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Organic–inorganic hybrid polyoxometalates: Efficient, heterogeneous and reusable catalysts for solvent-free synthesis of azlactones

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ABSTRACT

Two organic–inorganic hybrid polyoxometalates, consist of 1-butyl-3-methylimidazolium salts of $(W_{10}O_{32})^{4-}$ and $(PW_{12}O_{40})^{3-}$ polyanions were prepared and characterized by thermal analysis, X-ray diffraction, FT-IR, diffuse reflectance UV–Vis spectroscopic methods and nitrogen absorption–desorption determination (BET). These heterogeneous catalysts were used for synthesis of azlactones by the reaction of aldehydes with hippuric acid and acetic anhydride under solvent-free conditions. These catalysts were reused several times without loss of their activities.

1. Introduction

Azlactones are very interesting intermediates for the synthesis of a variety of bioactive molecules and show a wide range of pharmaceutical properties [1–5]. These compounds are especially active as anticancer [6], antitumor [7] and inhibitor of central nervous system. These valuable organic compounds are unique precursors for the synthesis of amino acids, peptides [8,9], heterocyclic compounds [10,11], biosensors [12] and *N*-substituted pyrroles [13].

Furthermore, some azlactones derivatives exhibit excellent nonlinear optical properties both in the solid state and in solution [14]. For instance 4-(4′-methoxybenzylidene)-2-phenyloxazoline-5-one is a nonlinear optical material with high SHG (second harmonic generation) efficiency and very good transparency [15]. By using new spectroscopic methods, it is easy to determine some photophysical and photochemical features of these compounds in various states, such as crystalline state, sol–gel and polymeric matrices [16]. Beside of all these unique applications, some of these compounds have been used as pH indicator [17]. Another brilliant application of some azlactone derivatives is their use as immunomodulator [18].

The most common and useful procedure for the azlactone synthesis is Erlenmeyer method. This reaction is based on the condensation of an aldehyde with hippuric acid in the presence of acetic anhydride as dehydrating agent and sodium acetate as catalyst [19]. After this report, several catalysts such as silica-supported heteropolyacids [20], $Yb(OTf)_3$ [21], $Ca(OAc)_2$ [22], organic bases [23], $Bi(OAc)_3$ [24], $Bi(OTf)_3$ [25], Al_2O_3 [26] and $POCl_3$ [27] have been used to perform this condensation.

In recent years, the green chemistry has been become an interesting research field for organic chemists. Among the different strategies for achieving this goal, the use of heterogeneous catalysts and solvent-free methods has received special attentions. These green methods offer several advantages such as cleaner products, higher selectivity, simpler work up and shorter reaction times [28].

Polyoxometalates have been found as useful materials in catalysis, photho- and electrochromism, optical materials, medicine and fuel cells. In the field of catalysis, these materials have enormous potential for catalyzing a wide variety of reactions and also have been developed for the synthesis of fine chemicals such as flavor, pharmaceutical and food industries [29–32]. A new class of these compounds is hybrid organic–inorganic polyoxometalates. These hybrid materials have different properties in comparison with original organic and inorganic components and this makes them very interesting materials for chemists. Different organic counter cations and polyoxametalate anions have been reported for preparation of this class of materials [33–39]. Introduction of imidazolium cation to the POMs is an efficient way for development of organic–inorganic hybrid materials. These compounds are used in thermally stable solid lubricants, biocatalysis, nanoparticle research [40–43] and electrochemical systems [44].

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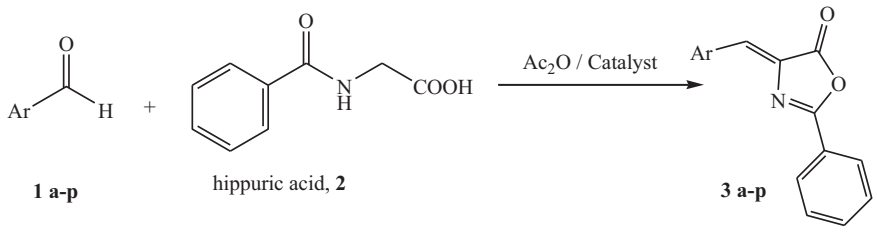


Scheme 1. The azlactones Erlenmeyer synthesis.

$$3[bmim]Cl + H_3PW_{12}O_{40}.nH_2O \longrightarrow [bmim]_3PW_{12}O_{40} + 3HCl$$

Scheme 2.

The organic salts of $W_{10}O_{32}^{4-}$ and $PW_{12}O_{40}^{3-}$ polyanions are able to catalyze several reactions such as epoxidation of alkenes and oxidation of alcohols [45–47].

Herein, we report the preparation and characterization of two heterogeneous organic–inorganic polyoxometalates hybrid using [bmim][Cl] and Keggin polyoxometalates, The catalytic activity of these catalysts in the synthesis of azlactones under solvent-free conditions was also investigated (Scheme 1).

2. Experimental

All chemicals and solvents were commercial reagent grade and were purified before use. FT-IR spectra were obtained as potassium bromide pellets in the range of 400–4000 cm^{-1} with a Nicolet Impact 400D instrument. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker-Arance AQS 500 MHz.

