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Ionic liquid gel: A heterogeneous catalyst for Erlenmeyer-Plochl and Henry reaction

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Abstract Ionic liquid gel has been prepared by entrapping 1-butyl-3-methylimidazolium hydroxide ([Bmim]OH) in an aqueous agar gel. The ionic liquid gel has been characterized by Fourier transform infrared (FT-IR), Fourier transform Raman (FT-Raman) spectroscopy, scanning electron microscopy (SEM), thermogravimetric analysis (TGA) and energy dispersive X-ray analysis (EDX). The ionic liquid gel has been successfully employed as a heterogeneous catalyst in the Erlenmeyer-Plochl reaction involving aldehydes, hippuric acid and acetic anhydride as well as in the Henry reaction between aldehydes and nitromethane in ethanol at a room temperature. The heterogeneity of ionic liquid gel has been confirmed by using hot filtration test and leaching studies. Additionally, the ionic liquid gel could be easily recovered by simple filtration and reused for five times without significant loss in catalytic activity.

Keywords 1-Butyl-3-methylimidazolium hydroxide; agar; Ionic liquid gel; Erlenmeyer-Plochl reaction; Henry reaction

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Introduction

As green chemistry is becoming a central issue in the 21st century, there has been a great deal of attention in redesigning synthetic processes in order to avoid use of harmful substances and generation of toxic waste.[1] An intriguing line of development in this regard is being fueled by a paradigm shift from the use of volatile organic solvents to an alternative reaction media in synthetic chemistry.[2] In this context, ionic liquids (ILs) have emerged as promising alternative reaction medium in recent years.[2a,3] The tempting properties of ILs such as diminutive vapor pressure, high thermal and electrical conductivity, large electrochemical window, low nucleophilicity and ability to provide non-coordinating environment have triggered enormous interest in these notorious solvents.[4] A unique attribute of ILs is their modularity which allows fine tuning of their physicochemical properties by alteration in cation–anion combinations making them process compatible.[5] However, despite these advantages, a series of drawbacks such as their high cost as compared to traditional solvents and reusability that requires energy consuming distillation have been major obstacles in implementing ILs at commercial levels. In addition, the processes applying ILs cannot be performed in continuous flow fixed bed reactors.[6] The recognition of these limitations has led to the flourishing activity of heterogenization of ILs. Several elegant strategies such as supported ionic liquid phase (SILP) catalysis have been developed for this purpose.[7] Nevertheless, there is plenty of room to explore new fundamental approaches in addition to currently employed strategies. From this perspective, we envisioned that the entrapment of ILs in the matrix of agar can provide a highly attractive strategy to circumvent drawbacks associated with ILs. Agar is a biopolymer composed of linear chains of repeating agarobiose units alternating between 3-linked–β-D-galactopyransoyl (G) and 4-linked 3,6-anhydro-α-L-galactopyransoyl (LA) units. Our interest in the use of agar for entrapment of

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ILs stems from its easy bioavailability, potent biocompatibility, cost effectiveness and good immobilization efficiency.[8] We hypothesized that the resulting heterogeneous class of IL referred as a ionic liquid gel can allow to conglomerate the properties of ILs with that of biopolymer support thereby facilitating significant enhancement in the catalytic activity. Moreover, we sought that the intact network of ionic liquid gel would allow facile separation and easy reuse thereby minimizing the energy consumption.

The Erlenmeyer-Plochl reaction is one of the most widely employed methods for synthesis of azlactones which are privileged scaffolds that possess anti-cancer,[9a-b] anti-inflammatory,[9c] anti-HIV,[9d] sedative,[9e] cardiotonic[9f] and anti-diabetic activities.[9g] Notably, azlactones are also used as intermediates in the synthesis of organic compounds comprising thiamine,[10a] polyfunctional molecules,[10b] amino acids[10c] and peptides.[10d] In the view of their dynamic properties, large number of methods have been reported for synthesis of azlactones. A most common process for the synthesis of azlactones includes the Erlenmeyer-Plochl reaction between aryl aldehydes and hippuric acid in the presence of acetic anhydride. A variety of catalytic systems have been reported for synthesis of azlactones using Erlenmeyer-Plochl reaction.[11] In addition, ILs such as $[Bnmim]H_2PO_4$,[12a] $[Et_3NH][HSO_4]$,[12b] $[Bmim]_3PW_{12}O_{40}/[Bmim]_4W_{10}O_{32}$,[12c] $[(C_{14}H_{24}N_4)_{22}W_{10}O_{32}].[Bmim]NO_3$,[12d] $[C_6(MIm)_2)_2W_{10}O_{32}].2H_2O$,[12e] [Bmim]OH[11e] and Zwitterium imidazolium salt[12f] have been reported to promote the efficiency of azlactones synthesis.

The Henry reaction is a classical carbon-carbon bond forming reaction[13] used for the construction of *β*-nitro alcohols from nitroalkane and aldehydes. This reaction has received overwhelming synthetic popularity as produced *β*-nitro alcohols offer considerable potential in the synthesis of natural products and pharmaceuticals.[14] In addition, *β*-nitro alcohols are used as

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an intermediates in synthesis of alkaloids,[15] amino sugar[16a] and antibiotics.[16b] Owing to the significant importance of *β*-nitro alcohols, development of novel protocols for the Henry reaction is a vibrant area of research in organic synthesis. Plethora of catalysts[17] including ILs such as $[C_4dabco]OH$,[18a] $[P_{4444}][Im]$,[18b] $[SFHEA][HSO_4]SO_3H$,[18c] [18-c-6k][OH],[18d] methoxy propylamine acetate,[18e] [EMIM]Cl,[18f] [TMG][Lac][18g] and [Bmim]OH[17e] have been reported to catalyze the Henry reaction between nitroalkane and aromatic aldehydes.

An insight into various catalytic systems reported for the Erlenmeyer-Plochl and Henry reactions reveal a number of drawbacks such as long reaction time, harsh reaction conditions and difficulty in recovery and reusability of the catalyst. Moreover, most of the IL mediated Erlenmeyer-Plochl and Henry reactions involve high catalyst loading and high energetic input or use of additional solvent for recycling. These concerns necessitate need to develop a facile protocol for the Erlenmeyer-Plochl and Henry reaction using a robust heterogeneous catalyst. Considering aforementioned aspects and in continuation of our work related to green chemistry,[19] we report herein preparation of ionic liquid gel by entrapping [Bmim]OH in agar and its application as heterogeneous catalyst in the synthesis of azlactones by the Erlenmeyer-Plochl reaction and *β*-nitro alcohols by the Henry reaction.

Experimental

Infrared spectra were recorded on the Perkin-Elmer FT-IR spectrometer. FT-Raman spectroscopy was done using a Bruker FT-Raman (MultiRAM) spectrometer. Thermal gravimetric analysis (TGA) curves were obtained using the instrument TA SDT Q600 in the presence of static air at a linear heating rate of 10 °C min^{-1} from 25 °C to 1000 °C. SEM was recorded using JSM-6701F, Japan. Elemental composition of materials was analyzed by energy-dispersive X-ray spectra (EDS) attached to the field emission scanning electron microscope (FE-

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SEM, Model Hitachi S 4800, Japan). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) spectrometer using $CDCl_3$ as a solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) are expressed in parts per million (ppm) values and coupling constants are expressed in hertz (Hz). Mass spectra were recorded on a Shimadzu QP2010 GCMS and all the chemicals including aromatic aldehyde, nitromethane, acetic anhydride and hippuric acid (Spectrochem) were used without further purification. Melting points were determined in an open capillary and are uncorrected. All reactions were carried out under air atmosphere in dried glasswares.

Preparation of [Bmim]OH

[Bmim]OH was prepared from [Bmim]Br by using ion exchange column. Amberlite®IRA-400 hydroxide resin was prepared in deionized water and poured into a glass column. [Bmim]Br (15g, 0.5M) was dissolved in 100 mL deionized water and resultant solution was loaded to the column. The column was then eluted with deionized water as eluent with the controlled flow rate of 0.7 mL/min. The evaporation of solvent from the eluted fractions under vacuo afforded [Bmim]OH as the viscous liquid. FT-IR (KBr): υ = 3406, 2966, 1644, 1403, 1268, 1168, 1007, 979, 831, 620 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.49 (t, 3H, *J* = 7.5 Hz, -C**H$_3$**), 0.88-0.95 (m, 2H, -C**H$_2$**), 1.45 (t, 2H, *J* = 7.5 Hz, -C**H$_2$**), 3.48 (bs, 1H, -O**H**), 3.65 (s, 3H, N-C**H$_3$**), 3.91 (t, 2H, *J* = 6.9 Hz, N-C**H$_2$**), 7.21-7.33 (m, 2H, C_4**H**, C_5**H** of Imi), 9.37 (s, 1H, -C_2**H** of Imi); ^{13}C NMR (75 MHz, $CDCl_3$): 13.5 (-**C**H_3), 19.5 (-**C**H_2), 32.0 (-**C**H_2), 36.6 (-N-**C**H_3), 49.6 (-N-C**H$_2$**), 121.9 (**C$_4$** of Imi), 123.6 (**C$_5$** of Imi), 135.8 (**C$_2$** of Imi) ppm.

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Preparation of [Bmim]OH@agar (1)

To a boiling mixture of agar-agar (10 g) in water (60 mL), 2.8 % w/v of [Bmim]OH was added. The resultant mixture was boiled with stirring for few minutes and cooled in ice bath to get the desired ionic liquid gel, [Bmim]OH@agar **(1)**. FT-IR (KBr, thin film): υ = 3401, 1634, 1373, 1260, 1175, 1070, 932, 890, 621 cm^{-1}; FT-Raman (cm^{-1}): 3665, 3470, 3408, 3343, 3265, 3246, 3224, 3187, 3119, 2990, 2968, 2955, 2939, 2850, 2828; Elemental analysis observed: % C 72.79, % N 1.96, % O 25.25; Loading: 0.51 mmol of functional group g^{-1} of agar.

General procedure for synthesis of azlactones (5)

A mixture of aromatic aldehyde (1 mmol), hippuric acid (1 mmol), acetic anhydride (1.2 mmol) and [Bmim]OH@agar (**1**) (100 mg) in ethanol (5 mL) was stirred at ambient temperature. After completion of a reaction as monitored by TLC, the reaction mixture was filtered to get the crude residue of azlactone which was purified by column chromatography over silica gel.

General procedure for synthesis of β-nitro alcohols (8)

A mixture of aromatic aldehyde (1 mmol), nitromethane (1 mmol) and [Bmim]OH@agar (**1**) (150 mg) in ethanol (5 mL) was stirred at ambient temperature. After completion of a reaction as monitored by TLC, the reaction mixture was filtered to get crude residue of β-nitro alcohol which was purified by column chromatography over silica gel.

Spectral data

4-[(4-Nitrophenyl)methylene]-2-phenyloxazol-5-one (Table 3, product entry **5a**)[20a]: MP 239 °C (lit.,238 °C)[20b]; IR (KBr, thin film): υ = 2923, 2845, 1804, 1652, 1600, 1514, 1341, 1167, 1106, 853, 760, 689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20 (s, 1H, -C-**H**), 7.52 (dd, 2H, *J* = 4.4, 10.4 Hz, Ar-**H**), 7.70 (m, 1H, Ar-**H**), 8.25 (dd, 2H, *J* = 1.2, 8.5 Hz, Ar-**H**), 8.34 (m, 2H, Ar-**H**), 8.40 (m, 2H, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 112.6 (**C**-H), 121.7 (Ar-**C**), 127.5 (Ar-**C**),

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128.7 (Ar-**C**), 129.5 (Ar-**C**), 130.2 (Ar-**C**), 131.3 (Ar-**C**), 131.7 (**C**-N), 141.1 (Ar-**C**), 147.8 (Ar-**C**), 160.4 (**C**=N), 165.9 (**C**=O); MS (EI): *m/z* 294 (M^+).

