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Fabrication of heterogeneous Zr-containing polyoxometalate as an efficient catalyst for the synthesis of a broad range of 1,5-benzodiazepine derivatives

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ABSTRACT

As an extension of our interest in polyoxometalate (POM) as catalysts, one heterogeneous catalyst $TBA_8[Zr(W_5O_{18})_2]\cdot 17H_2O$ (**$Zr(W_5)_2$**) (TBA^+: tetrabutylammonium) was synthesized and fully characterized by multiple spectroscopic techniques. In this catalyst, zirconium ion connected to two mono-lacunary Lindqvist $[W_5O_{18}]^{4-}$ anions to create anionic sandwich-type POM and this anionic unit was encapsulated by TBA^+ cations to form heterogeneous catalyst with hydrophobic nature. It is assumed that alkyl chains of TBA^+ can trap reactants on the surface of catalyst, thus in this regard, the probability of the interaction between reactants and POM center can increase which lead to the higher catalytic efficiencies of above catalysts. Using **$Zr(W_5)_2$** as a heterogeneous and efficient catalyst, a series of 1,5-benzodiazepines were synthesized *via* four mild and solvent-free reactions such as reaction of 1,2-phenylenediamine with ketones, chalcones, 1,3-diketones and aldehydes. According to the results, the presented protocol is superior to the previously reported methodologies in terms of reaction time and product yield. The facile work-up procedure and the reusability of this catalyst are other advantages of this protocol.

1. Introduction

The benzodiazepine skeletons are privileged heterocyclic ring systems containing nitrogen group because of its presence in many important pharmacological compounds. Among them, 1,5-benzodiazepine derivatives (1,5-BDs) have found applications as dyes for acrylic fibers in photography and sedative, anti-inflammatory and hypnotic agents [1]. Additionally, 1,5-BDs are key synthons for the preparation of numerous fused ring systems [2,3]. Over the past several years, various literatures for the preparation of 1,5-BDs reported [4–7]. However, several of them suffer from weaknesses such as low to poor yields and relatively long reaction times and above all, in most homogeneous catalytic systems, the major limitation is the separation of the catalyst after the completion of the reaction and poor reusability. Thus, due to the attractiveness of 1,5-BDs there is an imperative need to progress of proficient approaches and exploitation of green and heterogeneous catalysts that can be effortlessly isolated and simply reused at the end of reactions.

Polyoxometalates (POMs) are one class of inorganic and anionic metal-oxide clusters that have been investigated for about two centuries [8–10]. Generally, POMs can be classified into two groups; i) heteropolyanions (HPAs) include one or more metallic or nonmetallic heteroatom such as Keggin, Wells-Dawson, and Anderson-Evans and ii) isopolyanions (IPAs) with no heteroatom such as Lindqvist where only transition metal and oxygen atoms are involved in the structure. It is important to note that POMs have many merits, including mass, size and electron/proton storage capacities which produce many applications in different areas such as materials science, magnetism [11], medicine [12], catalysis [13–17] and so on. POMs benefit from fairly high thermal stability in the solid state, solubility in polar and non-polar solvents, high H^+ mobility and reversible redox properties that gave them the advantage to be employed as acid as well as oxidation catalysts. Totally, catalysts can be classified according to various criteria: structure, composition, area of application, or state of aggregation. Two large

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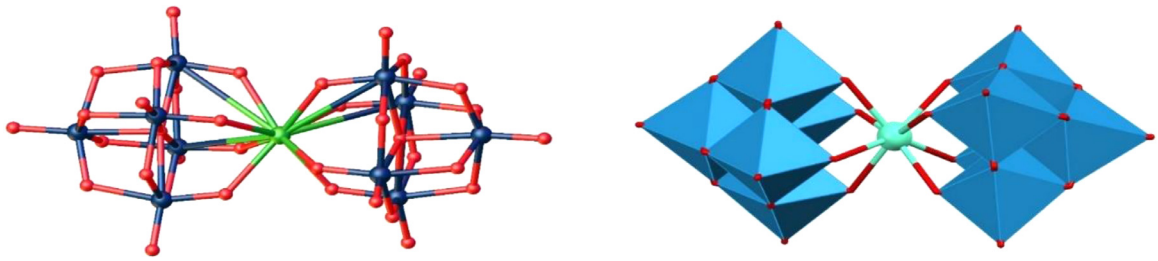


Fig. 1. Anionic representation of $[Zr(W_5O_{18})_2]^{8-}$ with ball and stick (left) as well as polyhedral (right) representation. This catalyst can act as Lewis acid/base catalyst: the oxygen enriched surfaces (Lewis base active sites) and the Zr^{4+} (Lewis acid active site). Color code: Zr, green; W, dark blue; O, red.

groups of classification of the catalysts according to the state of aggregation are commonly distinguished: homogeneous catalysts and heterogeneous catalysts (solid-state catalysts). Intermediate forms also exist such as homogeneous catalysts attached to solids (supported catalysts), also known as immobilized or heterogenized catalysts and finally, biocatalysts [18–20].

The rapid progress of POMs is inseparable from the modification of the lacunary structures. POMs are known to be unstable in alkaline condition. The formation of the lacunary POMs is mainly pH dependent. Controlling the pH of POMs involved solution will lead to some progressive degradations of the polyanion towards lacunary structures by the removal of some metal-oxide $[MO_x]^{n+}$ unites from the complete structures [13,21]. These lacunary species have generated a tremendous interest for researchers from structure to application. For example, the removal of one $[MO_x]^{n+}$ unit from the POMs expose 'cavity', which resulting in a remarkable increase of the charge density in the defective region due to the four new formed oxygen terminals[21]. This vacancy is proved much attractive for some metal ions to form transition metal-substituted POMs. The incorporation of a new metal in the cluster may bring significant electronic property changes, and consequently exhibit fantastic reactivity and electrochemistry. On the other hand, organic groups can also attach on the defect *via* electrostatic interactions, hydrogen bonds, van der Waals interactions, or covalent interactions to build the organic–inorganic POM hybrids [8,22,23].

