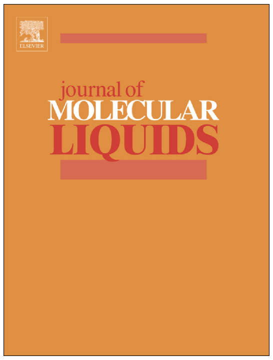

Heteropolyacid-based ionic liquid [Simp]3PW12O40 nanoparticles as a productive catalyst for the one-pot synthesis of 2H-indazolo[2,1-b]phthalazine-triones under solvent-free conditions

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Heteropolyacid-based ionic liquid $[Simp]_3PW_{12}O_{40}$ nanoparticles as a productive catalyst for the one-pot synthesis of 2H-indazolo[2,1-b]phthalazine-triones under solvent-free conditions

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Abstract

A novel Keggin-type heteropolyacid-based ionic liquid $[Simp]_3PW_{12}O_{40}$ was developed via the reaction of the as synthesized ionic liquid 3-sulfonic acid 1-imidazolopyridinium hydrogen sulfate $[Simp]HSO_4$ with an aqueous solution of $H_3PW_{12}O_{40}$. Then, the formulated $[Simp]_3PW_{12}O_{40}$ was changed to the nano-form via solvothermal processing in tetralin at 220 ºC. After that, the provided powdered solid nanomaterial was characterized by FT-IR, ^{1}H-NMR, XRD, SEM, EDX and TGA analyses. Then, the focused nanomaterial was handled as a productive and encouraging nanocatalyst for the establishment of 2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione attendants through one-pot, multi-component contraction of aldehydes, phthalhydrazide, and dimedone under solventless status and the generality and practical tolerance of this useful and environmentally benign method are illustrated. The simple work-up, smooth reaction conditions, good to excellent yields, and reasonably short reaction times are the particular benefits of this protocol. Besides, the new nano-powdered ionic liquid was a successful and modest catalyst that could definitely be recycled and reused several times without apparent decrease in its catalytic activity.

Keywords: ionic liquid; heterogeneous; $[Simp]_3PW_{12}O_{40}$; phthalazine-triones

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1. Introduction

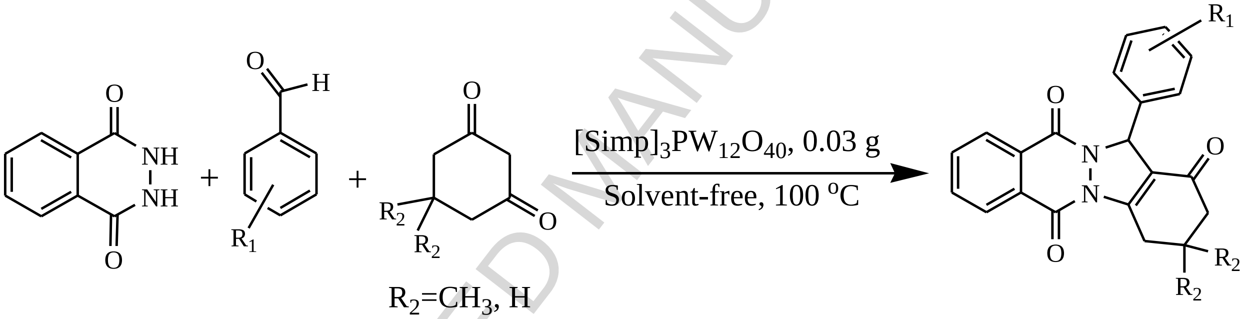
The use of green catalysts and gentle situations in synthetic reactions hold out critical considerations throughout organic synthesis approaches. This consideration can be credited to the lessening of natural squanders and the worth of the applied techniques. Multi-component reactions have been proved to be strikingly fruitful in producing molecular complexity in a single synthetic operation [1-5]. In the interim, ionic liquids have been evaluated as green disclosures in organic synthesis because of their great particular properties, for example poor vapor pressure, tunable polarity, wide liquid range, good solvating ability, high thermal stability, and simplicity of recyclability and common reusability without considerable decrease in their activities [6]. Among a wide range of ionic liquids, acidic counterparts, essentially ionic liquids including N-substituted reagents, are the most imperative ones which have been effectively utilized for the speeding up of various sorts of organic transformations via the multi-component reactions [7,8].

Heteropolyacids (HPAs) as an important class of inorganic transition-metal oxide clusters included an extensive variety of fabulous properties such as high stability, relatively non-toxicity, crystallinity, and ease of handling; which, have pulled in special interests in medicine, biology, catalysis and materials science [9-12]. Recently, ionic liquids involving polyoxometalates, which are comprised of heteropolyanions and appropriate organic cations, have attracted impressive interests as a new family of ionic liquids [13] and have been emerged as potential compounds in nanotechnology, electrochemistry, and catalysis [14–16].

Heterocycles containing phthalazine moiety have critical pharmacological properties such as anti-inflammatory [17], anti-convulsant [18], anti-microbial [19], anti-fungal [20] and anti-cancer [21] activities. Accordingly, synthesis of 2H-indazolo[2,1- b]phthalazine-triones has been the concentration of enthusiasm for as far back as decade and distinctive types of mediators such as silica sulfuric acid [22], trimethylsilyl chloride [23], cyanuric chloride [24], dodecylphosphonic acid [25], *p*-TSA [26], $H_3PW_{12}O_{40}$ in 1-butyl-3-methylimidazolium tetrafluoroborate [27], $Mg(HSO_4)_2$ [28], H_2SO_4 in water–ethanol [29], silica-supported poly phosphoric acid [30], *N*-halo sulfonamides [31], sulfonated poly(ethylene glycol) [32], wet cyanuric chloride [33], 1,1,1,3,3,3-hexafluoro-2-propanol [34], Fe(III)-based dicationic ionic liquid, $[C_4(mim)_2](FeCl_4)_2$ [35], Fe_3O_4@silica sulfuric acid nanoparticles [36], phosphomolybdic acid (PMA/SiO_2) [37], and tungstosilicic acid [38] have been applied for this transformation.

Taking into account disadvantages of the existing protocols, such as low product yields, long reaction times, costly motivators, poisonous reagents and solvents, and trouble in recovery and reuse of the catalysts, extension of new effective and environmentally benign methodology permitting simple synthesis of phthalazine heterocycles is therefore necessary.

As of late, a new ionic liquid [Simp]HSO_4 (3-sulfonic acid 1-imidazolopyridinium hydrogensulfate) is investigated and applied as catalyst; in any case, liquid nature of this catalyst made work-up and reuse troublesome [39, 40]. Herein, we wish to introduce devising, characterization, and application of a new heterogeneous catalyst $[Simp]_3PW_{12}O_{40}$ with upgraded catalytic activity in promoting synthesis of 2H-indazolo[2,1-b]phthalazine-trione derivatives (Scheme 1). The solid catalyst was set up by blending an aqueous solution of $H_3PW_{12}O_{40}$ with the liquid [Simp]HSO_4.



R_1=halogen, electron withdrawing (releasing) group

Scheme 1. Typical formulation for the synthesis of different phthalhydrazide-triones.

2. Experimental

2.1. Materials

Materials and reagents were obtained from Merck, Fluka, and Aldrich. All yields allude to the isolated products which were identified by comparison of their physical data and also their FT-IR and ^{1}H-NMR spectra with the previously reported and authentic. The purity assurance of the substrates and reaction monitoring were joined by TLC on silica gel polygram SILG/UV 254 plates. Solid state FT-IR spectra were recorded utilizing the KBr disk strategy on an 8700

Shimadzu Fourier Transform spectrophotometer. ^1H and ^{13}C NMR (300 and 100 MHz) spectra were reported on a Bruker-Avance spectrometer. Scanning electron microscope (SEM) micrographs were attained using a KYKY-EM3200 microscope (acceleration voltage 26 kV). Crystallinity was assessed by powder X-ray diffraction (XRD) on a PW1800-PHILIPS diffractometer with Cu K_α radiation ($\lambda = 1.5418$ Å) at 40 kV and 30 mA. Thermogravimetric (TGA) analysis was performed on a Bahr STA-503 instrument in air at a heating rate of 10 °C/min^{-1}. A freeze dryer, Model FD-10, Pishtaz Equipment Engineering Co, Iran, was used for occasional drying of the prepared nanocatalyst. Melting points were obtained in open capillaries on a Bamstead electrothermal type 9200 melting point apparatus.