4-[(3-Nitrophenyl)methylene]-2-phenyl-oxazol-5-one (Table 3, product entry **5b**)[20a]: MP 197 °C (lit., 195 °C)[20b]; IR (KBr): υ = 3093, 1792, 1762, 1658, 1531, 1491, 1325, 1168, 1095, 991, 885, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 1H, -C-**H**), 7.59-7.62 (m, 2H, Ar-**H**), 7.65-7.68 (m, 2H, Ar-**H**), 8.20-8.23 (m, 2H, Ar-**H**), 8.32-8.35 (m, 1H, Ar-**H**), 8.39 (d, 1H, *J* = 7.6 Hz, Ar-**H**), 9.17 (t, 1H, *J* = 1.7 Hz, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 112.2 (**C**-H), 120.5 (Ar-**C**), 121.6 (Ar-**C**), 128.7 (Ar-**C**), 129.4 (Ar-**C**), 129.7 (Ar-**C**), 130.1 (Ar-**C**), 131.4 (**C**-N), 131.7 (Ar-**C**), 132.7 (Ar-**C**), 135.9 (Ar-**C**), 148.5 (Ar-**C**), 160.4 (**C**=N), 165.8 (**C**=O); MS (EI): *m/z* 294 $(M)^+$.

4-(4-Fluorobenzylidene)-2-phenyloxazol-5-one (Table 3, product entry **5c**)[21]: MP 172 °C (lit., 170 °C)[20b]; IR (KBr): υ = 2951, 1798, 1774, 1664, 1598, 1500, 1327, 1296, 1158, 1096, 837 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.20-8.25 (m, 2H, Ar-**H**), 8.16 (dd, 2H, *J* = 1.4, 8.5 *Hz*, Ar-**H)**, 7.60 (t, 1H, *J* = 7.5 Hz, Ar-**H**), 7.49 (t, 2H, *J* = 7.5 Hz, Ar-**H**), 7.20 (s, 1H, C-**H**), 7.16 (t, 2H, *J* = 8.6 Hz, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 110.4 (**C**-H), 116.1(Ar-**C**), 128.6 (Ar-**C**), 129,0 (Ar-**C**), 130.4 (Ar-**C**), 131.1 (**C**-N), 133.2 (Ar-**C**), 134.5 (Ar-**C**), 134.9 (Ar-**C**), 163.1 (Ar-**C**), 163.5 (**C**=N), 167.6 (**C**=O); MS (EI): *m/z* 267 (M^+).

4-(4-Benzylidene)-2-phenyloxazol-5-one (Table 3, product entry **5d**)[20a]: MP 168 °C (lit.,170 °C)[20b]; IR (KBr): υ = 3052, 1805, 1756, 1720, 1640, 1290, 987, 860, 767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.27-8.30 (m, 2H, Ar-**H**), 8.10-8.13 (m, 2H, Ar-**H**), 7.59 (t, 1H, *J* = 7.5 Hz, Ar-**H**), 7.51 (t, 2H, *J* = 7.6 Hz, Ar-**H**), 7.39-7.48 (m, 3H, Ar-**H**), 7.20 (s, 1H, C-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 111.3 (**C**-H), 124.5 (Ar-**C**), 128.3 (Ar-**C**), 128.7 (Ar-**C**), 128.9 (Ar-**C**), 131.2 (**C**-

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N), 132.1 (Ar-**C**), 132.7 (Ar-**C**), 133.3 (Ar-**C**), 133.6 (Ar-**C**), 163.7 (**C**=N), 167.5 (**C**=O); MS (EI): *m/z* 249 (M^+).

4-(2-Hydroxybenzylidene)-2-phenyloxazol-5-one (Table 3, product entry **5e**)[22]*:* MP 106 °C (lit.,108-111 °C)[22]; IR (KBr): υ = 3411, 2924, 1791, 1644, 1446, 1415, 1328, 1295, 1152, 1096, 983, 859, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.89 (s, 1H, -O**H**), 7.95 (d, 2H, *J* = 6.9 Hz, Ar-**H**), 7.46-7.62 (m, 6H, Ar-**H**), 7.35-7.39 (m, 2H, Ar-**H**, -C**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 116.4 (**C**-H), 119.9 (Ar-**C**), 123.4 (Ar-**C**), 124.2 (Ar-**C**), 125.2 (Ar-**C**), 127.1 (Ar-**C**), 127.9 (Ar-**C**), 128.9 (Ar-**C**), 129.7 (Ar-**C**), 132.5 (**C**-N), 133.5 (Ar-**C**), 149.9 (Ar-**C**), 159.0 (**C**=N), 166.1 (**C**=O); MS (EI): *m/z* 265 (M^+).

4-[(4-Hydroxyphenyl)methylene]-2-phenyloxazol-5-one (Table 3, product entry **5f**)[23a]: MP 180 °C (lit., 182 °C)[23b]; IR (KBr): υ = 3465, 1812, 1635, 1599, 1130, 1061, 978, 724 cm^{-1}; ^1H NMR (300 MHz, DMSO): δ 10.36 (s, 1H, -O**H**), 8.18-8.89 (m, 4H, Ar-**H**), 7.64-8.11 (m, 5H, Ar-**H**), 7.42 (s, 1H, C**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 112.7 (**C**-H), 115.3 (Ar-**C**), 127.5 (Ar-**C**), 127.9 (Ar-**C**), 128.7 (Ar-**C**), 129.4 (Ar-**C**), 129.7 (Ar-**C**), 131.4 (Ar-**C**), 131.9 (**C**-N), 157.3 (Ar-**C**), 160.4 (**C**=N), 166.4 (**C**=O); MS (EI): *m/z* 296 (M^+).

4-(2-Methylbenzylidene)-2-phenyloxazol-5-one (Table 3, product entry **5g**)[13a]: MP 142 °C (lit.,141 °C)[13b]; IR (KBr): υ = 2921, 1798, 1640, 1586, 1544, 1487, 1456, 1324, 1294, 1252, 1227, 1165, 987, 866 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.71-8.76 (m, 1H, Ar-**H**), 8.14-8.19 (m, 2H, Ar-**H**), 7.57-7.63 (m, 1H, Ar-**H**), 7.54 (dd, 2H, *J* = 5.7, 4.4 Hz, Ar-**H**), 7.47 (dd, 1H, *J* = 5.0, 3.5 Hz, Ar-**H**), 7.29-7.33 (m, 2H, Ar-**H**), 7.30 (s, 1H, C**H**), 2.56 (s, 3H, C**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): 20.4 (**C**H_3), 125.2 (**C**-H), 126.4 (Ar-**C**), 128.2 (Ar-**C**), 128.7 (Ar-**C**), 129.0 (Ar-**C**), 130.4 (Ar-**C**), 130.9 (**C**-N), 132.1 (Ar-**C**), 133.4 (Ar-**C**), 133.4 (Ar-**C**), 133.5 (Ar-**C**), 139.7 (Ar-**C**), 163.9 (**C**=N), 167.4 (**C**=O); MS (EI): *m/z* 263 (M^+).

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4-(4-Methylbenzylidene)-2-phenyloxazol-5-one (Table 3, product entry **5h**)[21]: MP 147 °C (lit.,145 °C)[20b];IR (KBr): υ = 2926, 1795, 1647, 1667, 1556, 1490, 1330, 1227, 1162, 985, 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.17-8.20 (m, 2H, Ar-**H**), 8.08 (d, 2H, *J* = 8.0 Hz, Ar-**H**), 7.57 (dd, 1H, *J* = 4.7, 10.4 Hz, Ar-**H**), 7.50 (dd, 2H, *J* = 7.1, 8.0 Hz, Ar-**H**),7.32 (d, 2H, *J* = 8.1 Hz, Ar-**H**), 7.20 (s, 1H, C-**H**), 2.39 (s, 3H, C**H$_3$**); ^{13}C NMR (75 MHz, $CDCl_3$): 22.1 (**C**H_3), 125.9 (**C**-H), 128.1 (Ar-**C**), 128.7 (Ar-**C**), 128.9 (Ar-**C**), 130.4 (Ar-**C**), 132.2 (**C**-N), 133.5 (Ar-**C**), 133.3 (Ar-**C**), 133.7 (Ar-**C**), 142.4 (Ar-**C**), 163.2 (**C**=N), 167.9 (**C**=O); MS (EI): *m/z* 263 (M^+).

4-(4-Methoxybenzylidene)-2-phenyloxazol-5-one (Table 3, product entry **5i**)[23a]: MP 167°C (lit.,165 °C)[20b];IR (KBr): υ = 2907, 1740, 1670, 1594, 1555, 1480, 1111, 957, 845 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, 2H, *J* = 7.5 Hz, Ar-**H**), 8.18 (d, 2H, *J* = 7.5 Hz, Ar-**H**), 7.40-7.58 (m, 3H, Ar-**H**), 7.36 (s, 1H, **C**-H), 6.96-7.00 (d, 2H, *J* = 8.9 Hz, Ar-**H**), 3.84 (s, 3H, C**H$_3$**); ^{13}C NMR (75 MHz, $CDCl_3$): 56.1 (**C**H_3), 115.0 (**C**-H), 126.0 (Ar-**C**), 126.9 (Ar-**C**), 128.4 (Ar-**C**), 128.9 (Ar-**C**), 131.3 (**C**-N), 131.7 (Ar-**C**), 133.2 (Ar-**C**), 134.4 (Ar-**C**), 162.4 (Ar-**C**), 162.7 (**C**=N), 167.8 (**C**=O); MS (EI): *m/z* 264 (M^+).

4-[(4-Dimethylaminophenyl)methylene]-2-phenyloxazol-5-one (Table 3, product entry **5j**)[23c]: MP 212 °C (lit.,213 °C)[20b]; IR (KBr): υ = 3422, 2920, 1764, 1660, 1620, 1381, 1138, 923, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.11 (s, 6H, (-C**H$_3$**)**$_2$**), 5.9 (s, 1H, C-**H**), 6.2-6.7 (m, 9H, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 40.3 (**C**H_3), 112.2 (**C**-H), 121.5 (Ar-**C**), 125.7 (Ar-**C**), 127.3 (Ar-**C**), 128.2 (Ar-**C**), 129.1 (Ar-**C**), 132.4 (**C**-N), 133.6 (Ar-**C**), 134.5 (Ar-**C**), 152.4 (Ar-**C**), 160.7 (**C**=N), 168.7 (**C**=O); MS (EI): *m/z* 292 (M^+).

2-Phenyl-4-((thiophen-2-yl)methylene)oxazol-5-one (Table 3, product entry **5k**)[13a]: MP 178 °C (lit.,175 °C)[13c]; IR (KBr): υ = 2927, 1789, 1639, 1553, 1490, 1327, 1235, 1151, 1051, 978, 854 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.17-7.20 (m, 1H, C-**H**), 7.51-7.66 (m, 5H, Ar-**H**), 7.75 (d,

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1H, *J* = 5.1 Hz, Ar-**H**), 8.18-8.22 (m, 2H, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 124.8 (**C**-H), 125.6 (Ar-**C**), 127.9 (Ar-**C**), 128.3 (Ar-**C**), 128.9 (Ar-**C**), 130.9 (**C**-N), 133.1 (Ar-**C**), 134.9 (Ar-**C**), 135.3 (Ar-**C**), 137.6 (Ar-**C**), 162.5 (**C**=N), 166.9 (**C**=O); MS (EI): *m/z* 255 (M^+).

2-Phenyl-4-(4-pyridinyl)-oxazol-5-one (Table 3, product entry **5l**)[13a]: MP 170 °C (lit.,168-169 °C)[13a]; IR (KBr): υ = 3470, 2915, 1798, 1770, 1660, 1594, 1559, 869, 814 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.66 (d, 2H, *J* = 5.7 Hz, Ar-**H**), 8.18 (d, 2H, *J* = 7.4 Hz, Ar-H), 8.00 (d, 2H, *J* = 5.7 Hz, Ar-**H**), 7.69 (t, 1H, *J* = 7.3 Hz, Ar-**H**), 7.58 (t, 2H, *J* = 7.5 Hz, Ar-**H**), 7.11 (s, 1H, C-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 125.4 (**C**-H), 125.9 (Ar-**C**), 127.9 (Ar-**C**), 128.9 (Ar-**C**), 129.0 (Ar-**C**), 134.5 (Ar-**C**), 137.4 (**C**-N), 140.3 (Ar-**C**), 150.2 (Ar-**C**), 165.8 (**C**=N), 166.7 (**C**=O); MS (EI): *m/z* 250 (M^+).