Following our attempt to investigate the synthesis and utility of novel lacunary POM-based catalysts and development of environmentally benign synthetic methodologies for organic transformations [24–33], herein, we wish to present our findings towards the development of solvent free syntheses of 1,5-BDs by various cyclocondensation reactions under zirconium-containing isopolyoxometalate catalyst; $TBA_8[Zr(W_5O_{18})_2]\cdot 17H_2O$ (**$Zr(W_5)_2$**), in which these derivatives were synthesized in high yields. As we expected, this catalyst would simultaneously be acted as Lewis acid and base by combination of Zr^{4+} Lewis acid and terminal oxygen atoms of lacunary Lindqvist (Fig. 1). Moreover, the generality of this methodology and the reusability of the **$Zr(W_5)_2$** was also studied. Notably, the comparison of the efficiency of this study with the previously reported ones is covered.

2. Experimental

2.1. Chemicals and materials

The chemical compounds were purchased from Merck (Darmstadt, Germany, www.merckmillipore.com) and Sigma-Aldrich (St. Louis, MO, USA, www.sigmaaldrich.com) and used with no crystallization or purification. The chemicals employed for preparation of 1,5-BDs were 1,2-phenylenediamine, acetophenones, benzaldehydes and 1,3-diketones, toluene, ethanol, methanol, acetonitrile and deionized water were used.

2.2. Instrumentation

Electrothermal 9200 apparatus was employed to determine the melting point of products. Bruker Tensor 27 FT-IR spectrometer (400-4000 cm^{-1} region) was used to detect absorbance bands of KBr disk containing the compounds. Also, the infrared spectra of catalysts were recorded in the range of 4000–400 cm^{-1} on a Thermo Nicolet/AVATAR 370 Fourier transform spectrophotometer using KBr discs. Elemental analysis (CHN) was performed using a Thermo Finnigan Flash EA 1112 microanalyzer. Metal content was measured by the Spectro Arcos ICP-OES spectrometer model 76004555 using in the range of 130–770 nm and ICP-AES analyzer (Varian, Vista-pro) was used for metal leaching of the sample in the course of recycling. All organic products were known and for identification and their physical properties and spectral data were considered. Hence, some selected products were recognized by physical properties, NMR and FTIR spectroscopies. ^1H NMR and ^{13}C NMR spectra were obtained on a Bruker FUM-300 spectrometer using DMSO-d_6 as solvent and residual solvent signal as internal reference. The used instruments for performing FTIR spectroscopy by applying PERKIN/ELMER Spectrum 65 apparatus. Powder X-ray diffraction (PXRD) data were collected on ASENWARE/AW-XDM300 X-ray powder diffractometer using Cu Kα (λ = 1.54184 Å) radiation at room temperature with the scan range 2θ = 3 to 40° and step size of 0.05° and step time of 1s. Thermogravimetric analysis (TGA) was carried out under an air atmosphere from ambient temperature up to 1000 °C with a heating rate of 10 °C min^{-1} on a SDT Q600 SPECIFICATIONS. Melting points were measured by Electro thermal 9100. For monitoring of the organic transformation process, TLC on profitable aluminum-backed plates of silica gel 60 was applied and then visualized by UV-Vis light.

2.3. Preparation of catalyst

The sandwich-type isopolyoxometalate with molecular formula $[Zr(W_5O_{18})_2]^{8-}$ (hereafter: **$Zr(W_5)_2$**) was synthesized and identified by FT-IR, elemental analysis and NMR [34].

2.3.1. Synthesis of homogeneous $Na_8[Zr(W_5O_{18})_2]\cdot 28H_2O$

50 g (0.15 mol) $Na_2WO_4\cdot 2H_2O$ was dissolved in 100 ml of water and the pH of the solution was adjusted to 7.2 with glacial acetic acid. After that, warm solution of $ZrCl_4$ (2.6 g, 0.015 mol) was added dropwise to the above solution under continuous stirring and heated to 90 °C for 15 min. The whole solution was cooled down to 5 °C. Crystals of the product slowly separated and were collected.

2.3.2. Synthesis of heterogeneous $TBA_8[Zr(W_5O_{18})_2]\cdot nH_2O$

An aquas solution of $Na_8[Zr(W_5O_{18})_2]\cdot 28H_2O$ (1 mmol, 10 ml) was added to the chloroform solution of TBABr (8 mmol, 10 ml). Then, the reaction mixture was stirred for 2 h. After this time, $[Zr(W_5O_{18})_2]^{8-}$ was transferred into chloroform solution, so organic phase was separated and white precipitation of the prod-

uct was collected by evaporation of the solvent and washed with deionized water two times.

2.4. Typical procedure for synthesis of 1,5-BDs (Method a)

1,2-phenylenediamine (1 mmol), ketone (2.1 mmol) and **$Zr(W_5)_2$** (0.015 g) were mixed and heated at 40 °C. Upon completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and the reaction mixture diluted by hot EtOH (17 mL). Subsequently, the **$Zr(W_5)_2$** catalyst was easily seperated by filtration and the pure products were achieved by recrystallization in good to excellent yield. The structure of the product was confirmed by Mp, FTIR, ^{1}HNMR and ^{13}CNMR spectrometers.

2.5. Typical procedure for the synthesis 1,5-BDs (Method b)

A catalytic amount of heterogeneous **$Zr(W_5)_2$** catalyst (0.015 g) was introduced to a mixture of 1,2-phenylenediamine (1 mmol), chalcone (1 mmol) and then the mixture was heated at 40 °C. Upon completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and the reaction mixture diluted by hot EtOH (17 mL). Subsequently, the **$Zr(W_5)_2$** catalyst was easily seperated by filtration and the pure products were achieved by recrystallization in good to excellent yield.