2.2. Preparation of 3-sulfonic acid 1-imidazolopyridinium hydrogen sulfate [Simp]HSO_4

Caffeine (0.9710 g, 5 mmol) in dry CH_2Cl_2 (50 ml) was added to a round-bottomed flask. Then, chlorosulfonic acid (0.59 g, 5.1 mmol) was included drop-wise for 20 min at ambient temperature. Then, the reaction mixture was stirred for 12 h. The residue was washed with dry CH_2Cl_2 (3×50 ml) and dried to give 3-sulfonic acid imidazolopyridinium chloride [Simp]Cl as a viscous thick yellow-brown oil. At that point, sulfuric acid (0.49 g, 5 mmol) was added drop-wise to [Simp]Cl (1.155 g, 5 mmol) over a period of 5 min at room temperature to remove the produced HCl during the reaction. At long last, the subsequent mixture was stirred for 24 h at 60 °C under aerobic conditions to give [Simp]HSO_4 as a viscous yellow oil. FT-IR (KBr, cm^{-1}) υ_{max}: 582, 886, 1012, 1174, 1683, and 2395–3480.

2.3.Synthesis of 3-sulfonic acid 1-imidazolopyridinium tungstophosphate $[Simp]_3PW_{12}O_{40}$

$[Simp]_3PW_{12}O_{40}$ was prepared by following the procedure detailed by Ammam and Fransaer [41]. In an average arrangement, phosphotungstic acid ($H_3PW_{12}O_{40}$, 1.5 g) was dissolved in 5 ml deionized water. Then, [Simp]HSO_4 (0.7 g) was gradually added to the above solution with continuous stirring. Then, the reaction mixture was stirred at room temperature for 24 h to form a yellowish powder. The precipitate was filtered, washed with deionized water and dried under aerobic conditions. The resulting solid product was characterized by spectroscopic techniques and formulated as $[Simp]_3PW_{12}O_{40}$. To fragmentize the obtained ionic liquid particles to the nanoparticles, solvothermal technique was used. For this purpose, 0.2 g of $[Simp]_3PW_{12}O_{40}$ was added to 70 ml of tetralin with strong stirring for 30 min. Thereafter, the mixture was transferred to Teflon steel autoclave and the closed container was heated to 220 °C for 24 h. Finally, the container was gradually cooled to room temperature and the separated solid material was dried at 80 °C for 12 h. To study effect of drying conditions on the catalytic efficacy of $[Simp]_3PW_{12}O_{40}$, the prepared final material was dried under freeze conditions. Results showed no obvious improvements in the catalytic activity of this sample with the one dried under usual thermal conditions as described above.

2.4. General route for the synthesis of 2H-indazolo[1,2-b]phthalazine-triones

1,3-Diketones (0.25 mmol), phthalhydrazide (0.25 mmol), aromatic aldehydes (1 mmol), and the heterogeneous catalyst $[Simp]_3PW_{12}O_{40}$ (0.03 g) were thoroughly mixed in a test tube and heated at 100 °C in an oil-bath under solvent-free conditions for the required time. Fulfillment of the reaction was observed by TLC: n-hexane: ethyl acetate (8:2). After completion, the reaction mixture was cooled to room temperature and chloroform was added. After a minute, the heterogeneous catalyst was filtered and chloroform was dissipated from the residue. At that point, 5 ml of hot ethanol was added to the reaction mixture and stirred for 5 min. After wards, the reaction mixture was cooled to 5 °C and the acquired phthalazine-trione precipitate was separated. Further re-crystallization in ethanol afforded the highly pure product. All products were known compounds and were described by FT-IR, ^{1}H NMR, ^{13}C NMR, and determination of their melting points [27, 31, 38–40].

2.5. Spectral data for some representative 2H-indazolo[1,2–b]phthalazine-1,6,11(13H)-triones

3,4-dihydro-3,3-dimethyl-13-phenyl-2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione (Table 6, entry 1): IR (KBr) 2958, 1664, 1576 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.24 (s, 6H), 2.45 (s, 2H), 3.23 and 3.45 (d, AB system, J = 18.0 Hz, 2H), 6.45 (s, 1H), 7.32-8.35 (m, 9H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 28.4, 28.6, 34.7, 38.2, 50.9, 64.8, 118.2, 127.1, 127.6, 127.8, 128.7, 128.9, 129.1, 133.6, 134.5, 136.4, 150.9, 154.3, 156.2, 192.3.

3,4-dihydro-3,3-dimethyl-13-(4-chlorophenyl)-2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione (Table 6, entry 3): IR (KBr) 2957, 2931, 1688, 1654, 1622 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 6H, 2Me), 2.33 (s, 2H, CH_2C), 3.22-3.44 (AB system, *J* =19.2 Hz, 2H, CH_aH_bCO), 6.41 (s, 1H, CHN), 7.28-7.38 (dd, *J*= 8.4 Hz, 4H, ArCl), 7.84-8.38 (m, 4H, Ph); ^{13}C

NMR (100 MHz, CDCl$_3$): δ (ppm) 28.5, 28.7, 34.7, 38.0, 50.9, 64.31, 118.5, 127.1, 127.7, 127.8, 128.6, 128.6, 128.8, 129.1, 133.4, 134.5, 136.3, 150.8, 154.4, 156.0, 192.2.

3,4-dihydro-3,3-dimethyl-13-(4-nitrophenyl)-2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione (Table 6, entry 3): IR (KBr) 2965, 2375, 1666 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ (ppm) 8.29–8.08 (m, 4H), 7.80–7.79 (m, 2H), 7.53 (d, J = 8.4 Hz, 2H), 6.41 (s, 1H), 3.35–3.15 (AB system, J = 19.2 Hz, 2H), 2.25 (s, 2H), 1.13 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 192.1, 155.9, 154.5, 151.7, 147.8, 143.4, 134.8, 133.9, 128.9, 128.5, 128.2, 128.0, 127.7, 124.0, 117.2, 64.1, 50.7, 37.9, 34.7, 28.6, 28.3.

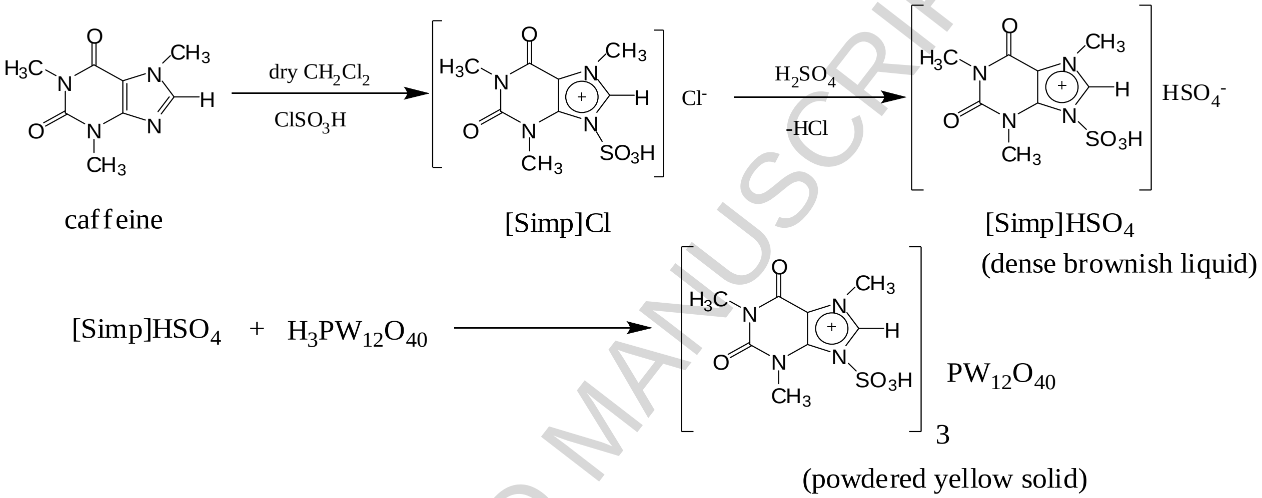
3,4-dihydro-3,3-dimethyl-13-(2-chlorophenyl)-2H-indazolo[1,2-b]phthalazine-1,6,11(13H)-trione (Table 6, entry 4): IR (KBr) 3058, 2957, 2894, and 1662 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ (ppm) 1.21 (s, 3H), 1.23 (s, 3H), 2.34 (s, 2H), 3.26 and 3.45 (d, AB system, J = 19.1 Hz, 2H), 6.66 (s, 1H), 7.24-8.41 (m, 8H, Ph); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 28.3, 28.7, 34.5, 37.9, 50.8, 63.9, 116.6, 127.1, 127.5, 127.9, 128.6, 129.0, 129.8, 130.4, 132.5, 133.0, 133.5, 134.4, 151.8, 154.1, 156.1, 192.0.