1-(4-Nitrophenyl)-2-nitroethanol (Table 6, product entry **8a**)[24]: MP 80 °C (lit.,82 °C)[24]; IR (KBr): υ = 3410, 2962, 1712, 1602, 1555, 1522, 1384, 1347, 1261, 1098, 856, 801, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (d, 2H, *J* = 8.7 Hz, Ar-**H**), 7.63 (d, 2H, *J* = 8.7 Hz, Ar-**H**), 5.59-5.63 (m, 1H, C-**H**), 4.60 (t, 2H, *J* = 3.3, 4.5 Hz, C**H$_2$**), 3.60 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 69.9 (**C**H), 80.7 (**C**H_2), 124.1 (Ar-**C**), 127.0 (Ar-**C**), 145.4 (Ar-**C**), 147.9 (Ar-**C**); GC-MS *m/z* : 194 (M^+-H_2O).

1-(3-Nitrophenyl)-2-nitroethanol (Table 6, product entry **8b**)[24]: MP 74 °C (lit.,70 °C)[24]; IR (KBr): υ = 3410, 2928, 1712, 1616, 1531, 1351, 1261, 1098, 806, 735 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (s, 1H, Ar-**H**), 8.23 (d, 1H, *J* = 8.1 Hz, Ar-**H**), 7.79 (d, 1H, *J* = 7.8 Hz, Ar-**H**), 7.62 (t, 1H, *J* = 7.8 Hz, Ar-**H**), 5.62 (q, 1H, C-**H**), 4.63 (t, 2H, C**H$_2$**), 3.45 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 69.84 (**C**H), 80.72 (**C**H_2), 121.15 (Ar-**C**), 123.79 (Ar-**C**), 130.10 (Ar-**C**), 131.99 (Ar-**C**), 140.32 (Ar-**C**), 148.58 (Ar-**C**); GC-MS *m/z* : 194 (M^+-H_2O).

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1-(2-Nitrophenyl)-2-nitroethanol (Table 6, product entry **8c**)[25a]: MP 68 °C (lit.,69 °C)[25b]; IR (KBr): υ = 3517, 2923, 1553, 1525, 1430, 1371, 1255, 1084, 899 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.51-8.12 (m, 4H, Ar-**H**), 6.04 (dd, 1H, *J* = 9.2, 2.6 Hz, C**H**), 4.87 (dd, 1H, *J* = 13.2, 2.5 Hz, C$\mathbf{H}_2$), 4.52 (dd, 1H, *J* = 9.1, 13.2 Hz, C$\mathbf{H}_2$), 3.57 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 69.98 (**C**-H), 80.74 (**C**H_2), 121.11 (Ar-**C**), 127.10 (Ar-**C**), 128.2 (Ar-**C**), 134.2 (Ar-**C**), 145.43 (Ar-**C**), 147.93 (Ar-**C**); GC-MS *m/z* : 194 (M^+-H_2O).

4-((1-Hydroxy)-2-nitroethyl)phenol (Table 6, product entry **8d**)[26]: MP 74 °C; IR (KBr): υ = 3356, 2929, 2844, 1687, 1596, 1547, 1523, 1485, 1456, 1374, 1255, 1160, 1104, 954, 847 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, 2H, *J* = 8.6 Hz, Ar-**H**), 6.86 (d, 2H, *J* = 8.6 Hz, Ar-**H**), 5.44-5.47 (m, 1H, O**H**), 4.96 (s, 1H, C**H**), 4.39-4.55 (m, 2H, C$\mathbf{H_2}$), 2.69 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 155.9 (Ar-**C**), 132.2 (Ar-**C**), 129.9 (Ar-**C**), 116.7 (Ar-**C**), 81.5 (**C**H_2), 70.4 (**C**H); GC-MS *m/z* : 165 (M^+-H_2O).

2-((1-Hydroxy)-2-nitroethyl)phenol (Table 6, product entry **8e**)[26]: MP 87 °C; IR (KBr): υ = 3416, 3036, 2931, 1546, 1517, 1444, 1426, 1377, 1265, 1232, 1115, 854, 647 cm^{-1}; ^1H NMR (300 MHz, CDCl3): δ 7.12-7.21 (m, 2H, Ar-**H**), 6.87-6.92 (m, 1H, Ar-**H**), 6.54 (d, 1H, *J* = 8.2 Hz, Ar-**H**), 5.76 (s, 2H, C$\mathbf{H_2}$), 4.77-4.87 (m, 2H, C**H**, O**H**), 4.37 (t, 1H, *J* = 6.7 Hz, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 153.4 (Ar-**C**), 131.2 (Ar-**C**), 130.5 (Ar-**C**), 121.6 (Ar-**C**), 120.2 (Ar-**C**), 116.7 (Ar-**C**), 89.3 (**C**H_2), 74.6 (**C**H); GC-MS *m/z* : 165 (M^+-H_2O).

1-Phenyl-2-nitroethanol (Table 6, product entry **8f**)[24]: MP 67 °C; IR (KBr): υ = 3452, 2924, 2853, 1600, 1561, 1454, 1384, 1271, 701, 526 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.39 (s, 5H, Ar-**H**), 5.41-5.45 (m, 1H, C$\mathbf{H}_2$), 4.59 (m, 1H, C$\mathbf{H}_2$), 4.49 (dd, 1H, *J* = 13.2, 9.9 Hz, C**H**), 3.15 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 71.0 (C**H**), 81.2 (**C**H_2), 125.9 (Ar-**C**), 128.9 (Ar-**C**), 129.0 (Ar-**C**), 138.2 (Ar-**C**); GC-MS *m/z* : 149 (M^+-H_2O).

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2-Nitro-1-p-tolylethanol (Table 6, product entry **8g**)[27a]: MP 49 °C (lit.,47 °C)[24]; IR (KBr): υ = 3551, 3035, 2938, 1559, 1509, 1450, 1370, 1278, 1067, 920, 816 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (d, 2H, *J* = 9.0 Hz, Ar-**H**), 7.20-7.23 (d, 2H, *J* = 9.0 Hz, Ar-**H**), 5.44-5.56 (m, 1H, C**H**), 4.40-4.63 (m, 2H, C$\mathbf{H_2}$), 2.87 (s, 1H, O**H**), 2.29 (s, 3H, C$\mathbf{H_3}$); ^{13}C NMR (75 MHz, $CDCl_3$): 138.7 (Ar-**C**), 135.4 (Ar-**C**), 129.6 (Ar-**C**), 125.7 (Ar-**C**), 81.6 (C$\mathbf{H_2}$), 70.6 (C**H**), 21.5 (C$\mathbf{H_3}$); GC-MS *m/z* : 163 (M^+-H_2O).

1-(4-Methoxyphenyl)-2-nitroethanol (Table 6, product entry **8h**)[27a]: MP 41 °C (lit.,43 °C)[27b]; IR (KBr): υ = 3436, 2925, 1549, 1510, 1456, 1377 , 1307, 1255, 1167, 1034, 867, 734 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.67 (s, 1H, O**H**), 3.87 (s, 3H, -O-C$\mathbf{H_3}$), 4.40 (dd, 1H, *J* = 3.7, 13.3 Hz, C**H**), 4.55 (dd, 1H, *J* = 9.1, 13.3 Hz, C$\mathbf{H_2}$), 5.38-5.41 (m, 1H, C$\mathbf{H}_2$), 6.88 (d, 2H, *J* = 8.7 Hz, Ar-**H**), 7.36 (d, 2H, *J* = 8.7 Hz, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 160.0 (Ar-**C**), 130.1 (Ar-**C**), 127.2 (Ar-**C**), 114.1 (Ar-**C**), 81.7 (**C**H_2), 70.2 (**C**H), 55.9 (O**C**H_3); GC-MS *m/z* : 179 (M^+-H_2O).

1-(3,4,5-Trimethoxyphenyl)-2-nitroethanol (Table 6, product entry **8i**)[27c]: MP 106 °C (lit.,108-109°C)[27d]; IR (KBr): υ = 3466, 2917, 1506, 1447, 1403, 1379, 1260, 1216, 1056, 857 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.58 (s, 2H, Ar-**H**), 5.36 (dd, 1H, *J* = 9.2, 3.2 Hz, C$\mathbf{H}_2$), 4.54 (dd, 1H, *J* = 13.1, 9.2 Hz, C$\mathbf{H}_2$), 4.44 (dd, 1H, *J* = 13.1, 3.2 Hz, C**H**), 3.81 (s, 6H, (OC$\mathbf{H_3})_2$), 3.74 (s, 3H, OC$\mathbf{H_3}$), 3.34 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 153.0 (Ar-**C**), 137.4 (Ar-**C**), 133.9 (Ar-**C**), 102.4 (Ar-**C**), 81.5 (**C**H_2), 71.6 (**C**H), 55.1 (O**C**H_3), 55.7 (O**C**H_3); GC-MS *m/z* : 239 (M^+-H_2O).

1-(2-Pyridyl)-2-nitroethanol (Table 6, product entry **8j**)[17a]: MP 68 °C (lit.,69 °C)[27e]; IR (KBr): υ = 3435, 2955, 1529, 1409, 1366, 1105, 1024, 866 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.12 (s, 1H, O**H**), 4.67-4.88 (m, 2H, C$\mathbf{H_2}$), 5.43-5.57 (m, 1H, C**H**), 7.15-7.44 (m, 2H, Ar-**H**), 7.68-7.80 (m, 1H, Ar-**H**), 8.47-8.51 (m, 1H, Ar-**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 157.4 (Ar-**C**), 149.1 (Ar-

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C), 137.7 (Ar-**C**), 123.7 (Ar-**C**), 121.1 (Ar-**C**), 81.6 (**C**H_2), 70.6 (**C**H); GC-MS *m/z*: 150 (M^+-H_2O).

1-(4-Pyridyl)-2-nitroethanol (Table 6, product entry **8k**)[28a]: MP 93 °C (lit.,95 °C)[28b]; IR (KBr): υ = 3427, 2945, 1529, 1460, 1357, 1109, 1010, 856 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (dd, 2H, *J* = 5.0, 1.6 Hz, Ar-**H**), 7.35 (m, 2H, Ar-**H**), 5.54 (dd, 1H, *J* = 7.5, 4.6 Hz, C**H**), 4.55 (m, 2H, C**H₂**), 3.64 (s, 1H, O**H**); ^{13}C NMR (75 MHz, $CDCl_3$): 149.6 (Ar-**C**), 147.0 (Ar-**C**), 120.0 (Ar-**C**), 79.0 (**C**H_2), 68.9 (**C**H); GC-MS *m/z* : 150 (M^+-H_2O).

Result and Discussion

Our initial task was to accomplish a reliable preparation of ionic liquid gel. [Bmim]OH was chosen as a prototype IL for synthesis of ionic liquid gel. Our interest in employing [Bmim]OH stems from its basic nature and ease of preparation. Owing to these properties, [Bmim]OH has been one of the most commonly employed IL in organic synthesis.[29a-c] Initially, a series of experiments were undertaken, in which different concentrations of [Bmim]OH (1-25 % w/v) were dissolved in a varying amount of agar in water. After a substantial experimentation, we found that 10 g of agar containing 2.8 % w/v [Bmim]OH resulted in the formation of soft gel, that served as a ionic liquid gel (acronymed as [Bmim]OH@agar (**1**)). [Bmim]OH@agar has a transparent gel like appearance and could be easily cut into pieces (Fig. 1).