2.6. Typical procedure for the synthesis 1,5-BDs (Method c)

A catalytic amount of heterogeneous **$Zr(W_5)_2$** (0.015 g) catalyst was added to the mixture of 1,2-phenylenediamine (1 mmol), 1,3-diketone (1 mmol) and aldehyde (1 mmol). The mixture was heated at 40 °C for approperite reaction time. Upon completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and the reaction mixture diluted by hot EtOH (17 mL). Subsequently, the **$Zr(W_5)_2$** catalyst was easily seperated by filtration and the pure products were achieved by recrystallization in good to excellent yield.

2.7. Characterization data

Spectral data for catalyst:

$Na_8[Zr(W_5O_{18})_2]\cdot 28H_2O$: Yield: 2.71 g (68 % based on W). Anal. Calc.: Na, 6.51; W, 55.25; Zr, 4.85. Found: Na, 6.73; W, 54.80; Zr, 4.96. FT-IR (KBr pellet, cm^{-1}): 497, 624, 716, 838, 882, 938, 1413, 1626, 3386.

$TBA_8[Zr(W_5O_{18})_2]\cdot nH_2O$: Yield: 3.27 g (76 % based on W). Anal. Calcd.: C, 34.33; W, 40.14; N, 2.50; H, 6.92 %. Found: C, 33.56; W, 38.75; N, 2.78; H, 7.45 %. FT-IR (KBr pellet, cm^{-1}): 3444, 2963, 2937, 2874, 1483, 1469, 1381, 1314, 1171, 1108, 1063, 975, 947, 883, 814, 665, 586, 445. ^{1}H NMR (d_6-DMSO, 300 MHz, RT) [δ, ppm] 0.93−0.98 (t, TBA-CH_3), 1.28−1.40 (h, TBA-CH_2), 1.54−1.65 (pd, TBA-CH_2), 3.17−3.22 (m, TBA-CH_2). ^{13}C NMR (d_6-DMSO, 300 MHz, RT) [δ, ppm] 14.01, 19.69, 23.57, 57.99 (all singlets).

Spectral data for selected compounds

2-Methyl-2,4-diphenyl-2,3-dihydro-1H-1,5-benzodiazepine **(4a):** Yellow solid, m.p. 150-151 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 3332 (NH), 2961 (C-H aromatic) 2855 and 1925 (C-H aliphatic), 1634 (C=N), 1594 and 1455 (C=C).^{1}H NMR: δ 1.271 (s, 3H, CH_3), 2.47 (d, 2H, CH_2 a,b), 4.64 (br s, 1H, NH), 6.89-7.12 (q, 3H, C_6H_4), 7.14–7.39 (m, 11H, C_6H_5); 13C NMR: δ 29.9 (CH_3), 43.3 (C-3), 73.7 (C-2), 119.7 (C-9), 119.9 (C-7), 125.9 (C-6), 125.9 (C-8), 126.7 (C-4"), 127.5 (C-2", 6"), 127.7 (C-3", 5"), 128.1 (C-3', 5'), 128.3 (C-2', 6'), 129.5 (C-4'), 138.1 (C-1'), 139.5 (C-5a), 140.1 (C-1"), 147.6 (C-9a), 167.8 (C-4).

2-Methyl-2,4-Bis(4-Bromophenyl)-2,3-dihydro-1H-1,5-benzodiazepine **(4c):** Yellow solid, m.p. 146-148 °C; (EtOH); ^{1}H NMR: δ 1.52 (s, 3H, CH_3), 2.60 (d, 1H, CHa), 2.83 (d, 1H, CHb), 3.29 (br s, 1H, NH), 6.80-6.83 (t, 1H, C_6H_4), 7.01-7.11 (m, 2H, C_6H_4), 7.25-7.30 (m, 2H, C_6H_4), 7.33-7.46 (d, 7H, C_6H_4). ^{13}C NMR: δ29.9 (CH_3), 43.3 (C-3), 72.1 (C-2), 121.2 (C-9), 121.3 (C-7), 122.2 (C-6), 124.7 (C-8), 126.8 (C-4"), 127.6 (C-4'), 128.7 (C-2", 6"), 128.8 (C-3", 5"), 131.4 (C-2', 6'), 131.5 (C-3', 5'), 137.7 (C-1'), 138.3 (C-5a), 140.2 (C-1"), 147.1 (C-9a), 166.2 (C-4).

2-Methyl-2,4-Bis(4-Methoxyphenyl)-2,3-dihydro-1H-1,5-benzodiazepine **(4f):** Yellowish solid,m.p. 119-120 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 3295 (NH), 3019 (C-H aromatic), 2964 and 2911 (C-H aliphatic), 1633 (C=N), 1594 and 1476 (C=C); ^{1}H NMR: δ 1.71 (s, 3H, CH_3), 2.90 (d, 1H, CHa), 3.03 (d, 1H, CHb), 3.06 (br s, 1H, NH), 3.52 (d, 3H, OCH_3), 3.79 (t, 3H, OCH_3), 6.74-6.94 (m, 5H, C_6H_4), 7.02-7.05 (t, 2H, C_6H_4), 7.24-7.30 (q, 1H, C_6H_4), 7.51-7.60 (q, 4H, C_6H_4); ^{13}C NMR: δ 29.9 (CH_3), 43.05 (C-3), 55.5 (OCH_3), 55.5 (OCH_3), 73.5 (C-2), 113.6 (C-9), 113.7 (C-3", 5"), 121.7 (C-3', 5'), 121.9 (C-7), 126.0 (C-6), 126.7 (C-1'), 128.3 (C-2', 6'), 129.0 (C-8), 132.3 (C-2', 6'), 138.3 (C-1"), 140.3 (C-5a), 140.8 (C-9a), 158.8 (C-4"), 161.2 (C-4'), 167.3 (C-4).

2-Methyl-2,4-Bis(4-Methylphenyl)-2,3-dihydro-1H-1,5-benzodiazepine **(4g):** Pale yellow crystalline solid, m.p. 98-100 °C (EtOH); ^{1}H NMR: δ 1.66 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.91 (d, 1H, CHa), 3.08 (d, 1H, CHb), 3.44 (br s, 1H, NH), 6.83 (t, 1H, C_6H_4), 7.08-7.12 (m, 3H, C_6H_4), 7.28-7.32 (q, 3H, C_6H_4), 7.49 (d, 2H, C_6H_4), 7.57 (d, 2H, C_6H_4).

