesis and catalysis, Chemical Review 99 (1999) 2071–2083.
- [8] R.L. Vekariya, A review of ionic liquids: Applications towards catalytic organic transformations, Journal of Molecular Liquids 227 (2017) 44–60.
- [9] Z.S. Qureshi, K.M. Deshmukh, B.M. Bhanage, Applications of ionic liquids in organic synthesis and catalysis, Clean Technologies and Environmental Policy 16 (2014) 1487–1513.
- [10] A. Oskarsson, M.C. Wright, Ionic Liquids: New Emerging Pollutants, Similarities with Perfluorinated Alkyl Substances, PFASs, Environmental Science and Technology 53 (2019) 10539–10541.
- [11] R.P. Swatloski, J.D. Holbrey, R.D. Rogers, Ionic Liquids are not always green: hydrolysis of 1-butyl-3-methyl-imidazolium hexafluorophosphate, Green Chemistry 2 (2003) 361–363.
- [12] M.G. Freire, C.M.S.S. Neves, I.M. Marrucho, J.A.P. Coutinho, A.M. Fernandes, Hydrolysis of tetrafluoroborate and hexafluorophosphate counter ions in imidazolium-based ionic liquids, Journal of Physical Chemistry A 114 (2010) 3744–3749.
- [13] S. Stolte, J. Arning, U. Bottin-Weber, M. Matzke, F. Stock, K. Thiele, M. Uredingen, U. Welz-Biermann, B. Jastorff, J. Ranke, Anion effects on cytotoxicity of ionic liquids, Green Chemistry 8 (2006) 621–629.
- [14] C. Chul-Woong, P.T.P. Thi, J. You-Chul, K. Vijayaraghavan, C. Woo-Seok, Y. Yeong-Sang, Toxicity of imidazolium salt with anion bromide to a phytoplankton *Selenastrum capricornutum*: Effect of alkyl-chain length, Chemosphere 69 (2007) 1003–1007.
- [15] R.S. Boethling, Cationic Surfactants, in Surfactant Science Series, Marcel Dekker, New York 53 (1994) 95–135.
- [16] P.H. Howard, R.S. Boethling, W. Stiteler, W. Meylan, J. Beauman, Development of a predictive model for biodegradability based on BIODEG, the evaluated biodegradation data base, Science Total Environment 109–110 (1991) 635– 641.
- [17] A. Wood, G. Baxter, F. Thies, J. Kyle, G. Duthie, A systematic review of salicylates in foods: estimated daily intake of a Scottish population, *Molecular Nutrition and Food Research* 55 (Suppl 1) (2011) S7–S14.

- [18] A.R. Swain, S.P. Dutton, A.S. Truswell, Salicylates in foods, Journal of American Dietetic association 85 (1985) 950–960.
- [19] K. Shahriar, J.M. Robin, Monocyclic Phenolic Acids, Hydroxy- and Polyhydroxybenzoic Acids: Occurrence and Recent Bioactivity Studies, Molecules 15 (2010) 7985–8005.
- [20] A. Kluczyk, T. Popek, T. Kiyota, P. de Macedo, P. Stefanowicz, C. Lazar, Y. Konishi, Yasuo, Drug Evolution: p-Aminobenzoic Acid as a Building Block, Current Medicinal Chemistry 9 (2002) 1871–1892.
- [21] T. Xin, L. Xiaomin, Y. Xiaokian, Z. Yaqin, J. Kun, Theoretical Study of Ionic Liquid Clusters Catalytic Effect on the Fixation of CO₂, Industrial & Engineering Chemistry Research 58 (2019) 34–43.
- [22] N. Thomas, Z. Dimitri, S. Anne, V. Alaxendar, L. Ralf, Cationic clustering influences the phase behaviour of ionic liquids, Scientific Reports 8 (2018) 14753.
- [23] G.A. Anthony, A.C. Penelop, P.D. Martin, R.S. Kenneth, W. Thomas, Evidence for Hydrogen Bonding in Solutions of 1-Ethyl-3- methylimidazolium Halides, and its Implications for Room-temperature Halogenoaluminate(III), Ionic Liquids, Journal of Chemical Society, Dalton Transaction (1994) 3405–3413.
- [24] Y. Cao, M. Tiancheng, Comprehensive Investigation on the Thermal Stability of 66 Ionic Liquids by Thermogravimetric Analysis, Industrial and Engineering Chemical Research 53 (2014) 8651–8664.