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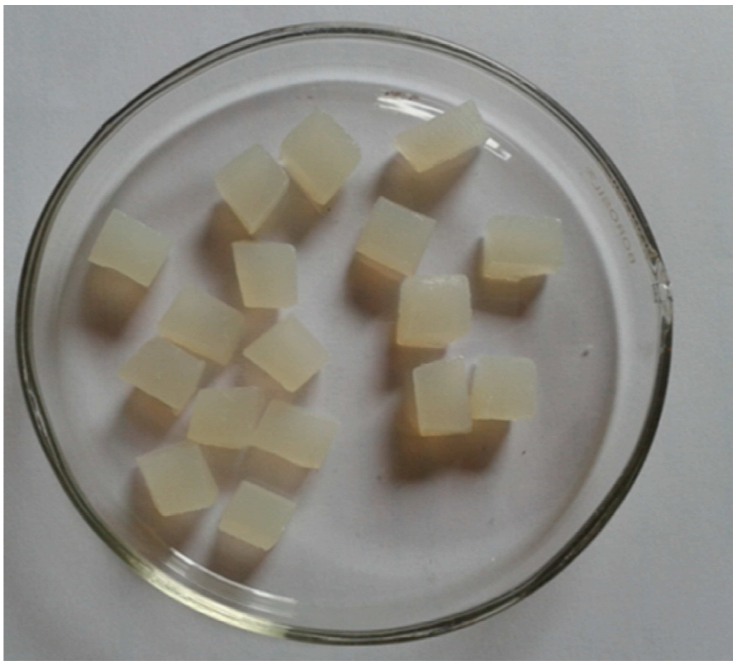

Fig. 1 Photograph of [Bmim]OH@agar (**1**)

Based on literature reports,[29d-e] the plausible structure of [Bmim]OH@agar (**1**) is established in Fig. 2 and is supported by interaction between IL and agar as evidenced by FT-IR analysis. The [Bmim]OH@agar (**1**) exhibits ion dipole interaction between oxygens of agarose with imidazolium cations and hydrogen bonding between agarose oxygen with C_2-H of imidazolium ring as revealed from FT-IR spectroscopic analysis. FT-IR spectra of [Bmim]OH, agar and **1** were recorded to study the interaction between IL and agar. The FT-IR spectrum of [Bmim]OH displayed characteristic peaks at 3406 cm^{-1} (O-H stretching vibrations), 1644 cm^{-1} (in-plane C-C and C-N stretching vibrations of imidazolium), 1403 cm^{-1} (C-H bending vibrations of $-CH_3$) and 831 cm^{-1} (C-H in plane vibrations of imidazolium) whereas that of pure agar gel showed characteristic peaks at 3434 cm^{-1} (O-H stretching vibrations of agarose and water), 1636 cm^{-1} (bending vibrations of water), 1252 and 1074 cm^{-1} (C-O-C and the glycosidic linkage of agarose). On contrary, FT-IR spectrum of [Bmim]OH@agar (**1**) displayed peaks at 3401 cm^{-1}

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(O-H stretching vibrations of agarose, IL and water), 1634 cm^{-1} (in-plane C-C and C-N stretching vibrations of imidazolium), 1373 cm^{-1} (C-H bending vibrations of $-CH_3$), 1260 cm^{-1} (symmetrical C-H vibrations of imidazolium), 1175 cm^{-1} (in plane C-H deformation vibrations of imidazolium), 1070 cm^{-1} (C-O-C and the glycosidic linkage of agarose) and 890 cm^{-1} (C-H in plane vibrations of imidazolium). A red shift in the position of O-H of pure agar gel from 3434 cm^{-1} to 3401 cm^{-1} in **1** and C-O-C stretching vibrations of glycosidic linkage of agarose from 1074 cm^{-1} to 1070 cm^{-1} in **1** are indicative of hydrogen bonding interactions.

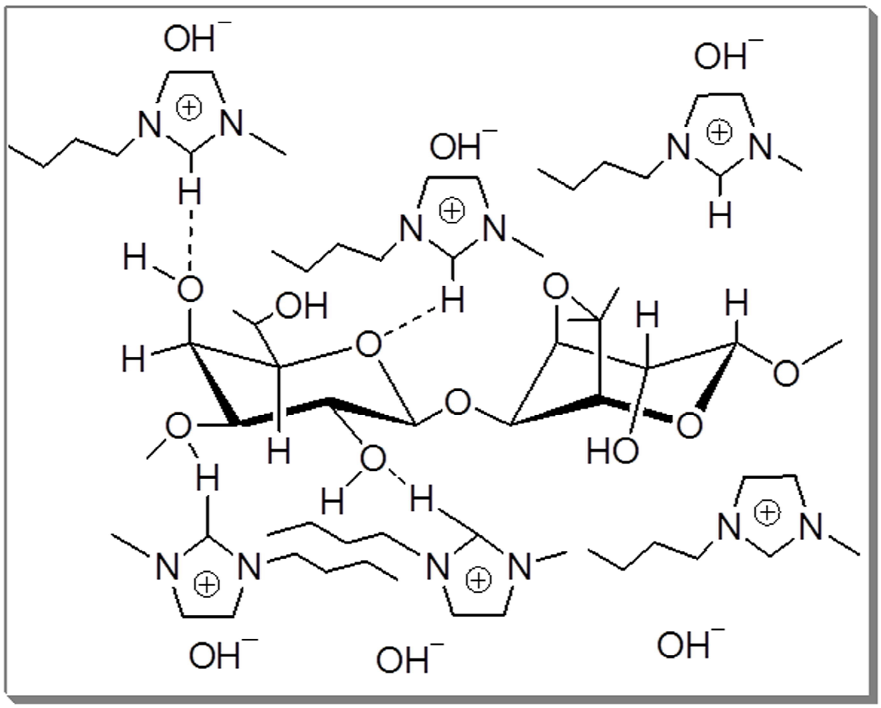

Fig. 2 Structure of [Bmim]OH@agar (**1**)

Next, we studied the effect of solvents on the physical nature of [Bmim]OH@agar (**1**). A gel was cut into 2.5 x 2.5 x 2.0 mm^3 pieces and stirred in different solvents at room temperature for 24 h. Subsequently, the gel was filtered and its physical dimensions were measured. The nature of gel remained intact in ethanol, methanol and acetone. The noticeable shrinkage in

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dimensions was found in dichloromethane and water. On the contrary, gel network collapsed in toluene.

A thermal profile of [Bmim]OH@agar (**1**) was studied by thermogravimetric analysis (TGA) and differential thermal analysis (DTA) (Fig. 3). An initial weight loss of 95% up to 162 °C in TGA curve is ascribed to desorption of water as evident from a strong endothermic peak in DTA at 90 ^{o}C. The second weight loss from 162 ^{o}C to 308 ^{o}C is attributed to the thermal decomposition of [Bmim]OH along with the agar into their corresponding carbonaceous material. The TGA analysis is consistent with the TGA profile of [Bmim]OH reported in the literature[30a] revealing no obvious changes in the thermal stability of [Bmim]OH even after entrapment.

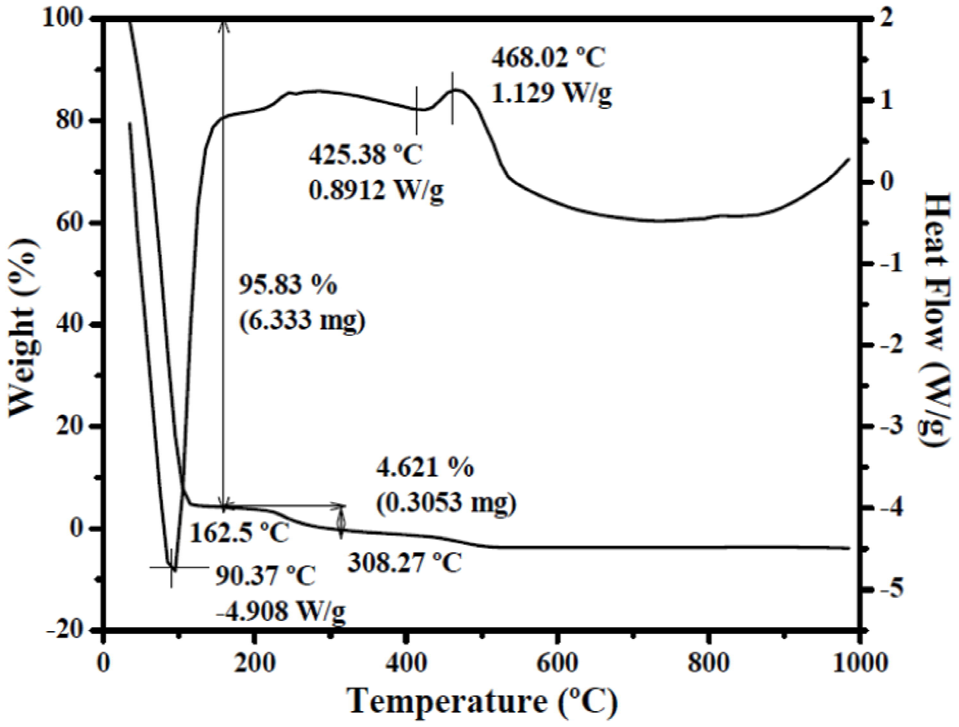

Fig. 3 TGA and DTA curve of [Bmim]OH@agar (**1**)

Surface morphology of [Bmim]OH@agar (**1**) was studied by Scanning Electron Microscopy (SEM) analysis (Fig. 4). The SEM micrograph of **1** revealed uniform gel type morphology with

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smooth surface which mimicked the morphology of gel obtained from only agar. This clearly indicates that morphology of agar gel is preserved even after entrapment of [Bmim]OH into agar gel.

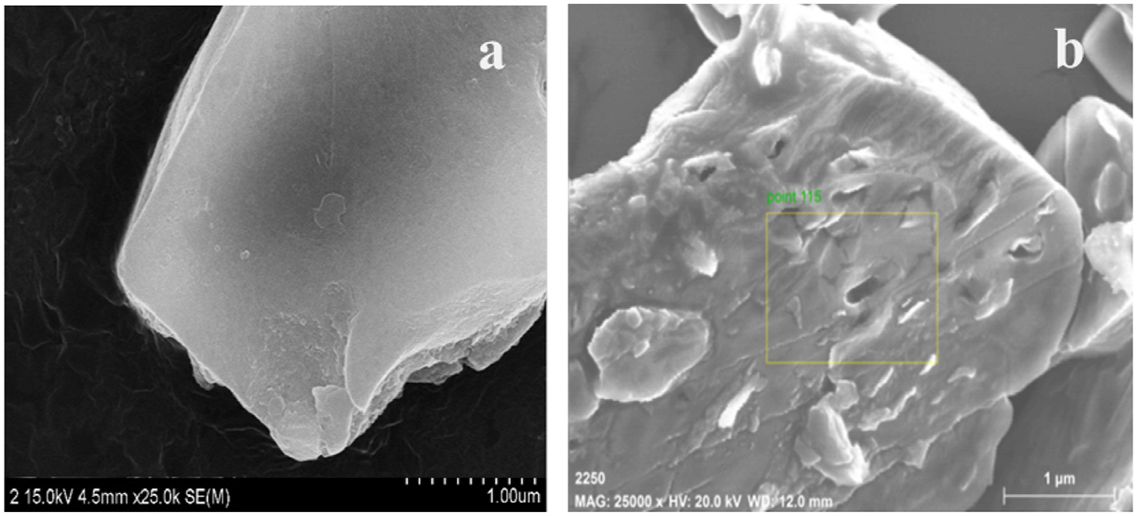

Fig. 4 SEM micrographs of (**a**) agar; (**b**) [Bmim]OH@agar (**1**)

Our next task was to assess the catalytic efficiency of [Bmim]OH@agar (**1**) in the synthesis of azlactones (**Scheme 1**). Initial studies to examine the effect of catalyst loading were carried out using a model reaction between hippuric acid **2** (1 mmol), *p*-nitrobenzaldehyde **3a** (1 mmol), acetic anhydride **4** (1.2 mmol) in ethanol. The reaction proceeded smoothly affording the expected azlactone viz. 4-[(4-nitrophenyl)methylene]-2-phenyl-5(4H)-oxazolone (**5a**) in 75% yield. When the quantity of (**1**) was increased from 50 mg (0.025 mmol) to 100 mg (0.051 mmol), yield of the product (**5a**) was elevated significantly from 75% to 90% (Table 1, entries 1−2). However, further increase in catalyst quantity did not markedly influence yield of the product (Table 1, entries 3-4).