2.1. Synthesis of $[bmim]_3PW_{12}O_{40}$

An aqueous solution of 1-butyl-3-methylimidazolium chloride [bmim][Cl] in the water (3.5 mmol, 0.61 g) was added drop-wise to an aqueous solution of $H_3PW_{12}O_{40}$ (1 mmol, 2.88 g; dried overnight at 80 °C) at room temperature and stirred for 1 h. The white precipitate was filtered and washed with deionized water. The catalyst was dried overnight at 80–100 °C [38] (Scheme 2).

2.2. Synthesis of $[bmim]_4W_{10}O_{32}$

To a solution of $Na_2WO_4{\cdot}2H_2O$ (5 mmol, 1.652 g) in H_2O (10 ml) was added aqueous HCl (9 ml, 3 M) and boiled until a clear yellow solution was obtained. A solution of 1-butyl-3-methylimidazolium bromide (10 mmol, 2.19 g; dried at 80 °C) was added to this solution and the precipitate was filtered, washed with water and dried overnight at 80 °C in vacuum [48] (Scheme 3).

2.3. General procedure for synthesis of azlactones

In a 25 ml round bottom flask, aldehyde (1 mmol), hippuric acid (1.2 mmol) and catalyst (5 mol%), were mixed and stirred for 5 min. Then freshly distilled acetic anhydride (2 mmol) was added to the reaction mixture and heated at 80 °C. The reaction progress was monitored by TLC (petroleum ether/ethyl acetate: 9/1). After the reaction was completed, the mixture was cooled to room temperature. An aqueous solution (20%) of $NaHCO_3$ (10 ml) was added, the solid products and the catalyst were filtered. The solid materials were dissolved in Et_2O to remove the catalyst. The solvent was evaporated and the pure products were recrystallized from hot ethanol. In addition, the blank experiment revealed that in the absence of catalyst only less than 10% of the corresponding azlactone was obtained under same reaction conditions.

2.4. Catalyst recycling

The reusability of the catalysts was also checked. In this manner, the reaction of 4-chlorobenzaldehyde was chosen as model reaction. At the end of each reaction, a 1:1 mixture of ethyl acetate/aqueous solution (20%) of $NaHCO_3$ (20 ml) was added to the mixture and the catalyst was filtered, dried and reused in the next run.

2.5. Spectral data

(4*Z*)-4-(4-chlorobenzylidene)-2-phenyloxazol-5(4H)-one **(3a)** [4]: mp 188–190 °C; IR (KBr): υ (cm^{-1}) 3049, 1796, 1654, 1588, 1486, 1449, 1325, 1160, 864, 824, 695; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.23 (1H, s), 7.48–7.49 (2H, d, J = 8.5), 7.57–7.60 (2H, t, J = 7.65), 7.65–7.68 (1H, t, J = 7.2), 8.18–8.20 (2H, d, J = 8.4), 8.21–8.23 (2H, m); Mass (*m*/*z*): 283.04, 105, 76.99.

(4*Z*)-4-(4-bromobenzylidene)-2-phenyloxazol-5(4H)-one **(3b)** [23]: mp 197–199 °C; IR (KBr): υ (cm^{-1}) 3053, 1794, 1651, 1581, 1324, 1162, 1071, 980, 862, 821, 694; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.21 (1H, s), 7.57–7.60 (2H, t, J = 8.5), 7.64–7.68 (3H, m), 8.11–8.12 (2H, d, J = 7.5), 8.21–8.23 (2H, m); Mass (*m*/*z*): 326.99, 104.97, 77.01.

(4*Z*)-4-(4-methoxybenzylidene)-2-phenyloxazol-5(4H)-one **(3c)** [26]: mp 153–155 °C; IR (KBr): υ (cm^{-1}) 3055, 2930, 1175, 1640, 1255, 1155, 825, 690; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.93 (3H, s), 7.03–7.05 (2H, d, J = 8.9), 7.27 (1H, s), 7.55–7.58 (2H, t, J = 7.3), 7.62–7.65 (1H, t, J = 7.5), 8.20–8.25 (4H, m); Mass (*m*/*z*): 279.09, 206.89, 105.01, 77.01, 59.08.

(4*Z*)-4-(4-(dimethylamino)benzylidene)-2-phenyloxazol-5(4H)-one **(3d)** [20]: mp 212–214 °C; IR (KBr): υ (cm^{-1}) 3055, 2923, 2857, 1763, 1647, 1606, 1529, 1448, 1375, 1195, 1162, 813, 694; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.14 (6H, s), 6.78–6.80 (2H, d, J = 9.1), 7.25 (1H, s), 7.52–7.60 (3H, m), 8.17–8.19 (4H, m); Mass (*m*/*z*): 292.08, 104.96, 77.06.

(4*Z*)-4-(4-(benzyloxy)benzylidene)-2-phenyloxazol-5(4H)-one **(3e)**: mp 152–154 °C; IR (KBr): υ (cm^{-1}) 3067, 2855, 1793, 1653, 1597, 1505, 1453, 1299, 1252, 1155, 981, 825,696; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.2 (2H, s), 7.10–7.12 (2H, d, J = 8.9), 7.26 (1H, s), 7.38–7.65 (7H, m), 8.20–8.24 (4H, m); ^{13}CNMR (125 MHz,

$$10Na_2WO_4.2H_2O + 4[bmim]Br \xrightarrow[H_2O]{HCl} [bmim]_4W_{10}O_{32} + NaCl + NaBr$$

Scheme 3.