3,4-dihydro-3,3-dimethyl-13-(4-methylphenyl)-2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione (Table 6, entry 5): IR (KBr) 2897, 1663, 1654, 1603, 1600, 1497, 1085, 827, 790, 687, 627, 495 cm^{-1}; ^{1}H NMR (300 MHz; CDCl$_3$): δ (ppm) 1.17 (s, 6H), 2.25 (s, 3H), 2.28 (s, 2H), 3.18-3.37 (AB system, s, 2H, J = 18.85 Hz), 6.36 (s, 1H), 7.08–7.2 (m, 4H), 7.8 (m, 2H), 8.2–8.3 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_{3,}$): δ (ppm) 21.6, 28.8, 29.1, 35.0, 38.4, 51.3, 65.1, 118.9, 127.4, 128.0, 128.3, 129.3, 129.5, 129.7, 133.8, 134.8, 138.8, 151.1, 154.6, 156.3, 192.4.

3. Results and Discussion

An acidic ionic liquid is characterized as a low melting ionic salt involving Bro□nsted, Lewis, or a combination of Bro□nsted and Lewis acidic characteristics. The acidic function(s) or group(s) can be either in the cation, anion, or both [6]. Apparently, in [Simp]$_3$PW$_{12}$O$_{40}$, Simp$^+$ cation and heteropolyoxometalate anion carry on as Bro□nsted and Lewis acid sites, individually. Scheme 1 provides the general pathway for the preparation of [Simp]$_3$PW$_{12}$O$_{40}$ from the reaction of [Simp]HSO$_4$, with the heteropolyacid H$_3$PW$_{12}$O$_{40}$. As indicated by our previous work, [Simp]HSO$_4$ was fabricated from the reaction of caffeine with chlorodulfonic acid in dry dichloromethane with subsequent substitution of the chloride counter ion with hydrogen sulfate.

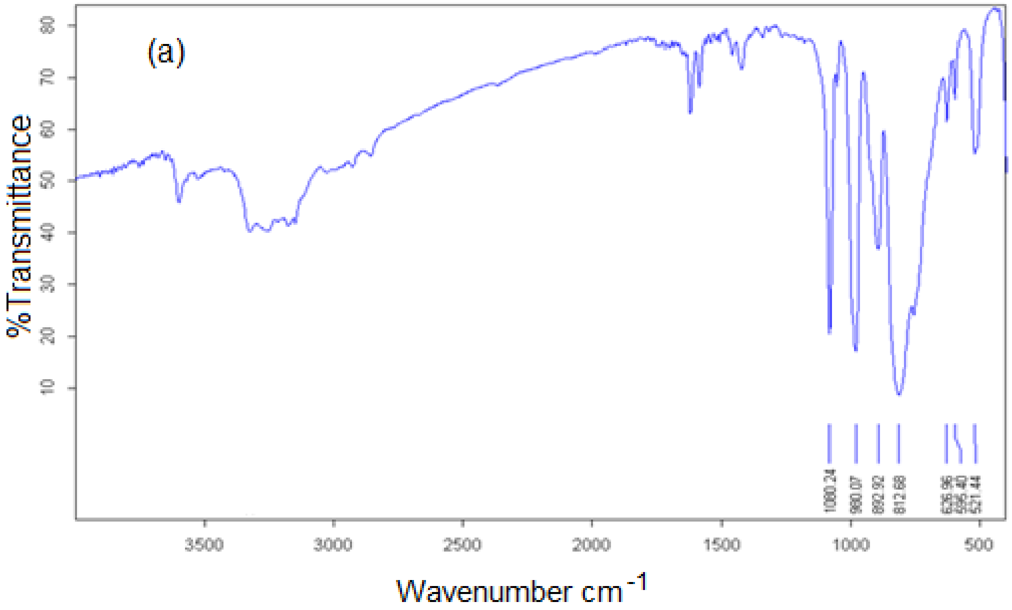
Then, the prepared high dense ionic liquid [Simp]HSO_4 was separated and treated with $H_3PW_{12}O_{40}$ in the second step to afford a pale yellow precipitate of $[Simp]_3PW_{12}O_{40}$ as an immaculate powder. From that point, this new fabricated catalyst was performed in the preparation of indazolophthalazine-trione derivatives. The structure of $[Simp]_3PW_{12}O_{40}$ provides functional Brønsted acidic hydrogen sulfate sites along with Lewis acidic sites of W^{+6} in the framework of *Keggin* anion. Subsequently, $[Simp]_3PW_{12}O_{40}$ behaved as an ideal acid catalyst in the desired organic transformation.



Scheme 2. A general route for the synthesis of 3-sulfonic acid 1-imidazolium hydrogen sulfate [Simp]HSO_4 and the heteropoly anion substituted $[Simp]_3PW_{12}O_{40}$.

3.1. *Structural identification of $[Simp]_3PW_{12}O_{40}$*

The infrared spectra of $H_3PW_{12}O_{40}$ and $[Simp]_3PW_{12}O_{40}$ are appeared in Fig. 1. $PW_{12}O_{40}^{3-}$ with the *Keggin* structure is communicated by the general formula of $[X^{n+}M_{12}^{m+}O_{40}]^{(80-12m-n)-}$ (heteroatom X= P, As, Si, etc., polyatom M= W, Mo, etc.) and provided strong peaks at 1080, 980, 892, and 812 cm^{-1} due to the four sorts of oxygen atoms P-O_i, W-O_t, W-O_b-W, and W-O_c-W, respectively (Fig. 1a). In the FT-IR spectrum of $[Simp]_3PW_{12}O_{40}$ (Fig. 1b) the strong stretching vibrations at 1100-800 cm^{-1} are distinctively credited to the above *Keggin* structure [41]. Hence, the *Keggin* structure is retained after exchanging of the protons with the imidazolopyridinium cation. In examination with the parent anion $PW_{12}O_{40}^{3-}$ in $H_3PW_{12}O_{40}$, the vibration frequencies of the polyoxometalate in the ionic liquid has slight shifts, which showed that the bonds of the heteropoly anion are fortified or weakened owing to the interaction with the organic cation. The FT-IR spectrum of $[Simp]_3PW_{12}O_{40}$ showed a broad peak at 3000–3700 cm^{-1} which can be related to the stretching of OH, SO_3H, and the adsorbed water molecules. Moreover, the C–H stretching vibrations are covered with above broad band. The strong peaks observed at 886, and 597 cm^{-1} related to the S–OH bending and symmetric S–O stretching vibrations, respectively [42,43]. Furthermore, the band at 887 cm^{-1} would be related to the N–SO_2 vibrations [44]. The bands at 1595 and 1638 cm^{-1} were due to C=N and C=C ring vibration of the imidazole part of the ionic liquid. The ^1H NMR spectrum of $[Simp]_3PW_{12}O_{40}$ showed the acidic hydrogen of $-SO_3H$ at 7.81 ppm in acetone.