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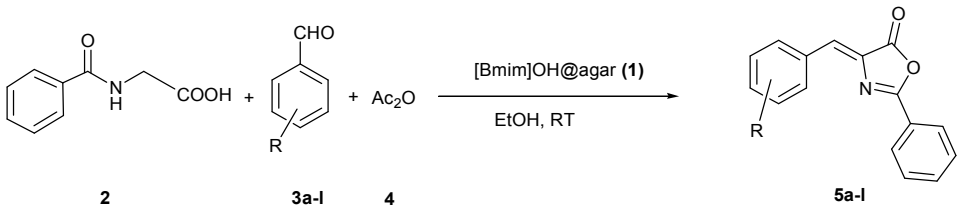
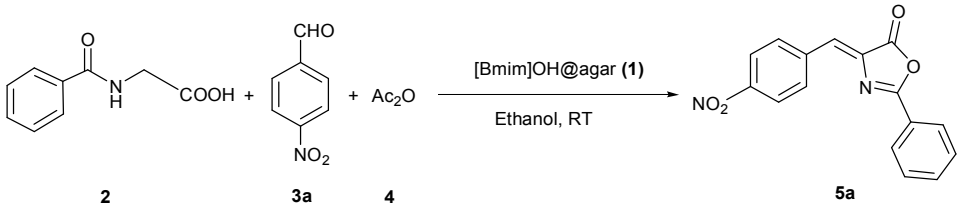


Scheme 1 [Bmim]OH@agar (**1**) catalyzed azlactones synthesis

Table 1. Optimization of catalyst loading in synthesis of azlactones[a]



Entry	Catalyst (mg)	Time (min.)	Yield[b] (%)
1	50 (0.025 mmol)	35	75
2	**100 (0.051 mmol)**	**20**	**90**
3	150 (0.077 mmol)	25	91
4	200 (0.103 mmol)	24	92

[a]Reaction conditions: **2** (1 mmol), **3a** (1 mmol), **4** (1.2 mmol) and EtOH (5 mL).
[b]Isolated yields after purification by column chromatography.

Next, we probed the effect of solvents on a model reaction by employing an array of solvents. The model reaction afforded good yields in polar protic solvents such as methanol and ethanol (Table 2, entries 1-2) while moderate yields were acquired in non-polar solvents such as CH_3CN, CH_2Cl_2, 1,4-dioxane, $CHCl_3$ and toluene (Table 2, entries 3-7). The reaction did not proceed to the synthetically useful degree in solvent like DMF (Table 2, entry 8). Among all the screened solvents, ethanol was found to furnish excellent yield of the product in shorter reaction time (Table 2, entry 2).

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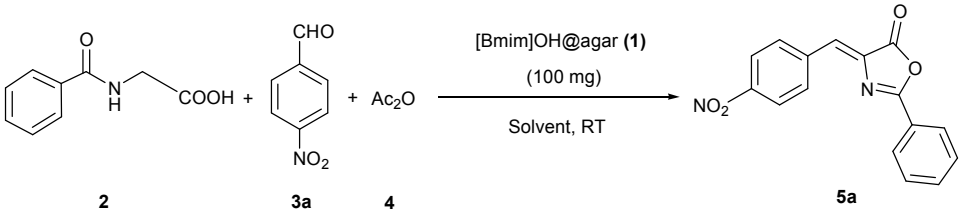
Table 2. Solvent optimization in the synthesis of azlactones[a]



Entry	Solvent	Time (Min.)	Yield[b] (%)
1	Methanol	25	78
2	**Ethanol**	**20**	**90**
3	CH_3CN	40	68
4	CH_2Cl_2	45	55
5	1, 4-dioxane	55	40
6	$CHCl_3$	65	45
7	Toluene	80	60
8	DMF	70	35

[a]Reaction conditions: **2** (1 mmol), **3a** (1 mmol), **4** (1.2 mmol), [Bmim]OH@agar (**1**) (100 mg) and solvent (5 mL).
[b]Isolated yields after purification by column chromatography.

With an optimal set of parameters in hand, we turned our focus on surveying scope of reaction by reacting structurally diverse aldehydes (**3a–l**) with hippuric acid (**2**) and acetic anhydride (**4**) under the optimized reaction conditions. The results are illustrated in Table 3. The present methodology is amenable to the presence of a variety of functional groups on aldehydes and provided the anticipated products in moderate to good yields (Table 3, entries **5a–l**). Notably, aldehydes with electron-withdrawing substituents (Table 3, entries **3a–c**) were found to be suitable for this transformation as corresponding products were obtained in high yields than aldehydes with electron-donating substituents (Table 3, entries **3f**, **3h-3j**). More significantly, sterically hindered aldehydes such as salicylaldehyde and *o*-tolualdehyde also performed well

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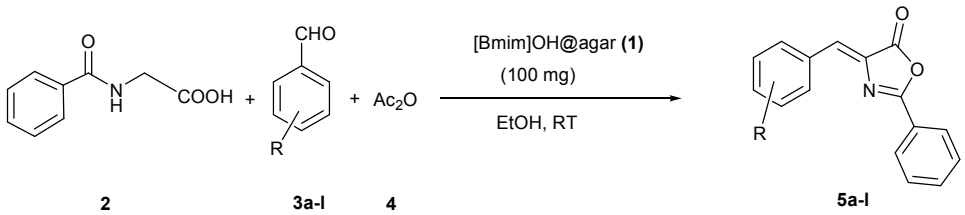
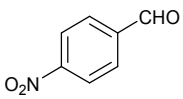
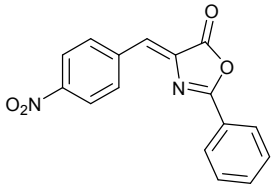
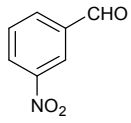
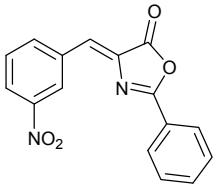
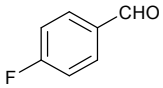
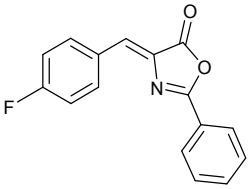
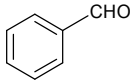
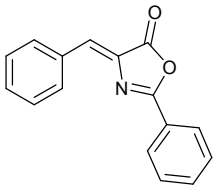
providing the desired azlactones in relatively good yields (Table 3, entries **3e, 3g**). It is noteworthy to mention that heteroaromatic aldehydes such as 2-thiophenecarboxaldehyde and 4-pyridinecarboxaldehyde also reacted efficiently furnishing the corresponding azlactones in good yields (Table 3, entries **3k–l**).

Table 3. [Bmim]OH@agar (**1**) mediated synthesis of azlactones[a]



Entry	Aldehyde (3)	Product (5)	Time (min.)	Yield[b] (%)
a			20	90
b			25	82
c			35	87
d			40	82

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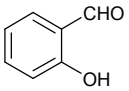
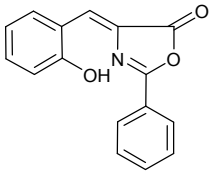
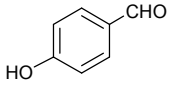
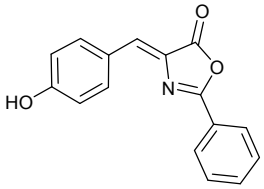
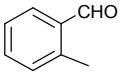
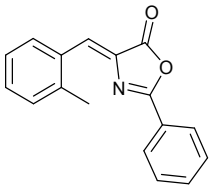
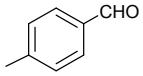
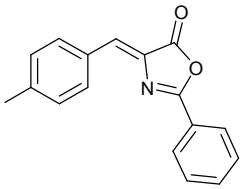
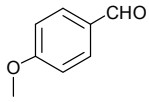
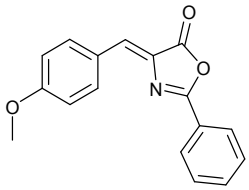
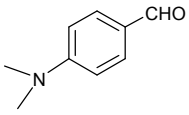
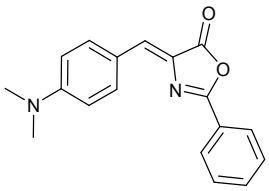
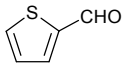
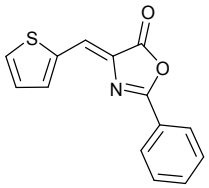
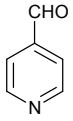
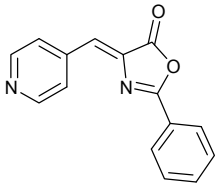
e			90	76
f			105	80
g			115	77
h			90	86
i			95	84
j			60	80
k			50	78
l			65	73

[a] Reaction conditions: **2** (1 mmol), **3** (1 mmol), **4** (1.2 mmol), [Bmim]OH@agar (**1**) (100 mg) and EtOH (5 mL).
[b] Isolated yields after purification by column chromatography.

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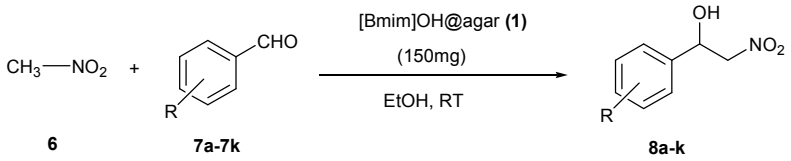
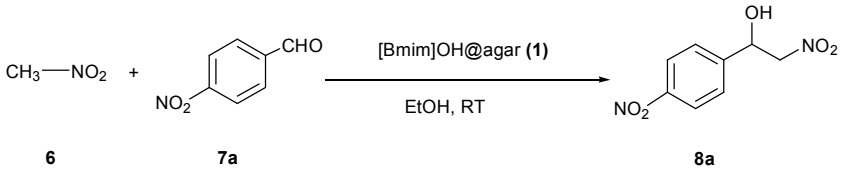
The successful application of [Bmim]OH@agar (**1**) in the synthesis of azlactones encouraged us to explore its compatibility in Henry reaction for synthesis of *β*-nitro alcohols (**Scheme 2**). To evaluate optimal reaction parameters, nitromethane (**6**) (1 mmol) and *p*-nitro benzaldehyde (**7a**) (1 mmol) were chosen as model substrates in presence of [Bmim]OH@agar (**1**) in ethanol. The impact of catalyst loading and solvents was investigated by employing different amounts of [Bmim]OH@agar (**1**) and variety of solvents (Table 4 and 5). The best results were obtained by performing a model reaction in the presence of 150 mg of [Bmim]OH@agar (**1**) (0.077 mmol) in ethanol as a solvent.



Scheme 2 [Bmim]OH@agar (**1**) catalyzed β-nitro alcohols synthesis

Table 4. Optimization of catalyst loading in synthesis of *β*-nitro alcohols[a]



Entry	Catalyst (mg)	Time (Min.)	Yield[b] (%)
1	50 (0.025 mmol)	160	50
2	100 (0.051 mmol)	55	70
3	**150 (0.077 mmol)**	**25**	**94**
4	200 (0.103 mmol)	25	95

[a]Reaction conditions: **6** (1 mmol), **7a** (1 mmol) and EtOH (5 mL).
[b]Isolated yields after purification by column chromatography.