2-Methyl-2,4-Bis(3-Nitrophenyl)-2,3-dihydro-1H-1,5-benzodiazepine **(4h):** Light brown crystal, m.p. 86-88 °C (EtOH); ^{1}H NMR: δ 1.90 (s, 3H, CH_3), 3.00 (d, 1H, CHa), 3.25 (d, 1H, CHb), 3.55 (br s, 1H, NH), 6.81-7.08 (m, 1H, C_6H_4), 7.10-7.13 (m, 2H, C_6H_4), 7.18-7.36 (m, 3H, C_6H_4), 7.83-7.99 (m, 3H, C_6H_4), 8.02-8.07 (t, 2H, C_6H_4), 8.30 (s, 1H, C_6H_4).

2,2,4-Trimethyl-2,3-dihydro-1H-1,5-benzodiazepine **(4j):** Yellow solid, m.p. 137-139 °C (EtOH); IR (KBr) ν_{max}/cm^{-1}: 3297 (NH), 2962 (C-H aromatic), 2955 and 2925 (C-H aliphatic), 1634 (C=N), 1594 and 1475 (C=C); ^{1}H NMR: δ 1.27 (s, 6H, CH_3), 2.16 (s, 2H, CH_2), 2.31 (s, 3H, CH_3), 4.47 (br s, 1H, NH), 7.22-7.28 (m, 2H, C_6H_4), 7.38-7.40 (q, 2H, C_6H_4).

3. Results and discussion

3.1. Synthesis and characterization of catalysts

A zirconium-containing isopolyoxometalate catalyst **$Zr(W_5)_2$** of this study was obtained by reaction of the zirconium ion with hot aqueous sodium tungstate at pH 7.2 (Fig. 1). Also, alkyl chains of TBA^+ can be located around the anionic unit of POM [35,36]. Also, the presence of TBA^+ can be proved by ^{1}H NMR and ^{13}C NMR spectra in which three peaks in the ^{1}H NMR located separately around 1.34, 1.59, and 3.19 ppm can be assigned to the CH_2 of TBA^+ and the CH_3 group located at 0.95 ppm (Figs. 2,3 and S1 and S2).

It is important to note that infrared spectroscopy is frequently employed technique for the characterization of POMs due to their characteristic metal–oxygen stretching vibrations that occur in the region between 400−1000 cm^{-1} which is known as the fingerprint region for the POMs. The absorption bands at 1626 and 3386 cm^{-1} attributed to the water molecules. Also, characteristic bands at 933, 882 and 716 cm^{-1} assigned to the W–O_t, W–O_b and W–O_c of POM, respectively (Fig. 4).

Also, the powder XRD pattern of the catalysts appears at around 9-10° for a 2θ value (similar to POMs) [37] (Fig. 5).

Thermogravimetric analysis (TGA) was performed on **$Zr(W_5)_2$** to determine the thermal stability and then calculate the number of its uncoordinated waters. There are a main weight-loss (Fig. 6) in which at temperatures between 50 and 194 °C 17 uncoordinated water molecules are removed and after that the mass remains constant and corresponds to the oxides of the respective metals.