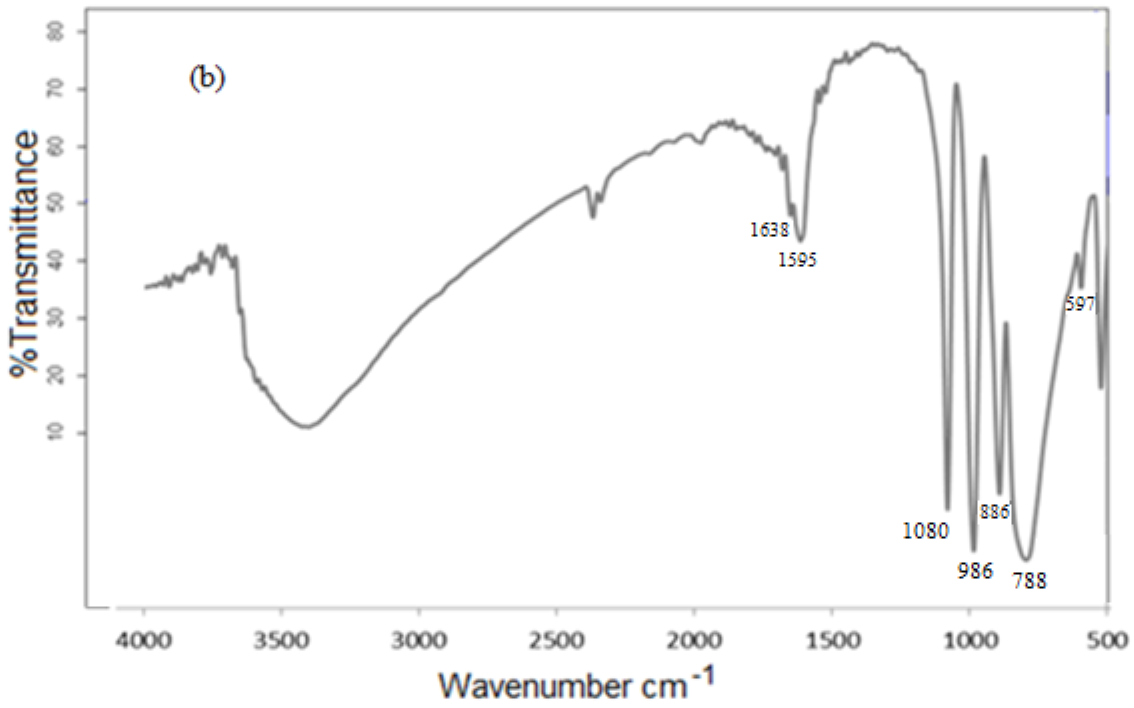


Fig. 1. FT-IR spectra of $H_3PW_{12}O_{40}$ (a) and $[Simp]_3PW_{12}O_{40}$ (b).

In the ^{1}H-NMR spectrum of $[Simp]_3PW_{12}O_{40}$ in DMSO, the number of the signals fitted exactly with the structure of ionic liquid (Fig. 2) which afforded four ^{1}H signals due to three methyl groups at 3.33, 3.44 and 3.88 and one proton attached to the aromatic ring at 8.02 δ ppm.

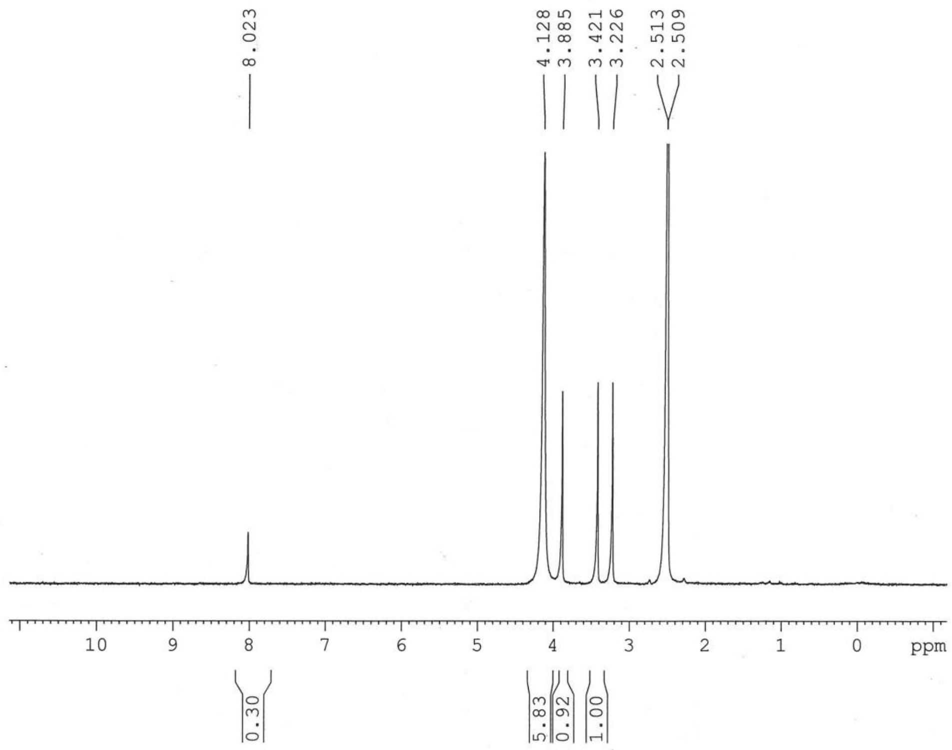


Fig. 2. ^{1}H-NMR spectrum of $[Simp]_3PW_{12}O_{40}$.

The synthesized nanopowdered ionic liquid $[Simp]_3PW_{12}O_{40}$ was likewise investigated by SEM with different amplifications for determining the particle size, shape, and surface morphology (Fig. 3). These pictures demonstrated that in view of synthetic alteration, formation of nanoparticles of $[Simp]_3PW_{12}O_{40}$ would provide an extended heterogeneous surface as catalyst for the targeted multi-component organic transformation. EDX investigation was additionally confirmed combination of the heteropoly anion with $[Simp]^+$. The peaks in the XRD patterns of $H_3PW_{12}O_{40}$ and $[Simp]_3PW_{12}O_{40}$ are situated at the wide-angle region of $2\theta = 10–50°$. Clearly, comparison of the two patterns confirms that a phase change is happened as a result of the substitution of the secondary structure protons in $H_3PW_{12}O_{40}$ with the organic cations. (Fig. 4).