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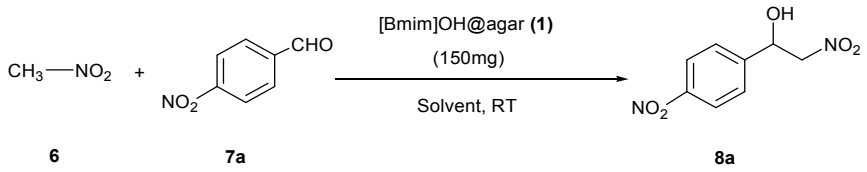
Table 5. Solvent optimization in the synthesis of *β*-nitro alcohols[a]



6 7a 8a

Entry	Solvent	Time (min.)	Yield[b] (%)
1	DMF	60	60
2	THF	45	57
3	Methanol	35	88
4	**Ethanol**	**25**	**94**
5	$CHCl_3$	55	30
6	CH_3CN	48	47
7	CH_2Cl_2	45	50
8	Toluene	65	35

[a]Reaction conditions: **6** (1 mmol), **7a** (1 mmol), [Bmim]OH@agar (**1**) (150 mg) and solvent (5 mL).
[b]Isolated yields after purification by column chromatography.

To establish generality of the method, substrate scope for the reaction was investigated under optimized reaction conditions by reacting structurally and electronically diverse aldehydes (**7a-k)** with nitromethane (**6**), the results of which are depicted in Table 6. In all the cases, reactions proceeded smoothly affording the corresponding *β*-nitro alcohols in good to excellent yields. In general, an electronic nature of the substituents attached to the aromatic ring had an impact on the yields of the products as aryl aldehydes with electron poor substituents (Table 6, entries **7a–b**) required shorter reaction time and afforded the anticipated products in high yield than those with electron rich substituents (Table 6, entries **7d, 7g-7i**). In addition, *ortho*-substituted benzaldehydes such as *o*-nitrobenzaldehyde, salicylaldehyde (Table 6, entries **7c, 7e**) underwent smooth reaction affording corresponding products in good yields. Moreover,

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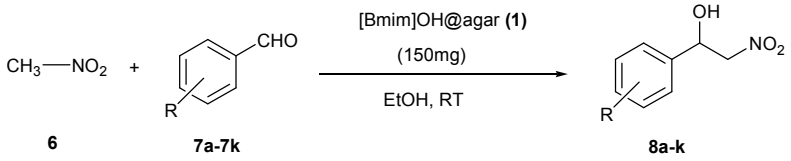
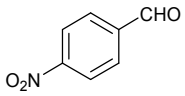
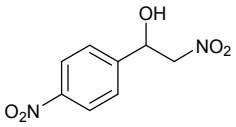
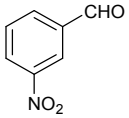
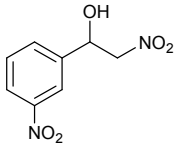
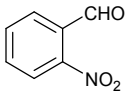
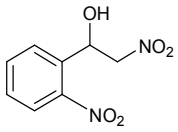
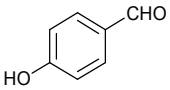
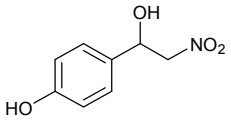
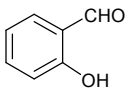
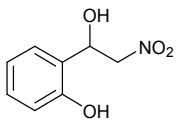
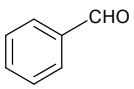
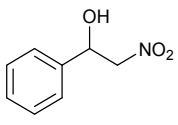
heterocyclic aldehydes such as 2-pyridinecarboxaldeyde, 4-pyridinecarboxaldehyde (Table 6, entries **7j-7k**) were found to react well furnishing related products in better yields.

Table 6. [Bmim]OH@agar (**1**) mediated synthesis of *β*-nitro alcohols[a]



6 7a-7k 8a-k

Entry	Aldehyde (7)	Product (8)	Time (min.)	Yield[b] (%)
a			25	94
b			35	90
c			40	85
d			40	75
e			55	72
f			120	79

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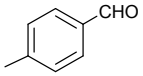
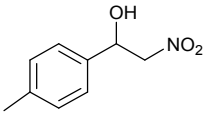
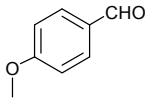
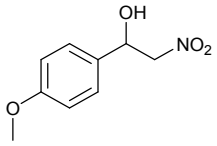
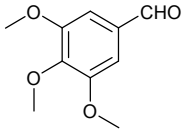
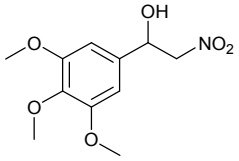
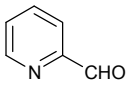
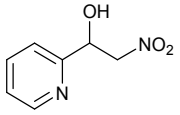
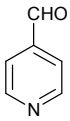
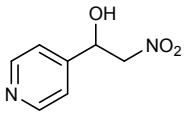
g			125	76
h			130	77
i			185	75
j			20	75
K			15	78

[a]Reaction conditions: **6** (1mmol), **7** (1 mmol), [Bmim]OH@agar (**1**) (150 mg) and EtOH (5 mL).
[b]Isolated yields after purification by column chromatography.

Identity of all the compounds was ascertained on the basis of IR, ^{1}H NMR, ^{13}C NMR spectroscopy and mass spectrometry. Spectroscopic data are consistent with the proposed structures and in harmony with the literature.

In order to gain insight into the main catalytic component of [Bmim]OH@agar (**1**), both the model reactions were carried out in presence of exclusively agar gel and [Bmim]OH. The agar gel failed to initiate both the reactions. On the contrary, [Bmim]OH could catalyze both Erlenmeyer-Plochl reaction (87% yield with 249 mol% catalyst loading) as well as Henry reaction (91% yield with 10 mol% catalyst loading). This is conclusive evidence for suggesting the prime role of [Bmim]OH in catalysis indicating that agar is unreactive immobilizing medium.

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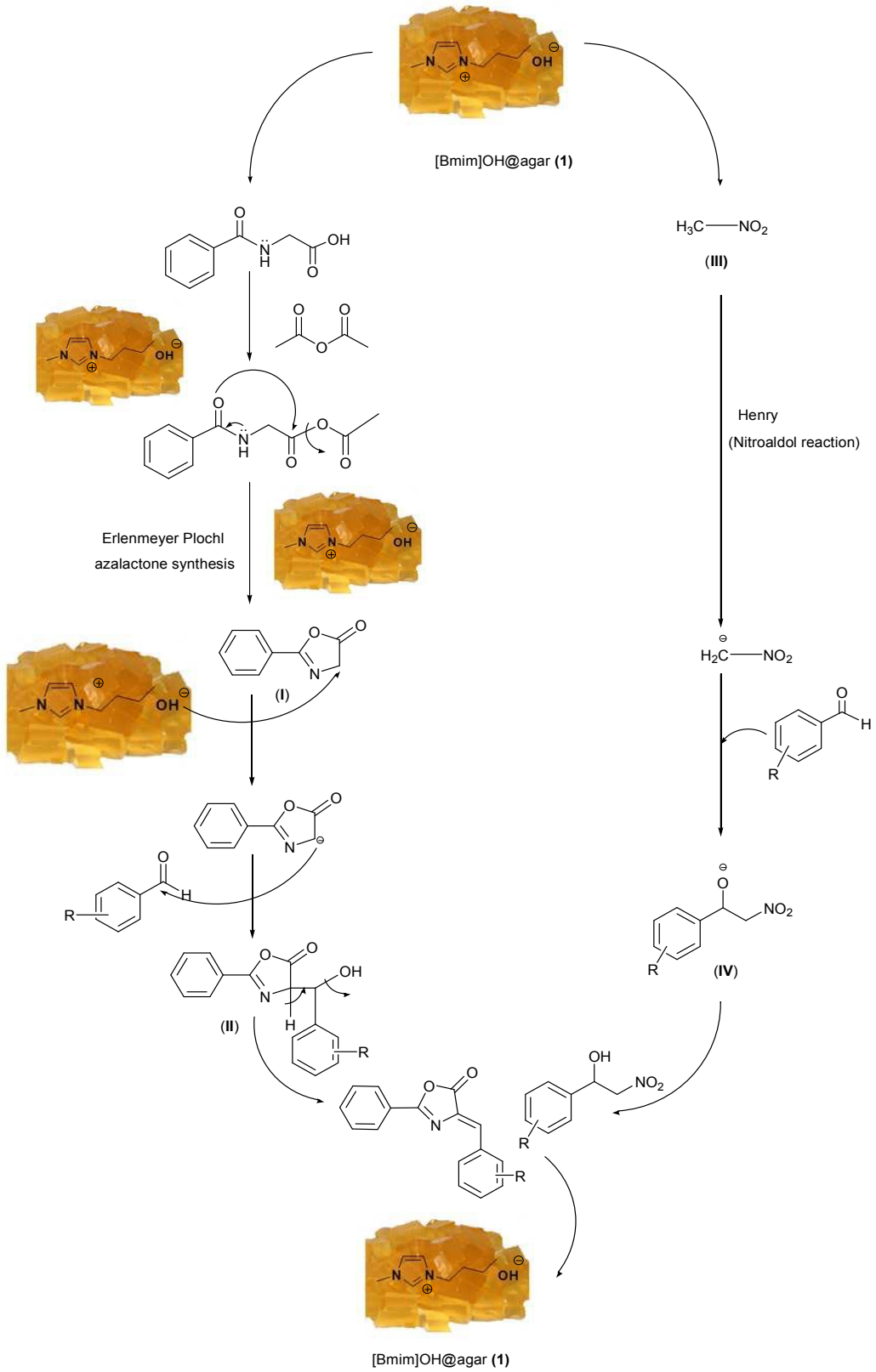

Scheme 3 A plausible mechanism for the synthesis of azlactones and *β*-nitro alcohols

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On the basis of literature reports,[30b-d] tentative mechanistic rational for the [Bmim]OH@agar (**1**) promoted Erlenmeyer-Plochl and Henry reaction is postulated in **Scheme 3**. In an initial step in the Erlenmeyer-Plochl reaction, cyclocondensation of hippuric acid in the presence of acetic anhydride generates intermediate 2-phenyl oxazol-5-one (**I**). The formation of intermediate **I** was confirmed by real time HRMS analysis of reaction mixture. The HRMS of reaction mixture displayed a peak at m/z = 160.98, which represents molecular ion (M^+) of intermediate (**I**). In the next step, [Bmim]OH from **1** abstracts proton of C_2 in **I** leading to the formation of carbanion which subsequently shows the nucleophilic attack on C=O group of aldehyde leading to the formation of **II**. In the last step, **II** eliminates water molecule furnishing the corresponding azlactone (**5**). In case of Henry reaction, initially, [Bmim]OH from **1** abstracts proton from nitromethane (**III**) leading to the formation of carbanion which subsequently shows the nucleophilic attack on C=O group of aldehyde generating intermediate **IV**. Finally, **IV** undergoes protonation to afford corresponding *β*-nitro alcohol (**8**).

In order to confirm the heterogeneous nature of [Bmim]OH@agar (**1**), a split test was performed with model Erlenmeyer-Plochl and Henry reaction. A catalyst was filtered off when 50% conversion was achieved (GC). The filtrate of the reaction mixture was stirred for additional 1 h. There was no increase in the amount of the corresponding product beyond 50%. These results revealed that entrapped IL is not being leached out from the agar matrix during the course of reaction. This greatly simplified the purification step and resulted in quantitative yields of product, without IL impurities.