$CDCl_3$) δ (ppm): 71.00, 112.00, 114.20, 127.30, 127.50, 127.65, 127.73, 128.87, 129.05, 129.25, 129.89, 131.23, 131.64, 141.40, 159.90, 161.12, 167.05, Mass (*m*/*z*): 355.25, 149.04, 115.10, 76.99, 56.97.

(4*Z*)-4-(4-nitrobenzylidene)-2-phenyloxazol-5(4H)-one **(3f)** [20]: mp 237–239 °C; IR (KBr): υ (cm^{-1}) 3063, 1795, 1661, 1559, 1513, 1450, 1345, 1284, 11167, 979, 865, 684; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.28 (1H, s), 7.60–7.63 (2H, t, *J* = 7.5), 7.7–7.73 (1H, t, *J* = 7.5), 8.25–8.27 (2H, m), 8.35–8.37 (2H, d, *J* = 8.8), 8.40–8.42 (2H, d, *J* = 8.8); Mass (*m*/*z*): 294.06, 105.11, 77.12.

(4*Z*)-4-(4-fluorobenzylidene)-2-phenyloxazol-5(4H)-one **(3g)** [26]: mp 177–179 °C; IR (KBr): υ (cm^{-1}) 3059, 1796, 1662, 1596, 1506, 1450, 124, 1242, 1157, 1094, 984, 834, 696; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.19–7.23 (2H, t, *J* = 8.5), 7.25 (1H, s), 7.56–7.59 (2H, t, *J* = 7.3), 7.65–7.68 (1H, t, *J* = 7.3), 8.21–8.22 (2H, d, *J* = 7.5), 8.25–8.28 (2H, m); Mass (*m*/*z*): 267.04, 105, 77.11.

(4*Z*)-4-(2-bromobenzylidene)-2-phenyloxazol-5(4H)-one **(3h)** [5]: mp 141–143 °C; IR (KBr): υ (cm^{-1}) 3054, 1793, 1650, 1551, 1325, 1292, 1167, 863, 763, 696; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37–7.69 (6H, m), 7.8 (1H, s), 8.22–8.24 (2H, d, *J* = 7.3), 8.96–8.97 (1H, d, *J* = 7.8); Mass (*m*/*z*): 326.99, 104.97, 77.01.

(4*Z*)-4-(3-bromobenzylidene)-2-phenyloxazol-5(4H)-one **(3i)** [25]: mp 147–149 °C; IR (KBr): υ (cm^{-1}) 3052, 1795, 1656, 1597, 1449, 1326, 1294, 1163, 982, 873, 776, 678; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.19 (1H, s), 7.37–7.40 (1H, t, *J* = 7.8), 7.58–7.62 (3H, m), 7.66–7.69 (1H, t, *J* = 7.3), 8.10–8.12 (1H, d, *J* = 7.8), 8.22–8.24 (2H, m), 8.47 (1H, s); Mass (*m*/*z*): 326.99, 194.06, 105.12, 77.08.

(4*Z*)-4-(2-chlorobenzylidene)-2-phenyloxazol-5(4H)-one **(3j)** [20,21]: mp 162–163 °C; IR (KBr): υ (cm^{-1}) 3056, 1793, 1652, 1554, 1328, 1294, 1169, 865, 764, 694, 565; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37–7.69 (6H, m), 7.8 (1H, s), 8.22–8.24 (2H, d, *J* = 7.3), 8.96–8.97 (1H, d, *J* = 7.8); Mass (*m*/*z*): 283.25, 105.06, 77.06.

(4*Z*)-4-(3-nitrobenzylidene)-2-phenyloxazol-5(4H)-one **(3k)** [4,21]: mp 174–176 °C; IR (KBr): υ (cm^{-1}) 3073, 1717, 1647, 1532, 1480, 1351, 1260, 1026, 691; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.32 (1H, s), 7.4–7.8 (4H, m), 8.12–8.55 (4H, m), 9.3 (1H, s); Mass (*m*/*z*): 294.06, 105, 76.95.

(4*Z*)-4-(2,4-dichlorobenzylidene)-2-phenyloxazol-5(4H)-one **(3l)** [27]: mp 181–183 °C; IR (KBr): υ (cm^{-1}) 3064, 2922, 2850, 1797, 1655, 1558, 1450, 1323, 1168, 1093, 979, 694; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.42–7.44 (1H, d, *J* = 8.6), 7.53 (1H, s), 7.57–7.60 (2H, m), 7.67–7.70(2H, m), 8.21–8.23 (2H, d, *J* = 8.1), 8.94–8.95 (1H, d, *J* = 8.6); Mass (*m*/*z*): 318.2, 105.12, 77.06.

(4*Z*)-4-((naphthalen-1-yl)methylene)-2-phenyloxazol-5(4H)-one **(3m)** [25]: mp 163–165 °C; IR (KBr): υ (cm^{-1}) 3060, 2923, 1792, 1645, 1549, 1488, 1448, 1323, 1167, 978, 874, 694; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.57–7.70 (6H, m), 7.94–7.96 (1H, d, *J* = 8), 8.01–8.02 (1H, d, *J* = 8.1), 8.19 (1H, s), 8.25–8.26 (2H, m), 8.35–8.37 (1H, d, *J* = 8.5), 9.07–9.09 (1H, d, *J* = 7.4); Mass (*m*/*z*): 299.09, 105, 77.01.