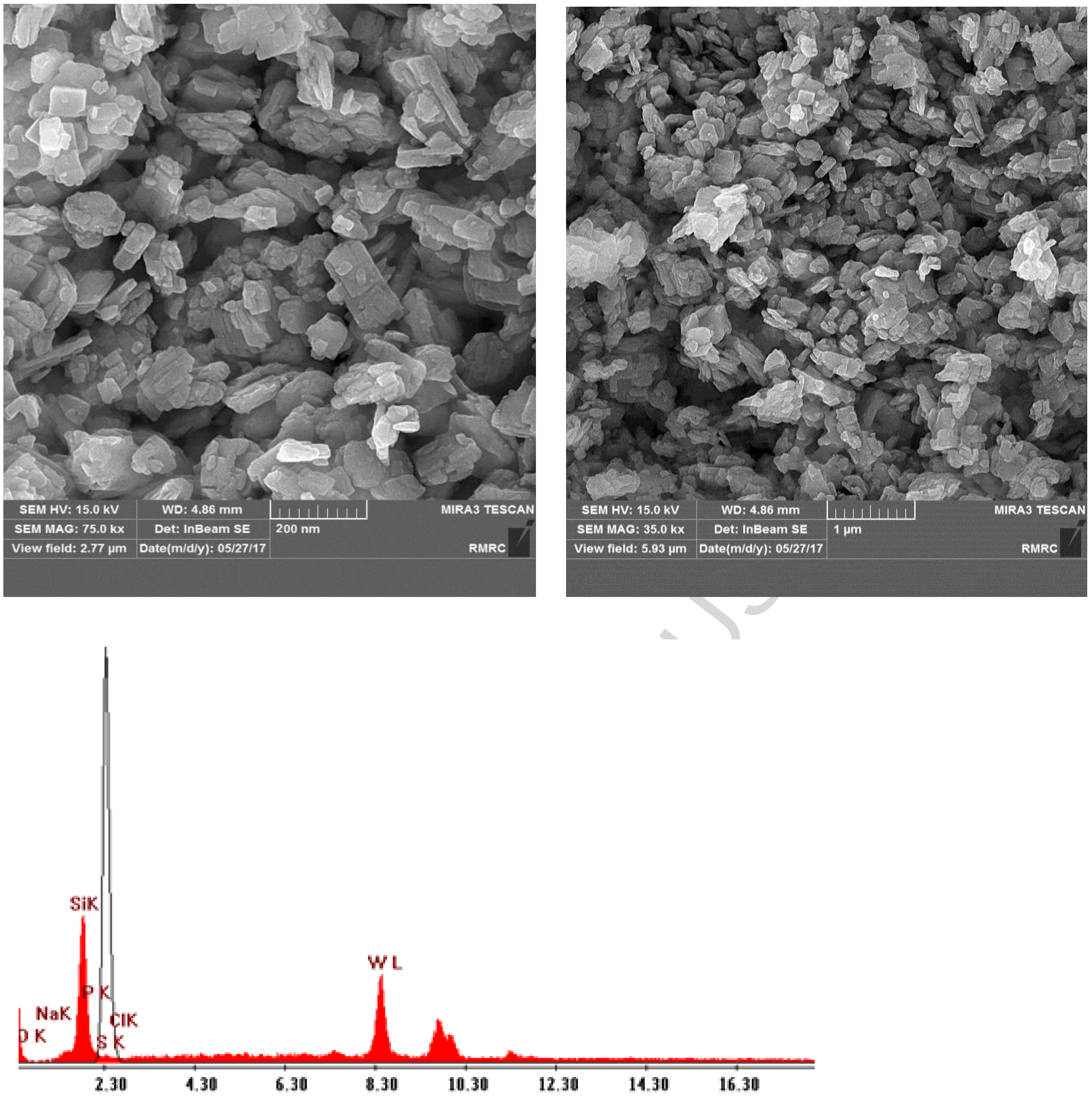


Fig. 3. SEM micrographs (up) and EDX (bottom) analysis of $[Simp]_3PW_{12}O_{40}$ nanoparticles.

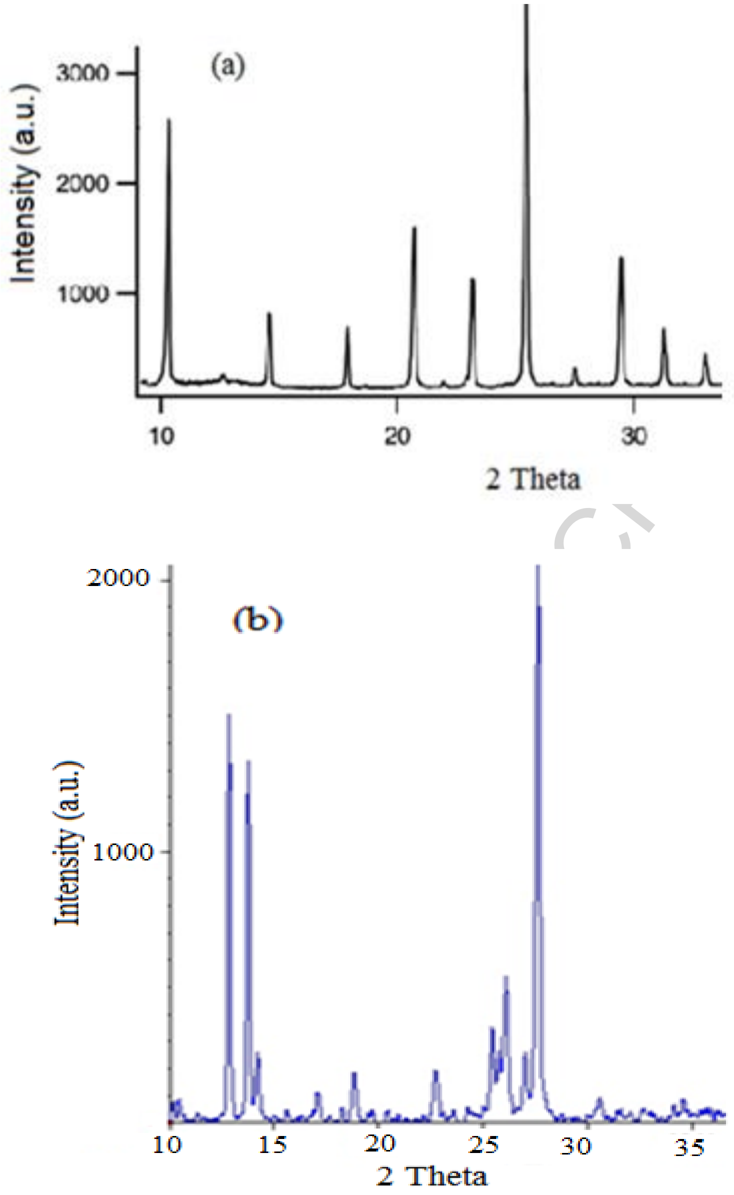


Fig. 4. XRD patterns of $H_3PW_{12}O_{40}$ (a) and $[Simp]_3PW_{12}O_{40}$ nanoparticles (b).

The heteropolyacid $H_3PW_{12}O_{40}$ in its non-reduced structures is generally characterized by oxygen-to-metal (O–M) charge transfer bands, which show up in the UV district around 265 nm. They are trademark bands of the *Keggin* structure, and relate to the charge transfer from the bridge oxygen atoms (O_b, O_c) to the metal atoms [41]. Be that as it may, it should be mentioned that the electronic transitions of n-σ^* and π-π^* due to nitrogen atoms and carbonyl groups in caffeine fragment provide an unmistakable absorption band at about 265-270 nm in the UV-Vis spectrum of [Simp]HSO_4 and [Simp]$_3PW_{12}O_{40}$. Furthermore, a little difference between the maximum absorption bands of [Simp]HSO_4 and [Simp]$_3PW_{12}O_{40}$ in Fig. 5, indicating that the wavelength of the band does not significantly vary with the counter cation.

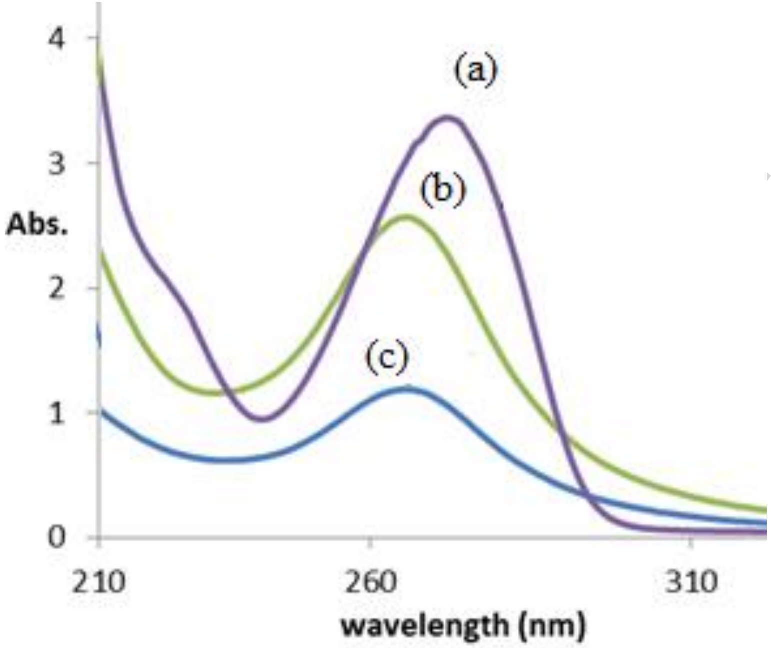


Fig. 5. UV-vis spectra of [Simp]HSO_4 (a), [Simp]$_3PW_{12}O_{40}$ (b), $H_3PW_{12}O_{40}$ (C).

The thermogravimetric behaviour of [Simp]$_3PW_{12}O_{40}$ is shown in Fig. 6. The initial low temperature weight loss was due to the removal of water molecules that occurred below 200 °C. The second step was for the beginning of the decomposition of organic parts that occurred in the range of 380–450 °C. The rapid weight loss started above 450 °C was mainly due to the decomposition of *Keggin* heteropolyacid moiety to WO_3 and P_2O_5 [45]. The thermal stability of the *Keggin* units have been affected because of their interaction with the imidazolopyridinium moieties.