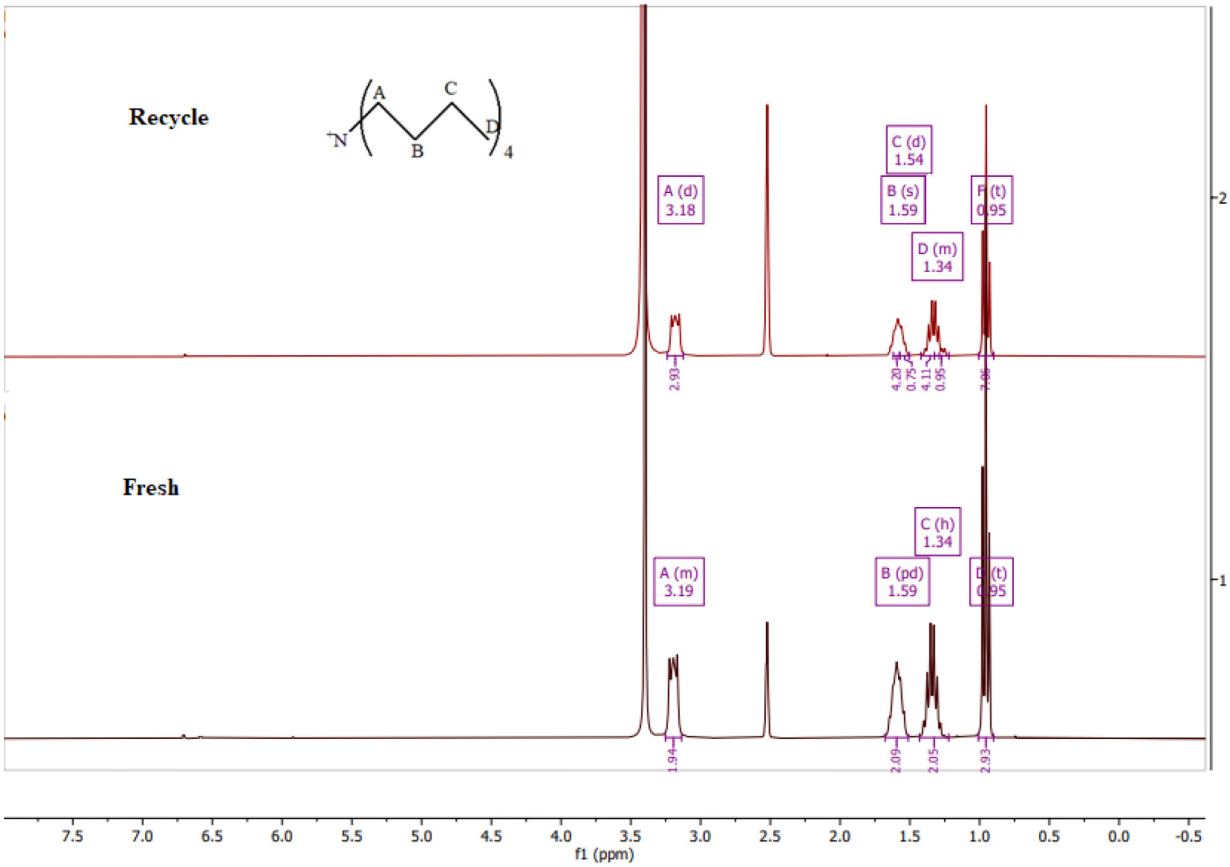


Fig. 2. ^{1}H NMR spectra of fresh and recycled $TBA_8[Zr(W_5O_{18})_2]\cdot nH_2O$.

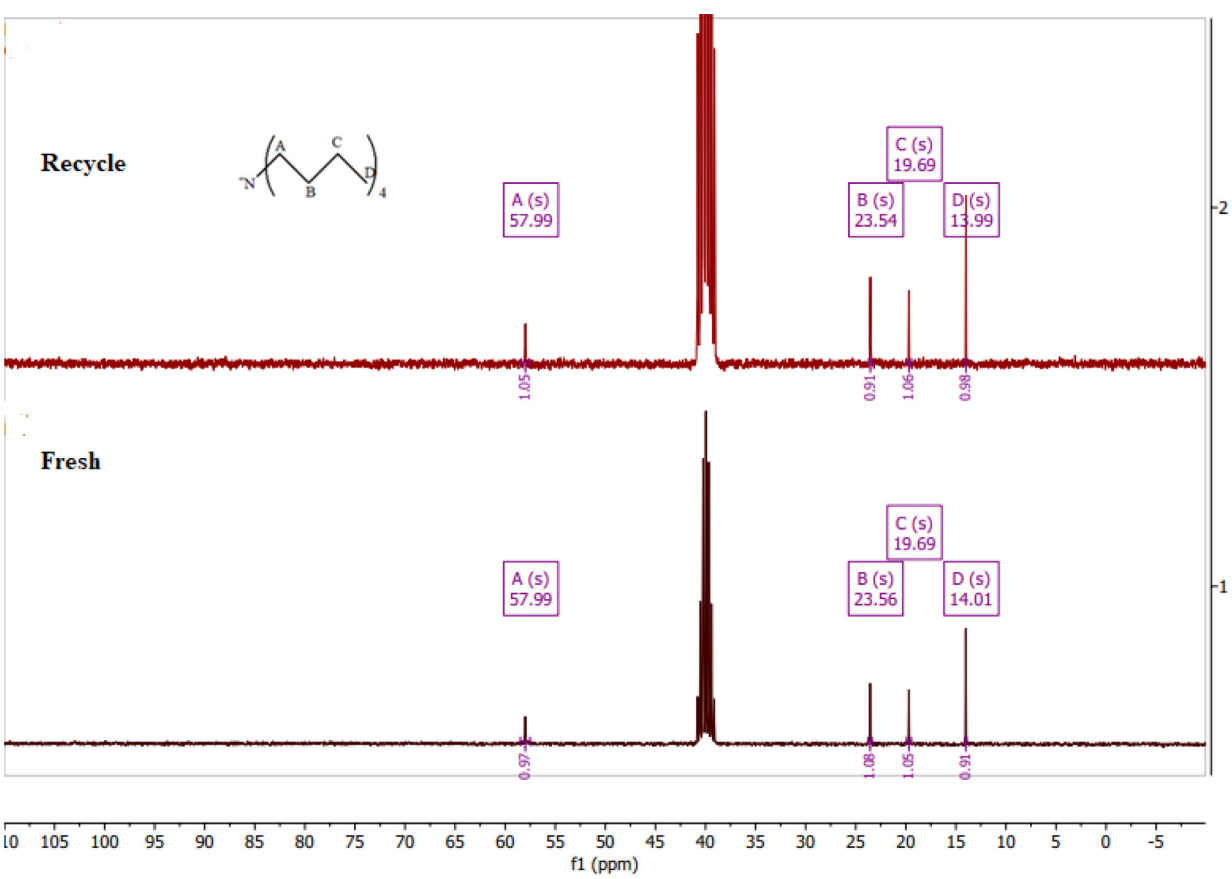


Fig. 3. ^{13}C NMR spectra of fresh and recycled $TBA_8[Zr(W_5O_{18})_2]\cdot nH_2O$.