(4*Z*)-4-((1H-indol-3-yl)methylene)-2-phenyloxazol-5(4H)-one **(3n)** [5,21]: mp 209–211 °C; IR (KBr): υ (cm^{-1}) 3328, 3052, 1730, 1644, 1508, 1459, 1288, 1124, 887, 743; ^{1}H NMR (500 MHz, C_3D_6O) δ (ppm): 7.32–7.62 (6H, m), 7.7 (1H, s), 8.05 (1H, bs), 8.17–8.19 (1H, dd, *J* = 9.5, *J* = 1.5), 8.65 (1H, s), 8.87 (1H, bs); ^{13}CNMR (125 MHz, C_3D_6O) δ (ppm): 112.23, 112.40, 119.62, 121.63, 123.24, 125.65, 126.45, 127.08, 127.52, 127.55, 129.13, 132.60, 134.42, 137.02, 160.03, 166.99; Mass (*m*/*z*): 288.04, 154.87, 104.88, 76.87.

(4*Z*)-4-((5-methylthiophen-2-yl)methylene)-2-phenyloxazol-5(4H)-one **(3o)**: mp 145–147 °C; IR (KBr): υ (cm^{-1}) 3070, 2922, 2852, 1726, 1639, 1510, 1440, 1375, 1230, 1132, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 2.63 (3H, s), 6.89 (1H, s), 7.43–7.63 (5H, m), 8.14–8.19 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 16.2, 125.6, 125.9, 126.9, 127.6, 128.2, 128.9, 133, 135.95, 136.35, 151.58, 160.56, 167.3; Mass (*m*/*z*): 269.12, 207.11, 105.14, 77.08.

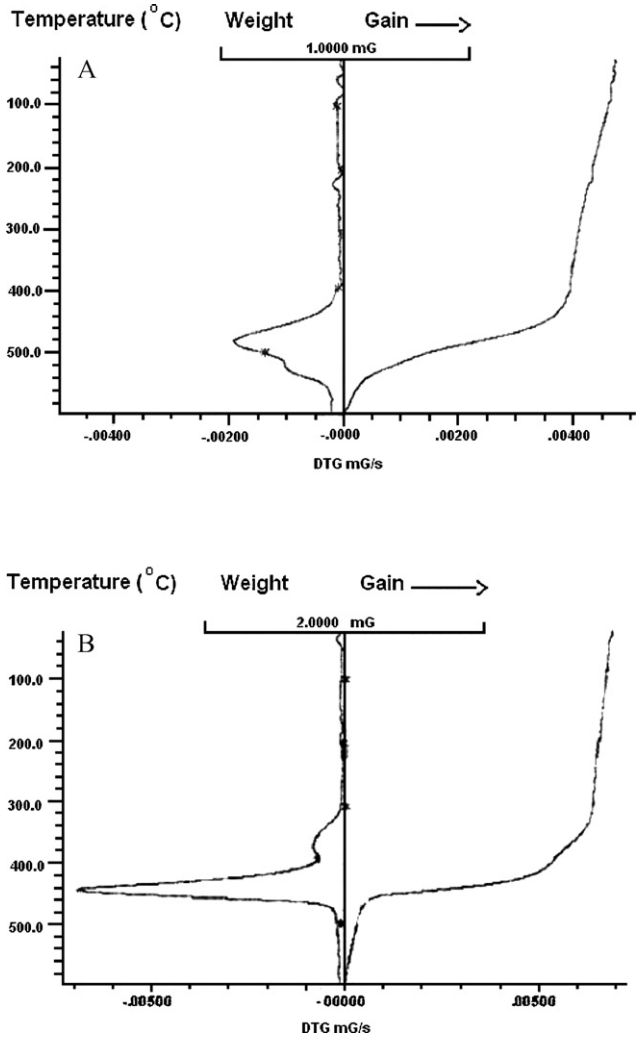


Fig. 1. TG-DTG analysis of: (A) $[bmim]_3PW_{12}O_{40}$ and (B) $[bmim]_4W_{10}O_{32}$.

3. Results and discussion

3.1. Preparation and characterization of catalysts

The prepared catalysts were characterized by TG-DTG, XRD, FT-IR and UV–Vis spectroscopic methods and nitrogen absorption–desorption determination (BET).

In TG-DTG analysis of $[bmim]_3PW_{12}O_{40}$ and $[bmim]_4W_{10}O_{32}$ no important weight loss or major endothermic peak was observed around 100 °C (Fig. 1a and b), and both catalysts were thermally stable up to 400 °C.

Fig. 2 shows the FT-IR spectra of $[bmim]_4W_{10}O_{32}$ and $[bmim]_3PW_{12}O_{40}$. The characteristic bands of [bmim]Cl, $[bmim]_4W_{10}O_{32}$, $[bmim]_3PW_{12}O_{40}$, $H_3PW_{12}O_{40}$ and $K_4W_{10}O_{32}$ are shown in Table 1. From these data, it is clear that both catalysts contain imidazolium cation and anionic Keggin parts.