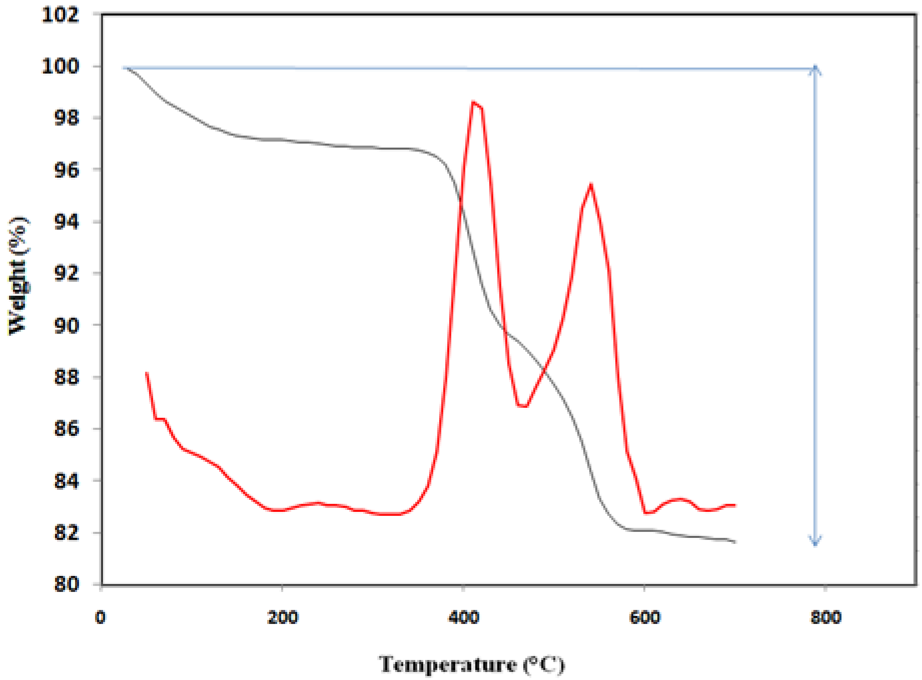


Fig. 6. TGA of $[Simp]_3PW_{12}O_{40}$ molecular nanohybrid material.

3.2. Performance of $[Simp]_3PW_{12}O_{40}$ in the catalytic preparation of different indazolo-phthalazine-triones

3.2.1. Effect of the heteropolyacid nature and structure

Catalytic activity of *Keggin* $H_3PW_{12}O_{40}$ was compared with some illustrative heteropolyacids in the preparation of 2,2-dimethyl-13-phenyl-2,3-dihydro-1H-indazolo[2,1-b]phthalazine-4,6,11(13H)-trione (DMP) (Table 1). Almost, all the examined *Keggin* and *Wells-Dawson* heteropolyacids are strong acids and showed good catalytic activity in the desired transformation. Results uncovered that both *Keggin* and *Wells-Dawson* heteropolyacids behaved as efficient catalysts and prompted to 82-85% yield after 20 min. Notwithstanding, the *Keggin* $H_3PMo_{12}O_{40}$ and the transition metal substituted *Wells-Dawson* $H_7FeP_2W_{17}O_{61}$ showed lower activity and gave 60 and 75% of conversion, respectively.

Table 1. Effect of the heteropolyacid nature and structure on the efficacy of the preparation of DMP.[a]

Catalyst	**Structure type**	**Time (min)**	**Yield (%)[b]**
$H_3PMo_{12}O_{40}$	*Keggin*	20	60
$H_3PW_{12}O_{40}$	*Keggin*	20	82
$H_7FeP_2W_{17}O_{61}$	*Wells-Dawson*	20	75
$H_5PW_{10}V_2O_{40}$	*Keggin*	20	83
$H_6P_2W_{18}O_{62}$	*Wells-Dawson*	20	85

[a] 0.03 g of catalyst was added to a mixture of phthalhydrazide (0.25 mmol), aldehyde (0.25 mmol), and dimedone (0.25 mmol) and the mixture was stirred at 100 ºC for 20 min. [b] Isolated yields.

3.2.2. Optimization of the reaction conditions

Condensation of benzaldehyde (0.25 mmol), dimedone (0.25 mmol) and phthalhydrazide (0.25 mmol) to 2H-indazolo[2,1-b]phthalazine-4,6,11(13H)-trione was chosen to afford the ideal conditions. In the first place, impact of $[Simp]_3PW_{12}O_{40}$ concentration was considered. It was found that 2*H*-indazolo[2,1-*b*]phthalazine-trione was created in a trace amount after 20 min in the absence of catalyst; whereas, 0.01g of catalyst led to 50% yield after 20 min. As appeared in Table 2, this transformation needs presence of catalyst; along these lines, the optimum amount of 0.03g was decided for the preparation of the desired phthalazine-triones. It should be noticed that higher amounts (>0.03 g) have no constructive outcome on the reaction time or yield%.

Table 2. Effect of the catalyst amount on the preparation of DMP. [a]

Entry	**$[Simp]_3PW_{12}O_{40}$**	**Time (min)**	**Yield (%)[b]**
1	0	20	0
2	0.01	20	50
3	0.02	20	61
4	0.03	20	85
5	0.04	20	83

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[a]General reaction conditions are as described below Table 1. [b]Isolated yields

3.2.3. Effect of reaction temperature, time, and solvent on the catalytic system

Effect of reaction temperature was researched in the synthesis of 3,4-dihydro-3,3-dimethyl-13-phenyl-2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione (DMP) in the sight of 0.03 g of $[Simp]_3PW_{12}O_{40}$(Figs. 7-8). Findings uncovered that yield% was expanded with improving reaction temperature from 25 to 100 °C. Impact of reaction time was also inspected. Findings showed that yield% was improved with time and the finest yield was gained after 20 min and no better outcomes were acquired under continued times.

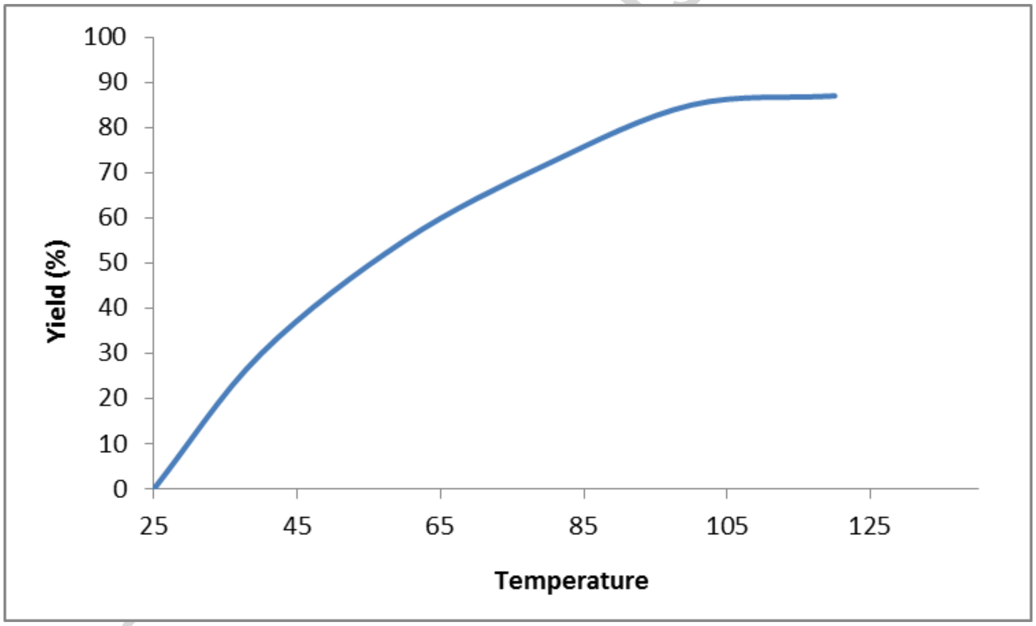


Fig. 7. Effect of temperature on the preparation of DMP.