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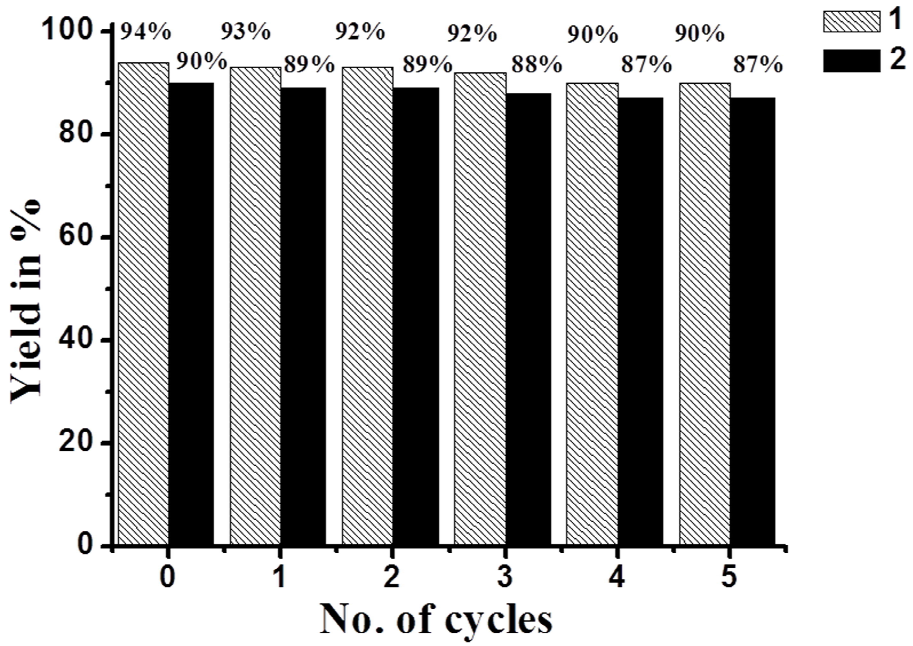

Fig. 5 Reusability of [Bmim]OH@agar (**1**) in the synthesis of-(1) β-nitro alcohols;

(2) Azlactones

A recyclability of the catalyst is a striking feature of heterogeneous catalysis and is a crucial parameter which designates the efficiency of the catalyst. Reusability of [Bmim]OH@agar (**1**) was tested for model Erlenmeyer-Plochl and Henry reactions. At the end of the reaction, the catalyst was isolated with the aid of simple filtration, washed several times with ethanol and subsequently reused in another catalytic cycle with identical substrates. The catalyst could be reused for five catalytic cycles, without a substantial decrease in catalytic activity and yield of product (Fig. 5).

In order to show merits of [Bmim]OH@agar (**1**) in comparison with other reported catalysts, we have summarized some of the previous reports for the preparation of 4-[(4-nitrophenyl)methylene]-2-phenyloxazol-5-one and 1-(4-nitrophenyl)-2-nitroethanol in Table 7 and 8 respectively. It is evident from these result that [Bmim]OH@agar (**1**) is more effective as compared to many of the reported catalysts in terms of yields as well as reaction time.

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Table 7. Comparison of various catalysts for synthesis of 4-[(4-nitrophenyl)methylene]-2-phenyloxazol-5-one (**5a**)

Sr. No.	Catalyst	Quantity	Temp (^{o}C)	Time	Yield (%)	Ref.
1	[Bnmim]H_2PO_4	2 mol%	US, RT	40 min.	90	12a
2	[Et_3NH][HSO_4]	10 mol%	100 ^{o}C	20 min.	96	12b
3	Mg/Al_2O_3	10 mol%	MW (300 W)	5 min.	90	31
4	K_3PO_4	5 mol%	80 ^{o}C	30 min.	93	11f
5	Iodine	5 mol%	MW (320 W)	65 sec.	94	11g
6	[Bmim]$_3PW_{12}O_{40}$	5 mol%	80 ^{o}C	75 min.	89	12c
	[Bmim]$_4W_{10}O_{32}$	5 mol%	80 ^{o}C	65 min.	90	
7	[C_6CmIm)$_2$]$_2W_{10}O_{32}$. $2H_2O$	5 mol%	US (RT)	24 min.	85	12e
8	[Bmim]OH	249 mol%	RT	90 min.	87	11e
9	**[Bmim]OH@agar (1)**	**5.37 mol%**	**RT**	**20 min.**	**90**	**Present work**

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Table 8. Comparison of various catalysts for synthesis of 1-(4-nitrophenyl)-2-nitroethanol (**8a**)

Sr. No.	Catalyst	Quantity	Temp (^oC)	Time (h or min.)	Yield (%)	Ref.
1	$[C_4dabco]OH$	10 mol%	RT	7 min.	99	18a
2	[18-C-6K][OH]	20 mol%	RT	10 min.	85	18b
3	Hexamethylene tetramine	20 mol%	RT	2.5 h	98	32a
4	Piperidine@dendritic sector (4-G_3)	10 mol%	RT	24 h	76	32b
5	K_2CO_3	10 mol%	60 ^oC	4 h	66	32c
6	Cyclen	5 mol%	RT	22 h	78	17a
7	Phosphine	10 mol%	RT	24 h	91	17b
8	$Mn(OAc)_2$, Schiff base	5 mol%	RT	24 h	95	17c
9	Ca^{2+}-Alginate	5 mol%	RT	24 h	88	17d
10	[Bmim]OH	10 mol%	RT	1 h	91	17e
11	**[Bmim]OH@agar (1)**	**7.75 mol%**	**RT**	**25 min.**	**94**	**Present work**

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Conclusions

In conclusion, we have synthesized the ionic liquid gel by entrapping [Bmim]OH in the matrix of aqueous agar gel. FT-IR analysis of ionic liquid gel demonstrated the hydrogen bonding and ion-dipole interaction between IL and agar. FT-Raman analysis ascertained the conservation of structural integrity of [Bmim]OH in the matrix of agar. FE-SEM micrographs of ionic liquid gel displayed no substantial alteration in the morphology of agar gel even after entrapment of IL. EDX analysis of ionic liquid gel confirmed the presence of respective elements. The ionic liquid gel exhibited outstanding catalytic activity in the synthesis of azlactones by using Erlenmeyer-Plochl reaction and β-nitro alcohols using Henry reaction. The ionic liquid gel could be reused for five cycles without substantial loss in catalytic activity. Mild reaction conditions, wide functional group tolerance, short reaction time, excellent catalytic activity and easy work up procedure are noteworthy merits of the protocol. We believe that the use of ionic liquid gel will contribute significantly to future developments aiming for sustainable processes.

Conflicts of interest

There are no conflicts of interest to declare.

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References

1 (a) S. C. DeVito, *Green Chem.*, 2016, **18**, 4332; (b) P. T. Anastas and J. C. Warner, Green Chemistry: Theory and Practice, Oxford University Press, New York, 1998; (c) M.

View Article Online
DOI: 10.1039/C8NJ00367J

Lancaster, Introduction to green chemistry, Royal Society of Chemistry, Cambridge, UK, 2002; (d) P. T Anastas and J. B. Zimmerman, *Environ. Sci. Technol*., 2003, **37**, 94A; (e) P. Anastas and N. Eghbali, *Chem. Soc. Rev.,* 2010, **39**, 301; (e) J. H. Clerk, *Nat. Chem.*, 2009, **1**, 12.

2 (a) R. L. Vekariya, *J. Mol. Liq.*, 2017, **227**, 44; (b) R. A. Sheldon, *Green Chem*., 2005, **7**, 267; (c) R. D. Rogers and K. R. Seddon, *Science*, 2003, **302**, 792; (d) Q. Zhang, S. Zhang and Y. Deng, *Green Chem.*, 2011, **13**, 2619; (e) J. Dupont and P. A. Suarez, *Phys. Chem. Chem. Phys.*, 2006, **8**, 2441.

3 (a) R. A. Sheldon, *Green Chem*., 2017, **19**, 18; (b) M. I. Qadir, J. Scholten and J. Dupont, *Catal. Sci. Technol.*, 2015, **5**, 1459; (c) C. V. Doorslaer, Y. Schellekens, P. Mertens, K. Binnemansb and D. De Vos, *Phys. Chem. Chem. Phys.*, 2010, **12**, 1741; (d) C. V. Doorslaer, A. Peeters, P. Mertens, C. Vinckier, K. Binnemansb and D. De Vos, *Chem. Commun.*, 2009, 6439; (e) H. Mehdi, A. Bodor, D. Lantos, I. T. Horvath, D. E. De Vos and K. Binnemans, *J. Org. Chem.*, 2007, **72**, 517; (f) M. Scott, P. J. Deuss, J. G. de Vries, M. H. G. Prechtl and K. Barta, *Catal. Sci. Technol.*, 2016, **6**, 1882; (g) P. A. Thomas and B. B. Marvey, *Molecules*, 2016, **21(2)**, 184.

4 (a) M. Kermanioryani, M. I. A. Mutalib, Y. Dong, K. C. Lethesh, O. B. O. Ben Ghanem, K. A. Kurnia, N. F. Aminuddin and J. M. Leveque, *J. Chem. Eng. Data*, 2016, **61**, 2020; (b) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (c) T. Boudewijns, M. Piccinini, P. Degraeve, A. Liebens and D. De Vos, *ACS Catal.*, 2015, **5**, 4043; (d) U. Schroder, J. D. Wadhawan, R. G. Compton, F. Marken, P. A. Z. Suarez, C. S. Consorti, R. F. de Souza and J. Dupont, *New J. Chem.*, 2000, **24**, 1009; (e) T. L. Greaves and C. J. Drummond, *Chem. Rev.,* 2008, **108 (1)**, 206; (f) A. S. Amarasekara, *Chem. Rev*. 2016, **116**, 6133; (g) A. –L. Girard, N.

View Article Online
DOI: 10.1039/C8NJ00367J

Simon, M. Zanatta, S. Marmitt, P. Gonçalves and J. Dupont, *Green Chem.*, 2014, **16**, 2815.

5 (a) K. S. Egorova, E. G. Gordeev and V. P. Ananikov, *Chem. Rev.*, 2017, **117 (10)**, 7132; (b) J. Hulsbosch, D. E. De Vos, K. Binnemans and R. Ameloot, *ACS Sustainable Chem. Eng.*, 2016, **4**, 2917; (c) V. I. Parvulescu and C. Hardacre, *Chem. Rev.,* 2007, **107**, 2615; (d) P. Wasserschied and T. Welton (eds.), Ionic Liquids in Synthesis, ed., VCH Wiley, Weinheim, 2nd edn., 2008; (e) J. P. Hallett and T. Welton, *Chem. Rev*., 2011, **111**, 3508; (f) J. Dupont, *Acc. Chem. Res.*, 2011, **44**, 1223.

6 (a) E. Garcia-Verdugo, B. Altava, M. I. Burguete, P. Lozanob and S. V. Luisa, *Green Chem.*, 2015, **17**, 2693; (b) A. Riisager, R. Fehrmann, M. Haumann and P. Wasserscheid, *Eur. J. Inorg. Chem*., 2006, 695; (c) R. Duque, D. J. Cole-Hamilton, ed. R. Fehrmann, A. Riisager and M. Haumann, Supported Ionic Liquids: Fundamentals and Applications, Wiley-VCH Verlag GmbH & Co., Weinheim, 2014, Supported Ionic Liquids, pp. 369-384.

7 (a) T. Bauer, R. Stepic, P. Wolf, F. Kollhoff, W. Karawacka, C. R. Wick, M. Haumann, P. Wasserscheid, D. M. Smith, A. –S. Smith and J. Libuda, *Catal. Sci. Technol*., 2018, **8**, 344; (b) C. V. Doorslaer, J. Wahlen, P. Mertens, K. Binnemans and D. De Vos, *Dalton Trans.*, 2010, **39**, 8377; (b) U. Hintermair, G. Francio and W. Leitner, *Chem. – Eur. J.*, 2013, **19**, 4538; (c) M. A. Gelesky, S. S. X. Chiaro, F. A. Pavan, J. H. Z. dos Santos and J. Dupont, *Dalton Trans.*, 2007, 5549; (d) C. P. Mehnert, E. J. Mozeleski and R. A. Cook, *Chem. Commun.*, 2002, 3010; (e) P. Agrigento, S. M. Al-Amsyar, B. Soree, M. Taherimehr, M. Gruttadauria, C. Aprile and P. P. Pescarmona, *Catal. Sci. Technol.*, 2014, **4**, 1598.