The UV–Vis spectroscopy, in the diffuse reflectance mode, was employed for characterization of these heterogeneous catalysts. The reflectance of these catalysts resembles solution counterpart spectra and two peaks at 235 and 260 nm for $H_3PW_{12}O_{40}$ and a peak at 320 nm for $K_4W_{10}O_{32}$ were observed. These

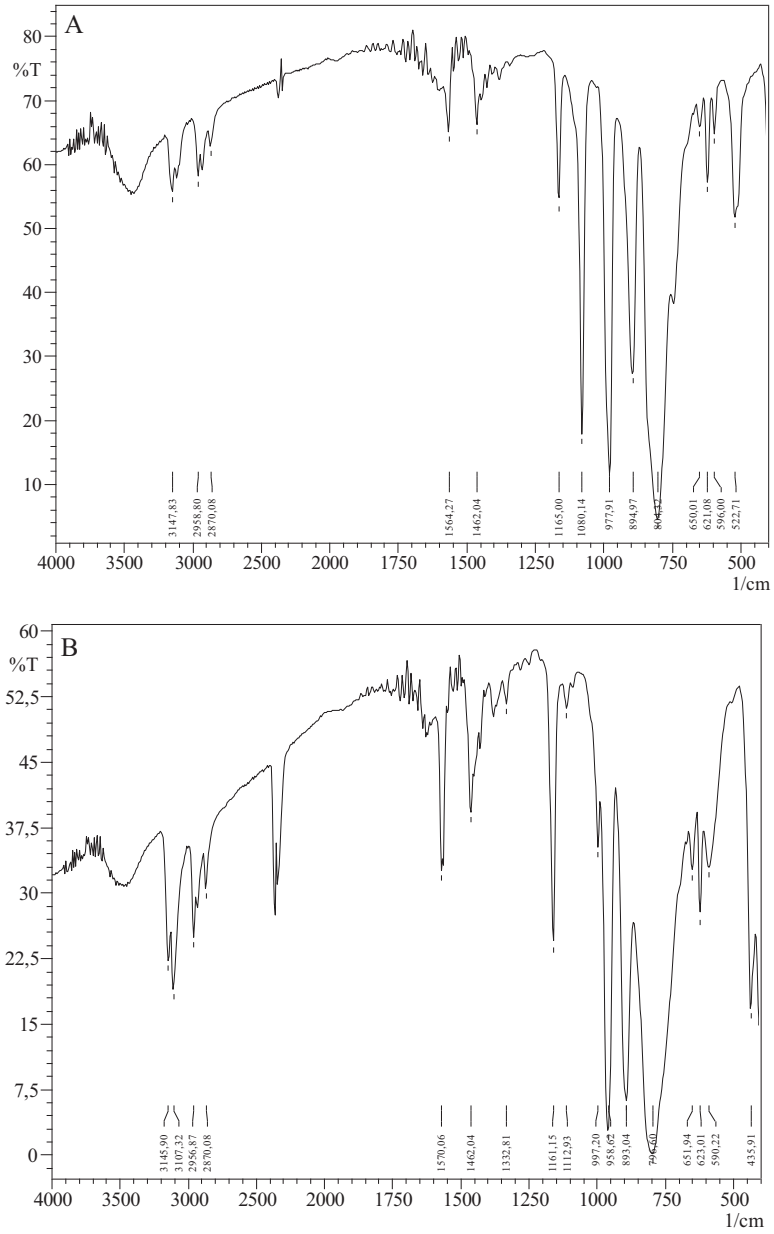


Fig. 2. FT-IR spectrum of: (A) $[bmim]_3PW_{12}O_{40}$ and (B) $[bmim]_4W_{10}O_{32}$.

observations clearly indicated the preparation of the catalysts (Fig. 3).

The Keggin type of the polyoxoanions exhibits typical peaks at 2θ: 8.8°, 9.2°, 10.3°, 27.9° and 29.2° in the X-ray diffraction (XRD) pattern [49]. These peaks are also observed in the XRD patterns of both catalysts (Fig. 4). From these observations, it is clear that the catalysts have been successfully prepared.

Table 1
IR bands of [bmim]Cl, $H_3PW_{12}O_{40}$ and $[bmim]_3PW_{12}O_{40}$, $K_4W_{10}O_{32}$ and $[bmim]_4W_{10}O_{32}$.

Vibration	Wave number (cm^{-1})				
	$[bmim]_4W_{10}O_{32}$	$[bmim]_3PW_{12}O_{40}$	$H_3PW_{12}O_{40}$	$K_4W_{10}O_{32}$	[bmim]Cl
Imidazole ring ν (C–H)	3145, 3107	3162, 3147, 3123, 3113, 3090	–	–	3147, 3090
Aliphatic ν (C–H)	2956, 2937, 2870	2957, 2938, 2870	–	–	2959, 2936, 2873
Imidazole ν (ring)	1572, 1563	1572, 1563	–	–	1572, 1563
Imidazole (H–C–C and H–C–N bending)	1161	1160	–	–	1168
ν (P–O)	–	1080	1080	–	–
ν (W–O_t)	958	980	987	968	–
ν (W–O_c–W)	893	892	886	894	–
ν (W–O_e–W)	796	807	810	796	–

Vibrational frequencies modes of both catalysts and parent components.