- [25] Y. Cao, M. Tiancheng, Stability of Ionic Liquids, in: S. Zhang (Ed.), Encyclopedia of Ionic Liquids, Springer, Singapore, 2020, https://doi.org/10.1007/978-981-10-6739-6_103-1.
- [26] L.N. Helen, L. Karen, H. Liesel, B.M. Alan, Thermal properties of imidazolium ionic liquids, Thermochimica Acta 357–358 (2000) 97–102.
- [27] Z. Ling, W. Ligang, Z. Shangru, Z. Dingwei, S. Jian, A. Qingda, Hydrogen bond promoted thermal stability enhancement of acetate based ionic liquid, Chinese Journal of Chemical Engineering 28 (2020) 1293–1301.
- [28] A.D.N. Brenno, S. John, The impressive chemistry, applications and features of ionic liquids: properties, catalysis & catalysts and trends, Journal of Brazilian Chemical Society 23 (2012) 987–1007.
- [29] P. Wasserschied, T. Welton (Eds.), Ionic Liquids in Synthesis, VCH Wiley, Weinheim, 2002.
- [30] D. Zhao, M. Wu, Y. Kou, E. Min, Ionic Liquids: Applications in Catalysis 74 (2002) 157–159.
- [31] R.A. Sheldon, Green solvents for sustainable organic synthesis: state of the art, Green Chemistry 7 (2005) 267–278.
- [32] N. Isambert, M. del, M.S. Duque, J.-C. Plaquevent, Y. Genisson, J. Rodriguez, T. Constantieux, Multicomponent reactions and ionic liquids: a perfect synergy for eco-compatible heterocyclic synthesis, Chemical Society Reviews 40 (2011) 1347–1357.
- [33] K. Li, T. Kobayashi, A FT-IR spectroscopic study of ultrasound effect on aqueous imidazole based ionic liquids having different counter ions, Ultrasonics Sonochemistry 28 (2016) 39–46.
- [34] G. Kaur, A. Sharma, B. Banerjee, Ultrasound and Ionic Liquid: An ideal Combination for Organic Transformations, Chemistry Select 3 (2018) 5283– 5295.
- [35] R. Baharfar, S. Asghari, N. Shariati, Green synthesis of 2-amino-3-cyclo-4Hchromenes in water using nano-silica bonded 5-N-propyl-octahydro-pyrtmido [1, 2-4] azepinium chloride as as effective and reusable nano catalyst, Journal of the Chilean Chemica; Society, 60 (2015) 2900-2904.
- [36] M. Esmaeilpour, J. Javidi, F. Dehghani, F.N. Dodeji, A green one-pot threecomponent synthesis of tetrahydrobenzo [b] pyran and 3, 4-dihydropyrano [c] chromene derivatives using a Fe 3 O 4@ SiO 2-imid-PMA n magnetic nanocatalyst under ultrasonic irradiation or reflux conditions, RSC Advances 34 (2015) 26625-26633.
- [37] N.M. Abd El-Rahman, R.M. Borik, Eco-friendly solvent-free synthesis of tetrahydrobenzo [b] pyran derivatives under microwave irradiation, World Applied Sciences Journal 31 (2014) 1–6.
- [38] D. Tahmassebi, J.A. Bryson, S.I. Binz, 1, 4-Diazabicyclo [2.2. 2] octane as an efficient catalyst for a clean, one-pot synthesis of tetrahydrobenzo [b] pyran derivatives via multicomponent reaction in aqueous media, Synthetic Communications, 41 (2011) 2701-2711.
 [39] D. Fang, D.; H.B. Zhang, Z. -L. Liu, Synthesis of 4H-benzopyrans catalyzed by
- [39] D. Fang, D.; H.B. Zhang, Z. –L. Liu, Synthesis of 4H-benzopyrans catalyzed by acyclic acidic ionic liquids in aqueous media, Journal of Heterocyclic Chemistry, 47 (2010) 63-67
- [40] W.-B. Sun, P. Zhang, J. Fan, S.-H. Chen, Z.-H. Zhang, Lithium bromide as a mild, efficient, and recyclable catalyst for the one-pot synthesis of tetrahydro-4 Hchromene derivatives in aqueous media, Synthetic Communications 40 (2010) 587–594.