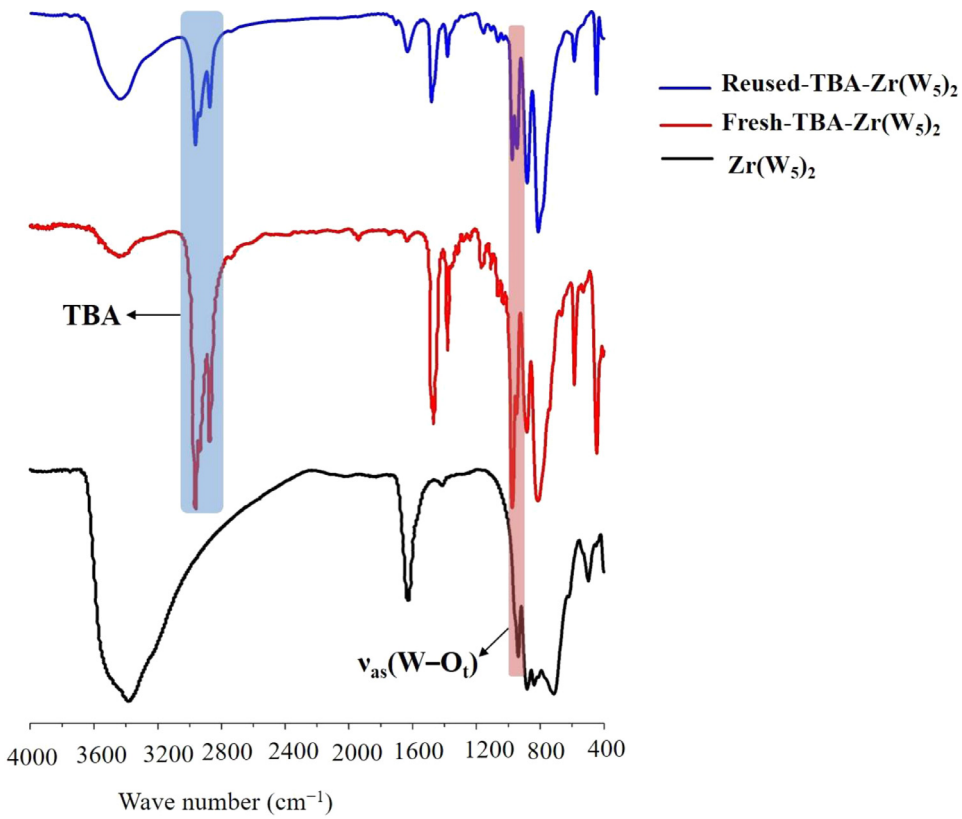


Fig. 4. FTIR spectra of $Zr(W_5)_2$ (homogeneous) and TBA-$Zr(W_5)_2$ (heterogeneous, fresh and reused catalyst).

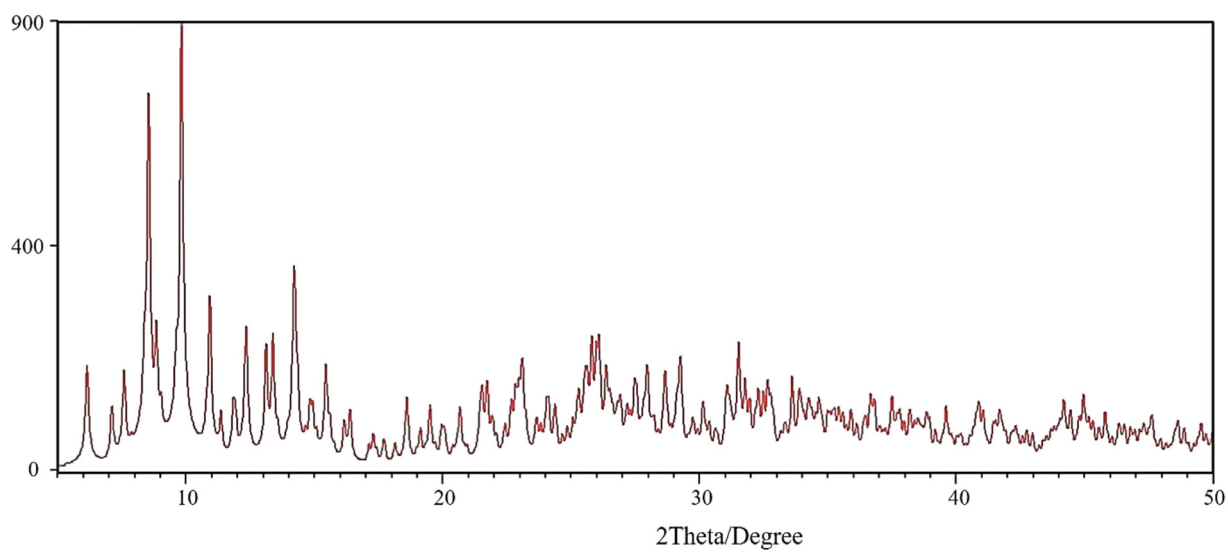


Fig. 5. XRD patterns of $Zr(W_5)_2$.

3.2. Catalytic activity

To extend the catalytic capacity of $\mathbf{Zr(W_5)_2}$ catalyst, herein we study the achievement of $\mathbf{Zr(W_5)_2}$ for the synthesis of a series of 1,5-BDs obtained from three reaction pathways, *i.e.* reaction of 1,2-phenylenediamine with ketones, chalcones and ethylactoacetate/benzaldehyde (Scheme 1). To this purpose, reaction between 1,2-phenylenediamine (1 mmol) and acetophenone (2 mmol) was selected as a model reaction and performed by 15 mg $\mathbf{Zr(W_5)_2}$ catalyst under solvent-free condition. Gratifyingly, the desired products were obtained in 98% yield after 30 min. Encouraged by the promising results; we optimized the reaction condition by investigating the effects of reaction variables on the yield of the product (Table 1). In this context, the selected reaction was accomplished under solvent free (S.F.) condition at different temperatures (r.t., 40 °C and 80 °C) in various solvents including H_2O, EtOH, CH_2Cl_2 and Toluene. The results established that the S.F. led to the highest yield. Moreover, the above reaction was investigated in the presence of 5-25 mg of the $\mathbf{Zr(W_5)_2}$ that 15 mg of the $\mathbf{Zr(W_5)_2}$ catalyst was the best catalyst amount and increasing this value did not improve the product's yield. Similarly, the reaction conditions of the methods b and c to synthesis 1,5-BDs were optimized by select-