Table 2
Optimization of reaction conditions in the reaction of 4-methoxybenzaldehyde with hippuric acid and acetic anhydride catalyzed by $[bmim]_4W_{10}O_{32}$ and $[bmim]_3PW_{12}O_{40}$ under solvent-free conditions.[a]

Entry	Catalyst amount (mol%)	Time (h)	T (°C)	Yield (%)[b]	
				$[bmim]_4W_{10}O_{32}$	$[bmim]_3PW_{12}O_{40}$
1	3	1	80	80	83
2	5	1	80	91	93
2	5	24	25	60	50
3	5	1	60	85	83
5	5	1	100	92	94
6	10	1	80	92	92

[a] *Reaction conditions*: aldehyde (1 mmol), hippuric acid (1.2 mmol) and acetic anhydride (2 mmol) and catalyst.
[b] Isolated yield.

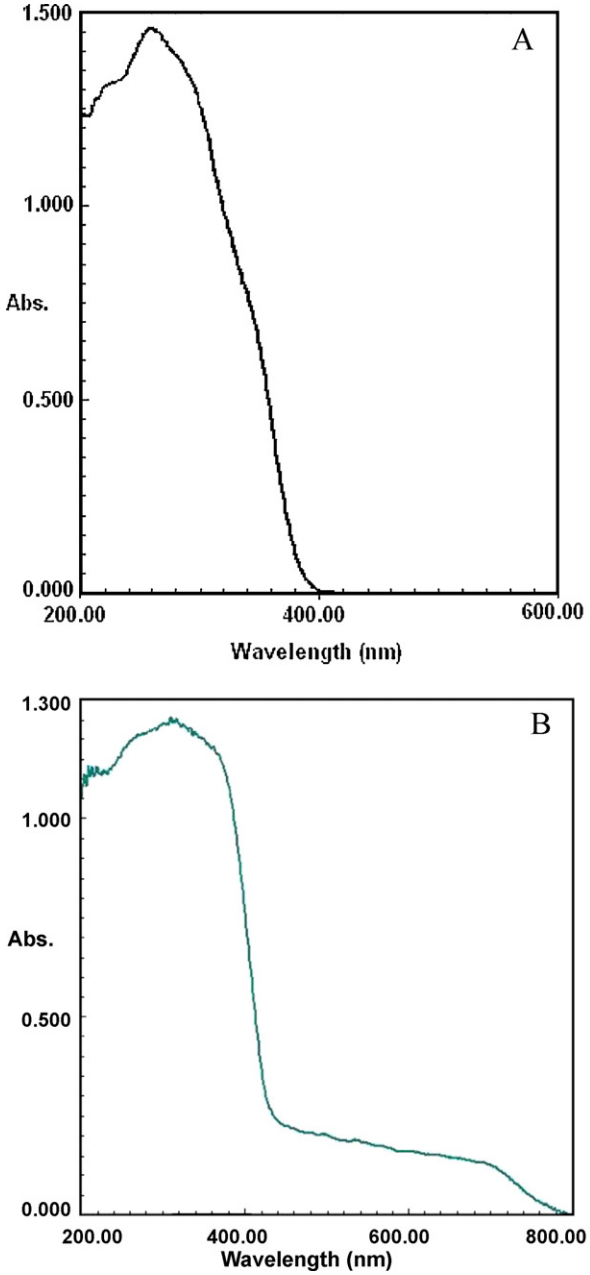


Fig. 3. Diffuse reflectance UV–Vis spectra of: (A) $[bmim]_3PW_{12}O_{40}$ and (B) $[bmim]_4W_{10}O_{32}$.

The specific surface area of both catalysts was determined by BET (nitrogen adsorption–desorption determination) analysis, The results showed that the specific surface area for $[bmim]_3PW_{12}O_{40}$ is 1.73 and for $[bmim]_4W_{10}O_{32}$ is 1.11 $m^2\,g^{-1}$.

3.2. Synthesis of azlactones

First, the reaction parameters were optimized in the reaction of 4-methoxybenzaldehyde with hippuric acid and acetic anhydride. In order to optimize the amount of catalysts, different amounts of both catalysts were used under solvent free conditions at 80 °C. The best results were obtained with 5 mol% of each catalyst after 60 min (Table 2). When the same reaction was carried out at room temperature, only 50–60% of azlactone was obtained after 24 h. Increasing the reaction temperature to 80 °C was led to shorter reaction times and higher product yields (Table 2, entries 2–5).

Under the optimized conditions, a wide variety of aromatic aldehydes bearing electron-withdrawing and electron-donating groups were reacted with hippuric acid and acetic anhydride in the presence of $[bmim]_4W_{10}O_{32}$ and $[bmim]_3PW_{12}O_{40}$ under solvent free