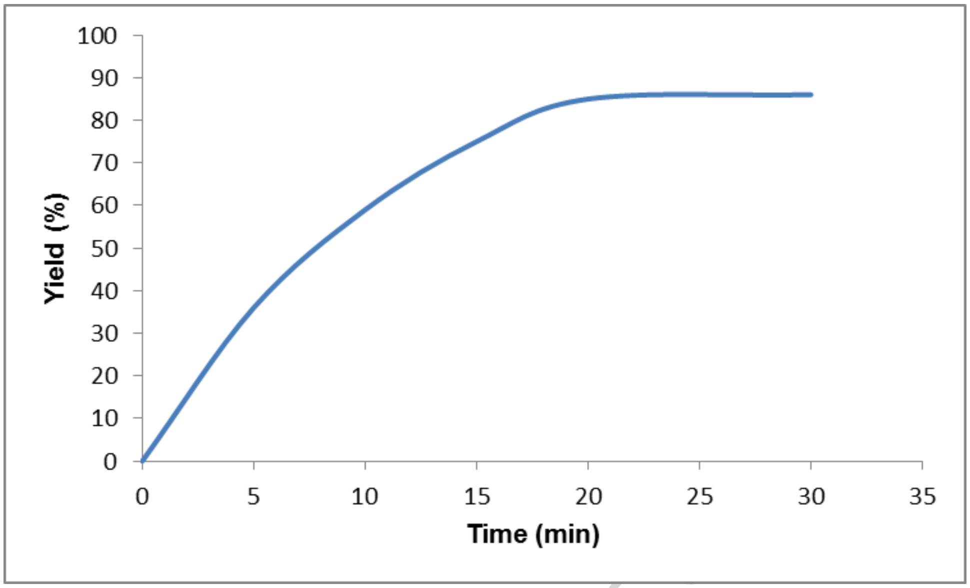


Fig. 8. Effect of time on the preparation of DMP.

Despite the way that this system is under solvent free conditions, even though, effects of some familiar solvents with various polarity were contemplated on the model reaction and the obtained results were compared with the solvent free case (Table 3). This study was carried out under reflux conditions for each solvent. Clearly, the solvent free approach was found to be more powerful than the solvent system considering both the reaction time and yield%.

Table 3. Effect of different solvents on the condensation of benzaldehyde, phthalhydrazide and dimedone.[a]

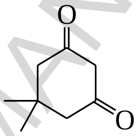
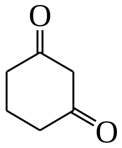
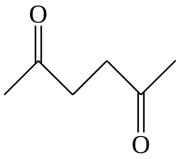
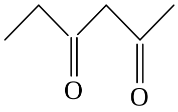
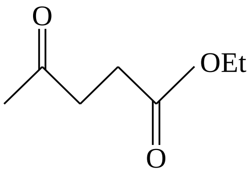
Entry	**Solvent**	**Condition**	**Time (min)**	**Yield (%)**[b]
1	H_2O	Reflux	120	48
2	CH_2Cl_2	Reflux	120	35
3	Chloroform	Reflux	120	45
4	Toluene	Reflux	120	46
5	Free-solvent	100 °C	20	85

General reaction conditions are as described below Table 1. [b]Isolated yields

3.3. Exploring condensation of phthalhydrazide and aromatic aldehydes with different diketones

To study impact of diketone structure on the condensation reaction, different acyclic diketones were chosen to react with phthalhydrazide and benzaldehyde in the presence of $[\mathrm{Simp}]_3\mathrm{PW}_{12}\mathrm{O}_{40}$ (Table 4). Among the examine diketones, 5,5-dimethyl-1,3-cyclohexane-dione (dimedone) and 1,3-cyclohexanedione prompted to the best yield (85 and 90% respectively). The two other linear dikenones, *i.e* 2, 5-hexane-dione and 3, 5-hexane-dione were clearly less compelling than the cyclic ones and led to 23 and 37% yield, respectively, after 20 min. Also, only a trace amount of the desired product was attained for ethyl acetoacetate as substrate.

Table 4. Studying reactivity of cyclic and linear hexanediones towards the condensation reaction.[a]

Diketone	**Structure**	**Time (min)**	**Yield (%)**[b]
5,5-dimethyl-1,3-cyclohexane-dione		20	85
1,3-cyclohexane-dione		20	89
2,5-hexane-dione		20	23
3,5-hexane-dione		20	37
ethyl acetoacetate		20	trace

[a]General reaction conditions are as described below Table 1. [b]Isolated yields.

3.4. Comparison of the catalytic activity of $[Simp]_3PW_{12}O_{40}$ with some reported catalysts

Catalytic activity of $[Simp]_3PW_{12}O_{40}$ was compared with some revealed catalysts as portrayed in Table 5. The general condensation reaction of dimedone, phthalhydrazide, and benzaldehyde was considered as a delegate illustration and the correlation was in terms of mol% or measure of the catalyst, reaction time, temperature, and yield%. The present new catalytic system behaved as one of the best protocols considering simplicity and cost of the procedure. Albeit, some of the introduced mediators catalyzed the reaction at a reduced temperature, however, they require toxic and costly solvents, higher amounts of catalyst, and longer reaction times.

Table 5. Comparison of the catalytic efficiency of $[Simp]_3PW_{12}O_{40}$ with some reported catalysts.

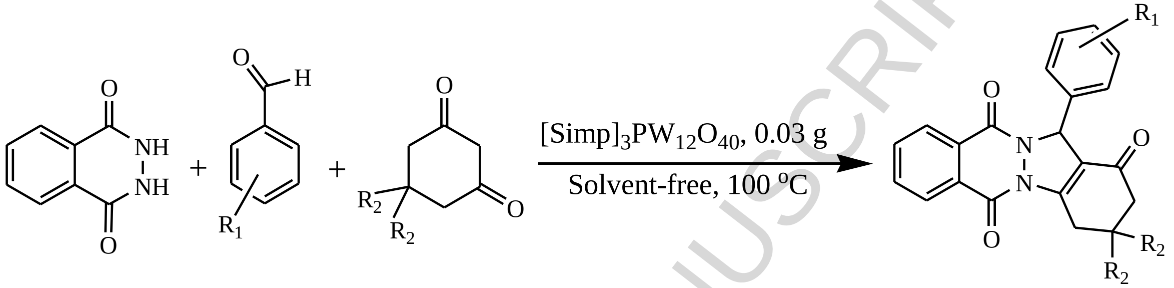
Entry	Catalyst and Conditions	Time (min)	Yield[a] (%)	Ref.
1	H_2SO_4[bmim][BF_4], 80 ºC	30	86	29
2	CAN, Solvent free, 50 ºC	120	94	33
3	Fe_3O_4@Silica sulfuric acid, Solvent free, 100 ºC	35	88	36
4	PMA–SiO_2 (0.05 mmol), Solvent-free, 80 ºC	30	85	37
5	$[Simp]_3PW_{12}O_{40}$	20	85	This work

[a] Isolated yields.

3. 5. Synthesis of substituted phthalazine-triones

All inclusive statement of the present convention was surveyed by applying condensation reaction with various substituted benzaldehydes. In all cases, the reactions provided the desired products in good to excellent yields. As shown in Table 6, a series of aromatic aldehydes containing either electron-withdrawing or electron-donating substituents effectively responded and afforded the corresponding pure products under the selected conditions. Although, aldehydes bearing electron-deficient groups led to better yields, however, the reactions proceeded easily and equally for both electron-withdrawing and electron-donating substituted. Therefore, the nature and electronic aspects of the substituents had no an evident and essential impact on the rate and reaction yield.

Table 6. Synthesis of different 2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-triones in the presence of $[Simp]_3PW_{12}O_{40}$ under solvent-free conditions.



Enty	R_1	R	Time (min)	Yield (%)[a]	m.p. / lit. m.p. (°C)	Ref.
1	Ph	Me	20	85	205-207/204-206	22
2	4-FPh	Me	80	80	220-222/218-220	22
3	4-ClPh	Me	80	83	261-263/261-263	22
4	4-NO_2Ph	Me	80	82	223-225/223-225	22
5	2-ClPh	Me	50	75	264-266/264-266	22
6	3-OMePh	Me	60	68	208-210/210-211	23
7	4-OMePh	Me	60	74	218-220/220-221	24
8	4-Me-Ph	Me	60	66	225-227/227-229	22
9	4-$(CH_3)_2$NPh	Me	80	70	256-258/257-259	34
10	3-ClPh	Me	60	73	205-207/207-209	28
11	2-NO_2Ph	Me	40	70	235-237/238-240	32
12	Ph	H	20	89	220-222/222-225	25
13	4-BrPh	H	20	90	280-282/279-282	25
14	3-NO_2Ph	H	15	92	230-232/228-231	25

[a] Yields point out to the isolated neat products. The desired pure products were described by comparison of their physical data with those of known samples.