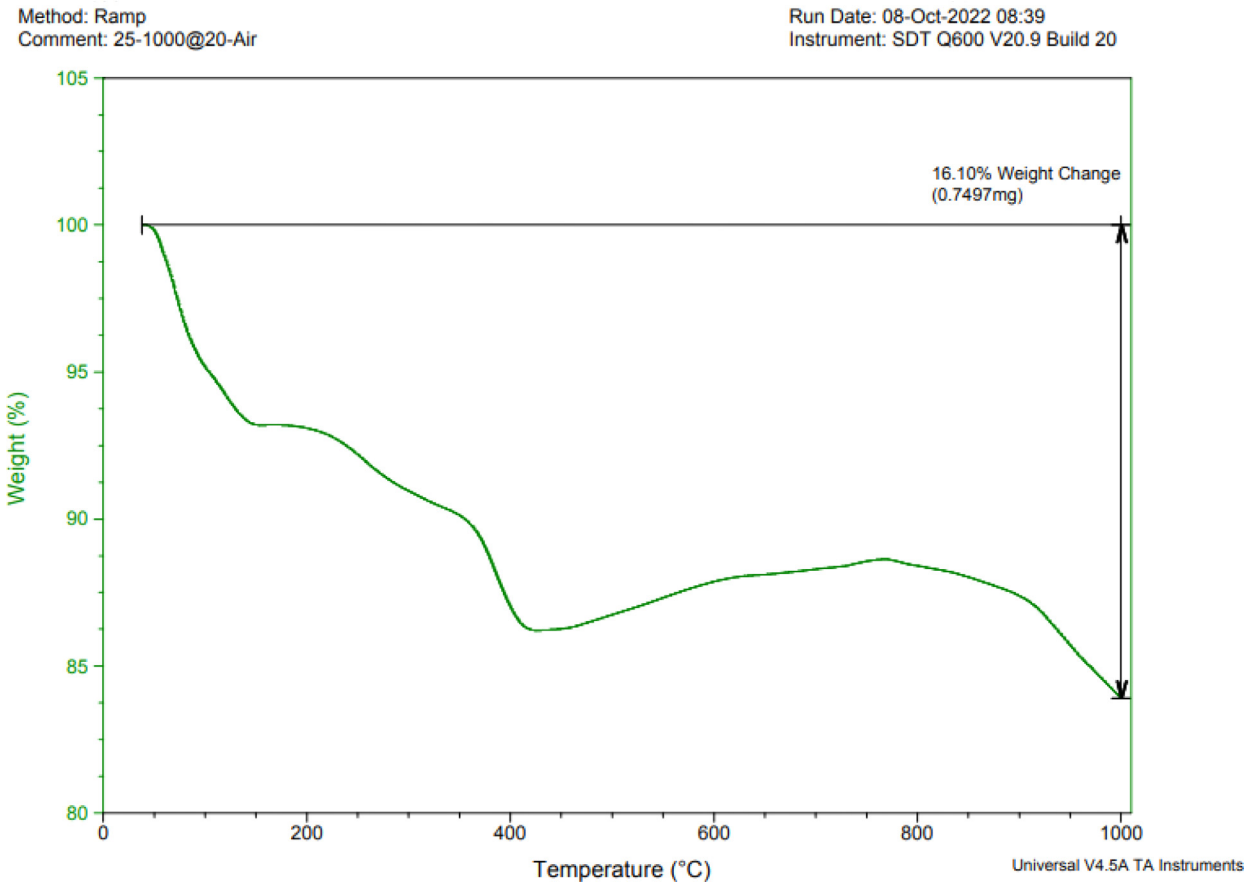
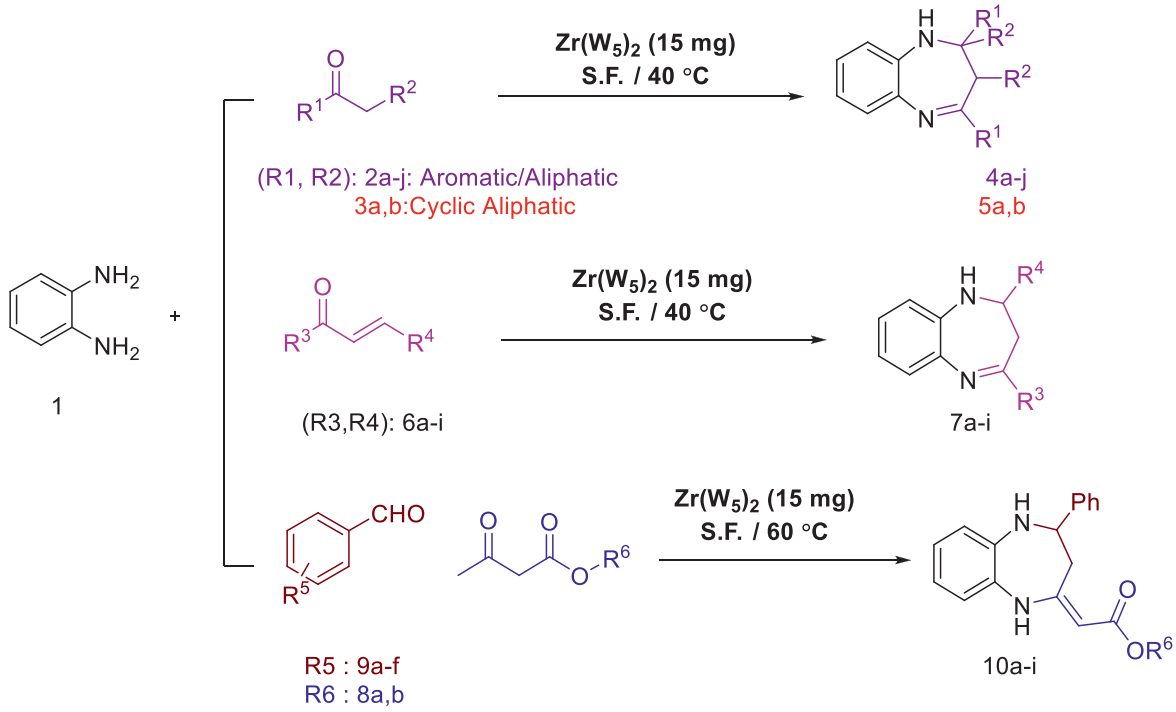
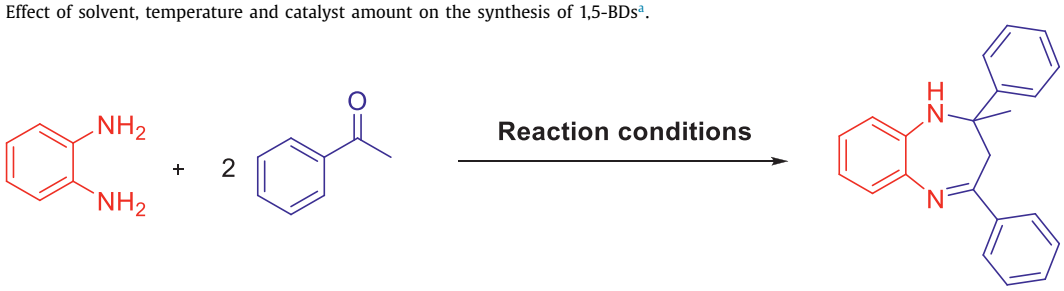


Fig. 6. TGA curves for $Zr(W_5)_2$.