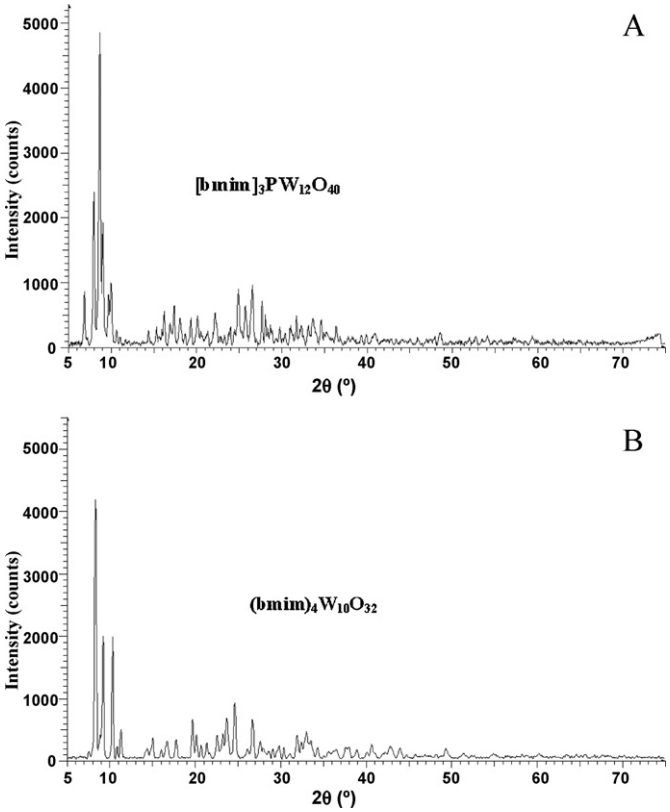
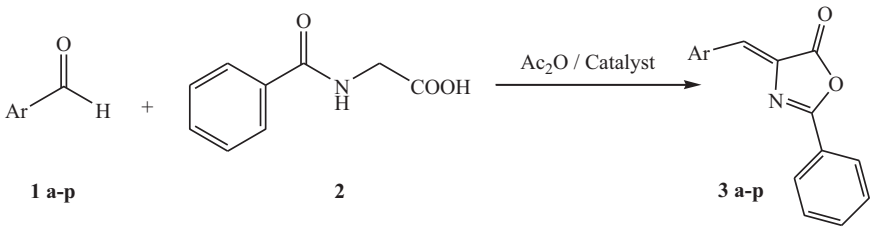


Fig. 4. XRD pattern of: (A) $[bmim]_3PW_{12}O_{40}$ and (B) $[bmim]_4W_{10}O_{32}$.

Table 3
Synthesis of azlactones with the use of (A) [bmim]3PW12O40 and (B) [bmim]4W10O32.[a]



1 a-p **2** **3 a-p**

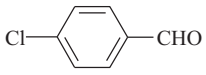
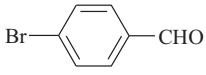
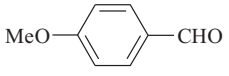
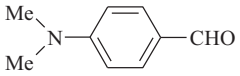
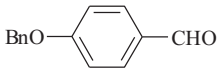
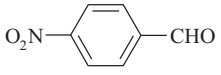
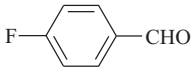
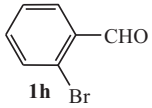
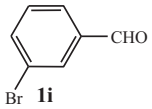
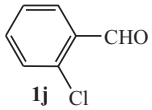
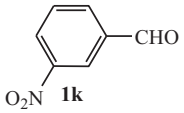
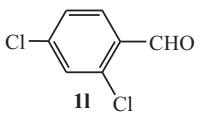
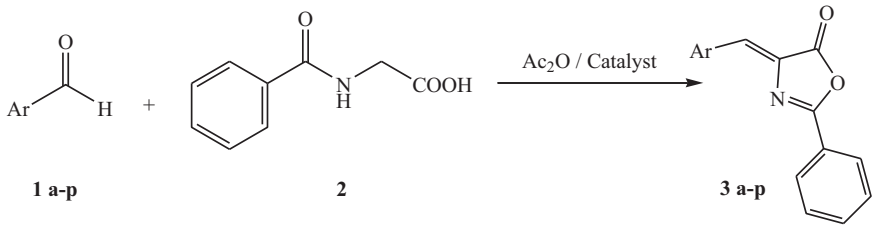
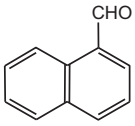
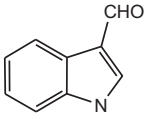
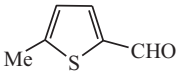
Aldehyde	Time (min)		Yield (%)[b]		TOF (h^{-1})[c]		M.p. (°C)	Azlactone
	A	B	A	B	A	B		
 **1a**	60	50	90	89	18.00	21.36	188–190	**3a**
 **1b**	50	45	91	92	21.84	24.53	197–199	**3b**
 **1c**	15	10	93	91	74.40	109.2	153–155	**3c**
 **1d**	5	5	95	94	228	225.6	212–214	**3d**
 **1e**	45	45	93	90	24.80	24	152–154	**3e**
 **1f**	75	65	89	90	14.24	16.61	237–239	**3f**
 **1g**	30	40	94	92	37.60	27.6	177–179	**3g**
 **1h**	45	45	91	92	24.27	24.53	141–143	**3h**
 **1i**	50	45	94	92	22.56	24.53	147–149	**3i**
 **1j**	45	40	92	90	24.53	27	162–163	**3j**
 **1k**	65	60	90	91	16.62	18.2	174–176	**3k**
 **1l**	50	45	93	94	22.32	25.07	181–183	**3l**

Table 3 (*Continued*)