View Article Online
DOI: 10.1039/C8NJ00367J

8 P. Laurienzo, *Mar. Drugs*, 2010, **8**, 2435.

9 (a) D. Benedlt and V. Daniel, *J. Med. Chem.*, 1994, **37**, 710; (b) F. C. Savariz, M. A. Foglio, J. E. de Carvalho, A. L. Ruiz, M. C. Duarte, M. F. da Rosa, E. Meyer and M. H. Sarragiotto, *Molecules*, 2012, **17(5)**, 6100; (c) K. Ando and N. Asai, *EUR PAT*, 1990, 385; (d) M. Witvrouw, C. Pannecouque, E. D. Clercq, E. Fernandez-Alvarez and J. L. Marco, *Arch. Pharm. Pharm. Med. Chem*., 1999, **352**, 163; (e) K. M. Khan, U. R. Mughal, M. T. H. Khan, Z. Ullah, S. Perveen and M. I. Choudhary, *Bioorg. Med. Chem. Lett.*, 2006, **14**, 6027; (f) R. A. Schnettler, W. D. Jones and G. P. Claxton, *US Patent*, 1987, US 4698353; (g) G. Marriappan, B. P. Saha, S. Datta, D. Kumar and P. K. Haldar, *J. Chem. Sci.*, 2011, **123**, 335.

10 (a) M. I. Ismail, *Can. J. Chem.*, 1991, **69**, 1886; (b) H. Matsunaga, T. Ishizuka and T. Kunieda, *Tetrahedron*, 2005, **61**, 8073; (c) J. Lamb and W. Robson, *Biochem. J.*, 1931, **25**, 1231; (d) D. Seebach, G. Jaeschke, K. Gottwald, K. Matsuda, R. Formisano and D. A. Chaplin, *Tetrahedron*, 1997, **53**, 7539.

11 (a) P. A. Conway, K. Devine and F. Paradisi, *Tetrahedron,* 2009, **65**, 2935; (b) F. M. Bautista, J. M. Campelo, A. Garcia, D. Luna, J. M. Marinas and A. A. Romero, *J. Chem. Soc., Perkin Trans*., 2002, **2**, 227; (c) K. M. Khan, U. R. Mughal, M. A. Lodhi and M. I. Chaudhary, *Lett. Drug Des. Discov.,* 2008, **5**, 52; (d) M. R. P. Heravi, *J. Univ. Chem. Technol. Metall.*, 2009, **44(1)**, 86; (e) S. G. Patil, R. R. Bagul, V. M. Kamble and V. A. Navale, *J. Chem. Pharm. Res.*, 2011, **3(4)**, 285; (f) T. Cleary, J. Brice, N. Kennedy and F. Chavez, *Tetrahedron Lett.*, 2010, **51**, 625; (g) M. B. M. Reddy and M. A. Pasha, *Synth. Commun.*, 2010, **40**, 1895; (h) C. A. B. Rodrigues, J. M. G. Martinho and C. A. M. Afonso,

View Article Online
DOI: 10.1039/C8NJ00367J

J. Chem. Educ., 2015, **92**, 1543; (i) G. Romanelli, J. C. Autino, P. Vazquez, L. Pizzio, M. Blanco and C. Caceres, *Appl. Catal. A.*, 2009, **352**, 208.

12 (a) K. F. Shelke, A. D. Badar and J. B. Devhade, *Chem. Biol.Interface*, 2016, **6(3)**, 157; (b) M. Praveen, F. Ahmad, A. M. Malla, S. Azaz, M. R. Silva and P. S. P. Silva, *RSC Adv.*, 2015, **5**, 52330; (c) M. Rostami, A. Khosropour, V. Mirkhani, M. Moghadam, S. Tangestaninejad and I. Mohammadpoor-Baltrok, *Appl. Catal. A*, 2011, **397**, 27; (d) M. Rostami, A. Khosropour, V. Mirkhani, I. Mohammadpoor-Baltrok, M. Moghadam and S. Tangestaninejad, *Monatsh Chem.*, 2011, **142**, 1175; (e) M. Rostami, A. Khosropour, V. Mirkhani, I. Mohammadpoor-Baltrok, M. Moghadam, S. Tangestaninejad, *C. R. Chimie*, 2011, **14**, 869; (f) B. Zhou and W. Chen, *J. Chem.*, 2013, 5.

13 (a) C. Palomo, M. Oiarbide and A. Laso, *Eur. J. Org. Chem.*, 2007, 2561; (b) J. Boruwa, N. Gogoi, P. P. Saikia and N. C. Barua, *Tetrahedron: Asymmetry*, 2006, **17**, 3315; (c) C. Palomo, M. Oiarbide and A. Mielgo, *Angew. Chem. Int. Ed.*, 2004, **43**, 5442; (d) M. Shibasaki and N. Yoshikawa, *Chem. Rev.*, 2002, **102**, 2187.

14 S. L. Liu and C. Wolf, *Org. Lett.*, 2008, **10**, 1831

15 M. A. Rizzacasa and M. V. Sargent, *J. Chem. Soc. Chem. Commun.*, 1990, **12**, 894

16 (a) S. Hanessian and J. Kloss, *Tetrahedron Lett.*, 1985, **26**, 1261; (b) H. Sasai, K. Matsuno and T. Suami, *J. Carbohydr. Chem.*, 1985, **4**, 99.

17 (a) C. V. –L. Bray, F. Jiang, X. –F. Wu, J. –B. Sortais and C. Darcel, *Tetrahedron Lett.*, 2010, **51**, 4555; (b) J. A. Weeden and J. D. Chisholm, *Tetrahedron Lett*., 2006, **47**, 9313; (c) G. P. Zhou, Y. H. Hui, N. N. Wan, Q. J. Liu, Z. F. Xie and J. D. Wang, *Chin. Chem. Lett*., 2012, **23**, 690; (d) D. Kuhbeck, J. Mayr, M. Haring, M. Hofmann, F. Quignard and D. Diaz Diaz, *New J. Chem*., 2015, **39**, 2306; (e) H. Wu, F. Zhang, Y. Wan and L. Ye, *Lett.*

View Article Online
DOI: 10.1039/C8NJ00367J

Org. Chem., 2008, **5**, 209; (f) M. Haring, A. Pettignano, F. Quignard, N. Tanchoux and D. Diaz Diaz, *Molecules*, 2016, **21**(**9**), 1122.

18 (a) S. Keithellakpam and W. S. Laitonjam, *Ind. J. Chem.,* 2016, **55B**, 110; (b) C. Wang, J. Liu, W. Leng and Y. Gao, *Int. J. Mol. Sci.*, 2014, **15**, 1284; (c) A. Ying, S. Xu, S. Liu, Y. Ni, J. Yang and C. Wu, *Ind. Eng. Chem. Res.*, 2014, **53**, 547; (d) Y. Song, H. Jiang, B. Li and D. Bai, *Chem. Eur. J.*, 2011, **17**, 8731; (e) W. Wang, W. Cheng, L. Shao, C. Liu and J. Yang, *Kinet. Catal*., 2009, **50**(**2**), 186; (f) A. Kumar and S. S. Pawar, *J. Mol. Catal. A Chem.*, 2005, **235**, 244; (g) T. Jiang, H. Gao, B. Han, G. Zhao, Y. Chang, W. Wu, L. Gao and G. Yang, *Tetrahedron Lett.*, 2004, **45**, 2699.

19 R. Kurane, J. Jadhav, S. Khanapure, R. Salunkhe and G. Rashinkar, *Green Chem.*, 2013, **15**, 1849.

20 (a) C. Yu, B. Zhou, W. Su and Z. Xu, *Synth. Commun.*, 2006, **36**, 3447; (b) A. Mobinikhaledi, H. Moghanian and S. Pakdel, *Chinese Chem. Lett.*, 2015, **26(5)**, 557.

21 T. Cleary, T. Rawalpally, N. Kennedy, F. Chavez, *Tetrahedron Lett.*, 2010, **51(12)**, 1533.

22 G. K. Rao, *Indian J. Heterocycl. Chem.*, 2010, **19(3)**, 303.

23 (a) D. Kaushik, S. A. Khan and G. Chawla*, Eur. J. Org. Chem.*, 2010, **45**, 3960; (b) M. Sudheer, K. K. Srinivas and D. Bukka, *Elixir Pharmacy*, 2013, **54**, 12315; (c) S. A. M. Tikdari, S. Fozooni and H. Hamidian, *Molecules*, 2008, **13**, 3246.

24 M. N. Elinson, A. I. Ilovaisky, V. M. Merkulova, F. Barba and B. Batanero, *Tetrahedron*, 2008, **64**, 5915.

25 (a) F. K. MacDonald, K. M. M. Carneiro and I. R. Pottie, *Tetrahedron Lett.*, 2011, **52(8)**, 891; (b) J. Boileau, *B. Soc. Chim. Fr.*, 1953, 1007.

26 J. Fan, G. Sun, C. Wan, Z. Wang and Y. Li, *Chem. Commun.*, 2008, **32**, 3792.

View Article Online
DOI: 10.1039/C8NJ00367J

27 (a) Y. Y. Liu, S. W. Wang and L. J. Zhang, *Chin. J. Chem.*, 2008, **26**, 2267; (b) M. A. Allais, *Bull. Soc. Chim. Fr.*, 1949, 536; (c) F. A. Khan, C. Sudheer and N. Sahu, *Synth. Commun.,* 2005, **35**, 201; (d) K. Wismayr, O. Schmid and G. Zoeless, 1967, DE 1233410 B; (e) E. Profft, F. Schneider and H. Beyer, *J. Prakt. Chem.,* 1955, **2**, 147.

28 (a) B. Eduardo, G. F. Vicente and V. Gotor, *Org. Process Res. Dev.*, 2011, **15**, 236; (b) F. Zymalkowski, *Arch Pharm Ber. Dtsch Pharm. Ges.*, 1956, **289**, 52.

29 (a) A. R. Hajipour and F. Rafiee, *J. Iran. Chem. Soc.*, 2009, **6(4)**, 647; (b) Z. S. Qureshi, K. M. Deshmukh and B. M. Bhanage, *Clean Techn. Environ. Policy*, 2014, **16**, 1487; (c) C. Yue, D. Fang, L. Liu and T. –F. Yi, *J. Mol. Liq.*, 2011, **163**, 99; (d) P. Bharmoria and A. Kumar, *RSC Adv.*, 2013, **3**, 19600; (e) R. Leones, F. Sentanin, L. C. Rodrigues, I. M. Marrucho, J. M. S. S. Esperanca, A. Pawlicka and M. M. Silva, *Express Polym. Lett.*, 2012, **12**, 1007.

30 (a) F. Zhang, X. Bao, Q. Liu and M. Huang, *Journal of Materials and Chemical Engineering*, 2014, **2(4)**, 86; (b) A. Mobinikhaledi, H. Moghanian, S. Pakdel, *Chin. Chem. Lett.*, 2015, **26(5)**, 557; (c) T. Cleary, T. Rawalpally, N. Kennedy, F. Chavez, *Tetrahedron Lett.*, 2010, **51**, 1533; (d) R. Ballini, G. Bosica, *J. Org. Chem.*, 1997, **62(2)**, 425.

31 N. Rostamizadeh, A. Khajeh-Amiri and H. Moghanian, *Synth. React. Inorg. M.*, 2016, **46**, 631

32 (a) S. Fathi and A. R. Sardarian, *Iran. J. Sci. Technol. Trans. Sci.*, 2016, **40**, 103; (b) B. Yi, Y. Yin, Z. Yi, W. Zhou, H. Liu, N. Tan and H. Yang, *Tetrahedron Lett.*, 2016, **57**, 2320; (c) G. Bosica and K. Polidano, *J. Chem.*, 2017, 9.

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DOI: 10.1039/C8NJ00367J

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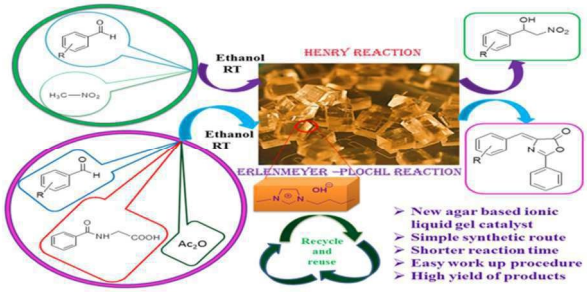

Agar gel entrapped [Bmim]OH has been prepared and employed as efficient heterogeneous catalyst for synthesis of β-nitro alcohols and azlactones.