- [41] M.R. Islami, E. Mosaddegh, Sulfur,; Silicon, Ce (SO4) 2. 4H2O as a Recyclable Catalyst for an Efficient, Simple, and Clean Synthesis of 4H-Benzo [b] pyrans, Phosphorous, Sulfur and Silicon and the Related Elements 184 (2009) 3134– 3138.
- [42] R. Balaskar, S. Gavade, M. Mane, P. Pabrekar, M. Shingare, D. Mane, Triethylammonium Acetate [TEAA]: An Efficient Catalyst for One Pot Synthesis of Tetrahydro-4H-chromene Derivatives, Letters in Organic Chemistry 8 (2011) 282.
- [43] A. Patra, T. Mahapatra, T Synthesis of tetrahydrobenzo [b] pyran derivatives catalysed by Aliquat[®] 336 in water under microwave irradiation, Journal of Chemical Research 34 (2010) 689–693.
- [44] A. Khazaei, F. Gholami, V. Khakyzadeh, A.R. Moosavi-Zare, J. Afsar, Magnetic core-shell titanium dioxide nanoparticles as an efficient catalyst for domino Knoevenagel-Michael-cyclocondensation reaction of malononitrile, various aldehydes and dimedone, RSC Advances 5 (2015) 14305–14310.

- [45] B. Eshtehardian, M. Rouhani, Z. Mirjafary, Green protocol for synthesis of MgFe 2 O 4 nanoparticles and study of their activity as an efficient catalyst for the synthesis of chromene and pyran derivatives under ultrasound irradiation, Journal of the Iranian Chemical Society 17 (2019) 1–13.
- [46] H.F. Niya, N. Hazeri, M.R. Kahkhaie, M.T. Maghsoodlou, Preparation and characterization of MNPs-PhSO 3 H as a heterogeneous catalyst for the synthesis of benzo [b] pyran and pyrano [3, 2-c] chromenes, Research on Chemical Intermediates 46 (2019) 1–20.
- [47] M.A. Zolfigol, A. Khazaei, A.R. Moosavi-Zare, J. Afsar, J.; V. Khakyzadeh, O. Khaledian, Knoevenagel-Michael-cyclocondensation Tandem Reaction of Malononitrile, Various Aldehydes and Dimedone Catalyzed by Sulfonic Acid Functionalized Pyridinium Chloride as a New Ionic Liquid and Catalyst, Journal of the Chinese Chemical Society, 62 (2015) 398-403
- [48] A. Davoodnia, S. Allameh, S. Fazli, N. Tavakoli-Hoseini, One-pot synthesis of 2amino-3-cyano-4-arylsubstituted tetrahydrobenzo [b] pyrans catalysed by silica gel-supported polyphosphoric acid (PPA-SiO 2) as an efficient and reusable catalyst, Chemical Papers 65 (2011) 714–720.

Journal of Molecular Liquids 336 (2021) 116329

- [49] A.K. Chakraborti, S.R. Roy, On catalysis by ionic liquids, Journal of the American Chemical Society 131 (2009) 6902–6903.
- [50] V. Gauchot, A.R. Schmitzer, Asymmetric aldol reaction catalyzed by the anion of an ionic liquid, The Journal of Organic Chemistry 77 (2012) 4917–4923.
- [51] Y. Tao, R. Dong, I.V. Pavlidis, B. Chen, T. Tan, Using imidazolium-based ionic liquids as dual solvent-catalysts for sustainable synthesis of vitamin esters: inspiration from bio-and organo-catalysis, Green Chemistry 18 (2016) 1240– 1248.
- [52] P.P. Salvi, A.M. Mandhare, A.S. Sartape, D.K. Pawar, S.H. Han, S.S. Kolekar, An efficient protocol for synthesis of tetrahydrobenzo[b]pyrans using amino functionalized ionic liquids, Comptes Rendus Chimie 14 (2011) 878–882.
- [53] L. Cammarata, S.G. Kazarian, P.A. Salter, T. Welton, Molecular states of water in room temprature ionic liquids, Phys. Chem. Chem. Phys. 3 (2001) 5192–5200.
- [54] Huiyong Wang, Jianji Wang, Shibiao Zhang, Xiaopeng Xuan, Structural Effects of Anions and Cations on the Aggregation Behavior of Ionic Liquids inAqueous Solutions, The Journal of Physical Chemistry B 112 (51) (2008) 16682–16689, https://doi.org/10.1021/jp8069089.