1 a-p **2** **3 a-p**

Aldehyde	Time (min)		Yield (%)[b]		TOF (h^{-1})[c]		M.p. (°C)	Azlactone
	A	B	A	B	A	B		
 **1m**	25	20	92	90	44.16	54	163–165	**3m**
 **1n**	25	15	90	93	43.20	74.4	209–211	**3n**
 **1o**	20	15	93	91	55.80	72.8	145–147	**3o**

[a] *Reaction conditions*: aldehyde (1 mmol), hippuric acid (1.2 mmol) and acetic anhydride (2 mmol) and catalyst (5 mol%).
[b] Isolated yield.
[c] TOF = (mmol of product/mmol of catalyst)/time (h).

conditions. The results, which are summarized in Table 3, showed that the corresponding azlactones were obtained in 89–95% isolated yield in 15–75 min. The aldehydes bearing electron-donating groups were more reactive than the others. On the other hand, aldehydes with lower melting points and liquid ones gave higher product yield. This is due to the fact that solid aldehydes should melt first and then react.

As can be seen, the $[bmim]_3PW_{12}O_{40}$ is slightly more reactive than $[bmim]_4W_{10}O_{32}$. This can be attributed to the higher surface area of $[bmim]_3PW_{12}O_{40}$ in comparison with $[bmim]_4W_{10}O_{32}$.

Several attempts were done to understand the catalyst active site. First, the acidity of both catalysts was determined by potentiometric titration and the results (7.05 $[bmim]_4W_{10}O_{32}$ and 6.97 for $[bmim]_3PW_{12}O_{40}$) revealed that both catalysts were neutral. These data showed that these catalysts have no BrØnsted acid character.

In order to understand more about the catalytic activity of these catalysts, a set of reactions were performed for the synthesis of ((4*Z*)-4-(4-chlorobenzylidene)-2-phenyloxazol-5(4H)-one) (**3a**) under similar reaction conditions. As can be seen in Table 4, different catalysts bearing different anions and cations were used. While [bmim]Cl gave only 20% of **3a** [bmim]OTf was more efficient and 60% of **3a** was produced. On the other hand in the presence of potassium salt of both catalysts (these catalyst are homogeneous and cannot be recovered), 46–53% of **3a** was produced. The [bmim] salts of these catalysts gave **3a** in 89–90%.

The property of ionic liquids depends on the three-dimensional network of the anions and cations. Anion identity has an important impact on its property. It seems that in these catalysts ($[bmim]_3PW_{12}O_{40}$ and $[bmim]_4W_{10}O_{32}$) a special microenvironment is formed which is very dependent on the interactions between anion and cation. By changing these interactions, the catalytic activity can change [50,51]. It seem that the higher catalytic activity of $[bmim]_3PW_{12}O_{40}$ and $[bmim]_4W_{10}O_{32}$ in comparison with $K_3PW_{12}O_{40}$ and $K_4W_{10}O_{32}$ can be attributed to these effects.

However, it is proved that the catalytic activity of these heterogeneous catalysts is originated from crystal-water molecules in the $[bmim]_3PW_{12}O_{40}$ and $[bmim]_4W_{10}O_{32}$ structures [52].

3.3. Catalyst reusability

The reusability of the catalysts was investigated in the sequential reaction of aldehyde **1d** with hippuric acid and acetic anhydride. At the end of each run, the catalyst was removed, washed with ethyl acetate, heated at 250 °C and reused. The results which are summarized in Table 5, showed that the catalysts were reused five consecutive runs, no appreciate loss of their catalytic activities were observed. Also, the catalytic behavior of the separated liquids was tested by addition of fresh aldehyde, hippuric acid and acetic anhydride to the filtrates after each run. Execution of the oxidation reactions under the same reaction conditions, as with

Table 4
The results obtained in the synthesis of ((4*Z*)-4-(4-chlorobenzylidene)-2-phenyloxazol-5(4H)-one) in the presence of different catalysts.[a]

Entry	Catalysts	Time (h)	Yield (%)[b]
1	[bmim]Cl	1	20
2	[bmim]OTf	1	60
3	$[bmim]_3PW_{12}O_{40}$	1	90
4	$[bmim]_4W_{10}O_{32}$	1	89
5	$K_3PW_{12}O_{40}$	1	53
6	$K_4W_{10}O_{32}$	1	46

[a] *Reaction conditions*: 4-chlorobenzaldehyde (1 mmol), hippuric acid (1.2 mmol), acetic anhydride (2 mmol), catalyst (0.05 mmol).
[b] Isolated yield.

Table 5
Investigation of catalysts reusability in the reaction of aldehyde 1d with hippuric acid and acetic anhydride under solvent-free conditions.[a]

Run	Yield (%) after 5 min[b]	
	$[bmim]_4W_{10}O_{32}$	$[bmim]_3PW_{12}O_{40}$
1	95	94
2	93	91
3	90	87
4	88	86
5	85	84

[a] *Reaction conditions*: aldehyde (1 mmol), hippuric acid (1.2 mmol) and acetic anhydride (2 mmol) and catalyst (5 mol%).
[b] Isolated yield.

catalyst, showed that the obtained results were as same as blank experiments.

4. Conclusion

In this study, 4-benzylidene-2-phenyloxazoline-5-ones was synthesized via the Erlenmeyer synthesis by the reaction of different aldehydes with hippuric acid and acetic anhydride. The corresponding azlactones were obtained in good to excellent yields. These heterogeneous catalysts were reused several times without loss of their activities.

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