3.6. Hot filtration test

With a specific end goal to affirm that the catalytic activity was started from the ionic liquid catalyst $[Simp]_3PW_{12}O_{40}$ and not from the drained segments (if possible) in the reaction mixture, a hot filtration test was done. In this technique, the condensation reaction of benzaldehyde was performed at 100 °C for 10 min in the presence of the $[Simp]_3PW_{12}O_{40}$. Then, the reaction mixture was cooled to room temperature and the yield of 59% was accomplished as depicted in the experimental section. A short time later, the heterogeneous catalyst was filtered and chloroform was evaporated from the residue and the reaction was continued with the filtrate at 100 °C for another 20 min (total time 30 min). However, no corresponding increase in the product yield beyond 59% was watched. This outcome affirmed the heterogeneous nature of the catalyst and that no leaching of the components occurred during the course of the reaction. FT-IR, XRD, UV-Vis, and ^{1}H NMR of the recycled catalyst after 4th run were compared to the fresh one. In agreement with the results of recyclability, no observable spectral changes were detected for the recycled catalyst.

3.7. Reusability and reproducibility of $[Simp]_3PW_{12}O_{40}$

The reusability of the catalyst was tested in the synthesis of DMP, as shown in Fig. 9. The catalyst was recouped after each run, washed three times with chloroform, dried in an oven at 80 ºC for 4 h and tested in a subsequent run. The catalyst was approved for 5 runs. It was observed that the catalyst displayed very good reusability. Additionally, to ensure reproducibility of the transformation, duplicated typical experiments were carried out under similar reaction conditions. The obtained yields were observed to be reproducible within ±3% variation.

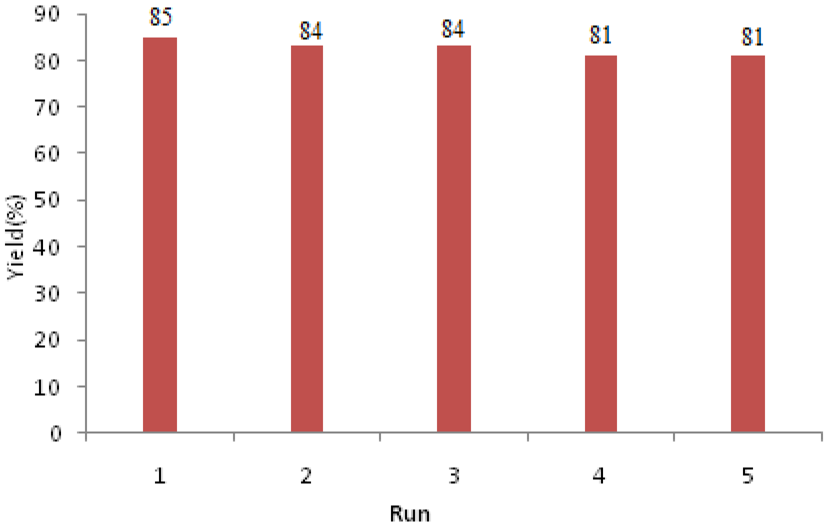


Fig. 9. Yield% *vs* of reusability of $[Simp]_3PW_{12}O_{40}$ catalyst.

4. Conclusion

In outline, a new ionic nanomaterial $[Simp]_3PW_{12}O_{40}$ was fabricated and utilized as a proficient impetus for the one-vessel synthesis of 2H-indazolo-phthalazine-triones via the contraction of dimedone, phthalhydrazide and aromatic aldehydes. The catalytic reactions were adjusted under thermal solventless conditions in brief times. Besides, the catalyst could be profitably renewed and reused at least for five runs without serious loss of activity. The one-pot feature and utilization of heterogeneous solid acid catalyst, as an eco-friendly mediator, provided the current protocol suitable for multi-step approaches. This methodology bears significant improvements such as the heterogeneous impetus of the catalyst, scope of the transformation, accessible operation and simple work up.

5. Acknowledgments

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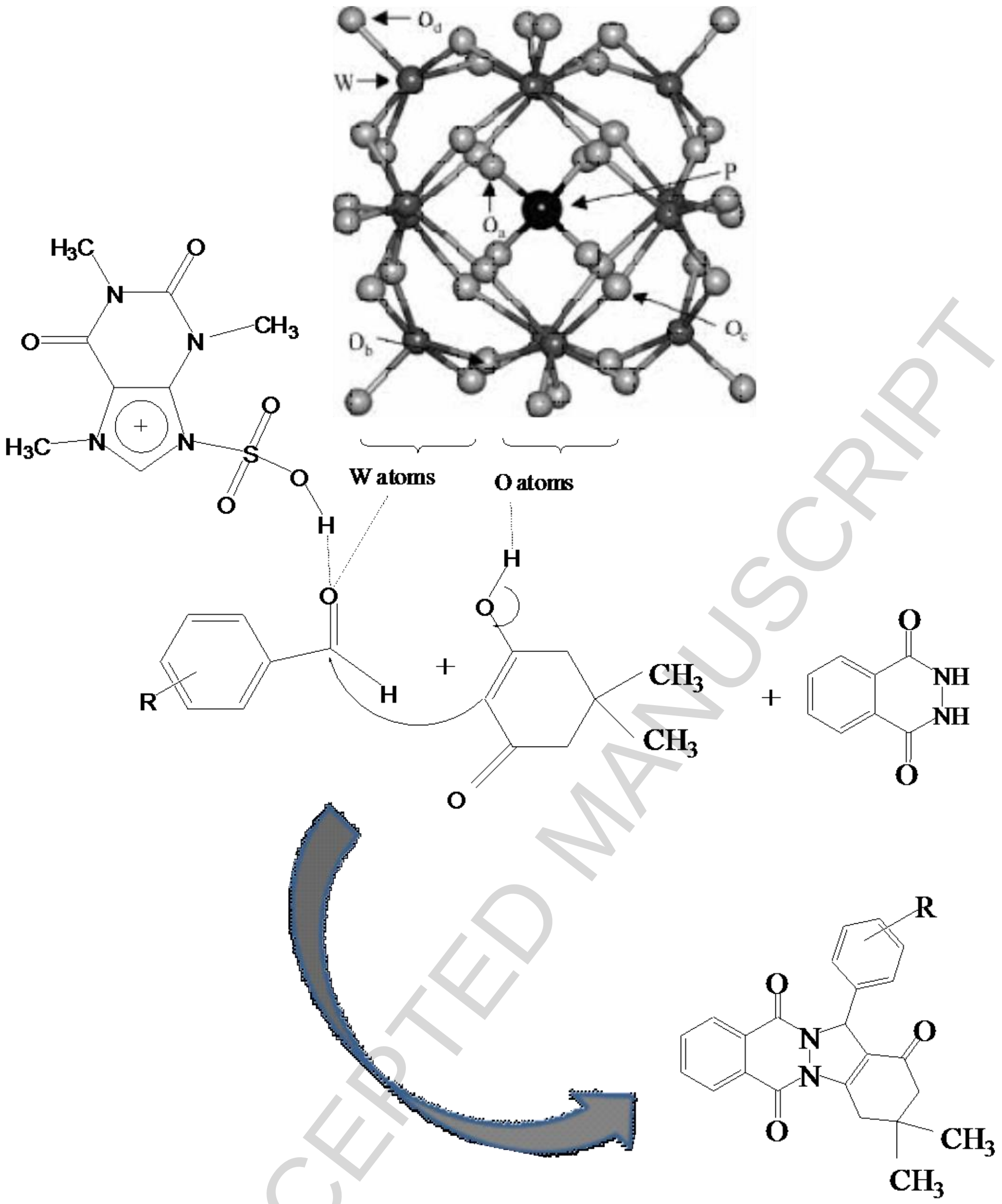

Graphical abstract

Highlights

- Preparation of a new powdered ionic liquid $[\mathrm{Simp}]_3\mathrm{PW}_{12}\mathrm{O}_{40}$
- The catalyst was an inexpensive and efficient catalyst with high recycle ability without significant loss of activity
- The entire synthetic sequence is cost-effective, environmentally friendly, and possesses acceptable generality