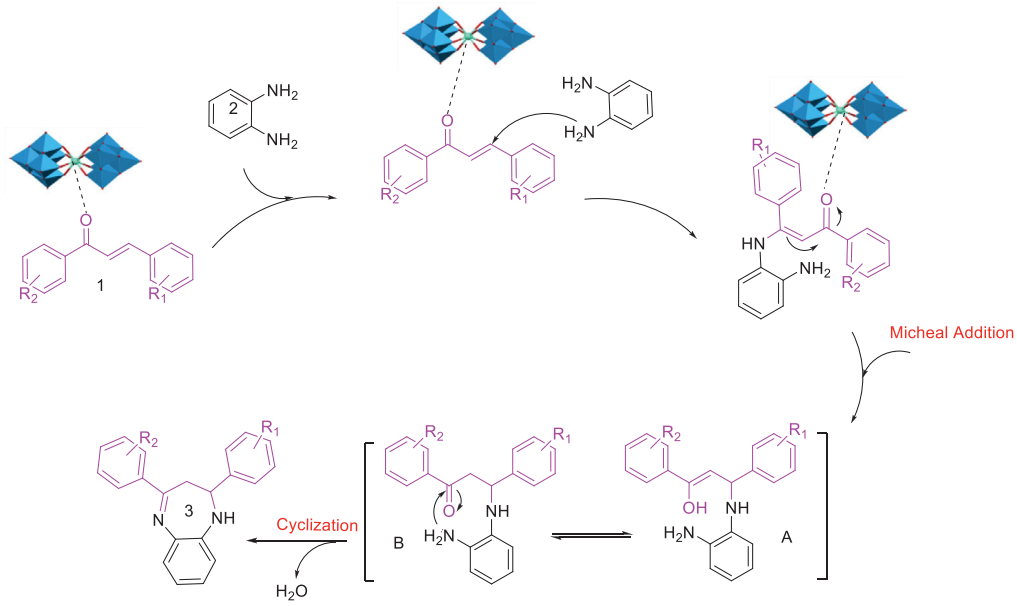
Scheme 1. Synthesis of broad ranges of 1,5-BDs catalyzed by $Zr(W_5)_2$ *via* three methods.

Table 1
Effect of solvent, temperature and catalyst amount on the synthesis of 1,5-BDs[a].



Entry	Catalyst (mg)	Conditions	Time (h:min)	Yield[b] (%)
1	$Zr(W_5)_2$ (None)	S.F./ 40°C	02:00	Trace
2	$Zr(W_5)_2$ (5)	S.F./ 40°C	00:20	55
3	$Zr(W_5)_2$ (10)	S.F./ 40°C	00:20	86
4	$Zr(W_5)_2$ (15)	S.F./ 40°C	00:20	98
5	$Zr(W_5)_2$ (25)	S.F./ 40°C	00:20	90
6	$Zr(W_5)_2$ (15)	S.F./ r.t.	00:20	40
7	$Zr(W_5)_2$ (15)	S.F./ 80°C	00:20	72
8	$Zr(W_5)_2$ (15)	H_2O/ Reflux	00:20	85
9	$Zr(W_5)_2$ (15)	EtOH/ Reflux	00:20	60
10	$Zr(W_5)_2$ (15)	CH_2Cl_2/ Reflux	00:20	53
11	$Zr(W_5)_2$ (15)	Toluene/ Reflux	00:20	Trace

[a] 1,2-phenylenediamine (1 mmol), acetophenon (2.1 mmol) with one drops deionized water.
[b] Isolated yield.



Scheme 2. Plausible mechanism for synthesis 1,5-BDs from 1,2-phenylenediamine and chalcone by $Zr(W_5)_2$ catalyst.

ing model reactions and altering the reaction variables (Table 1). In the case of using chalcones as the starting compound, employing 15 mg of the **$Zr(W_5)_2$** catalyst under solvent free condition at 40 °C was obtained as the optimum condition while in the case of using ethylactoacetate using 15 mg **$Zr(W_5)_2$** catalyst under S. F. at 60 °C led to the highest yield.

Armed with the optimum reaction conditions, three series of 1,5-BDs were synthesized through the first three pathways to prove the generality of the protocols (Table 2). As obvious, various carbonyl containing compounds with different electron densities could tolerate these reactions to furnish the desired products in high yields.

Aiming to evaluate the benefits of this study and investigating the active site in the **$Zr(W_5)_2$** catalyst towards the condensation reaction of 1,2-phenylenediamine and acetophenone, the activity of several catalysts such as various Zr salts and Zr-free POM catalysts were considered and their results were compared. It is noted that, Zr-free POM catalysts have been synthesized and reported by our research group [15,16]. As expected and shown in Table 3, the presence of Zr as an active site to promote this reaction and condensation is necessary, because in its absence, the reaction was incomplete and final product was achieved less than 50% yield. By comparing other Zr salts with **$Zr(W_5)_2$** catalyst, it can be stated that Zr salts are able to promote the reaction and their difference with **$Zr(W_5)_2$** catalyst is in recovery and separation process. Actually, **$Zr(W_5)_2$** catalyst was easily separated by filtration from the reaction mixture and it was recycled up to 3 times with high yields, while Zr salts were difficult to separate and it was not possible to investigate the recovery steps for them. Based on these observations, it can be concluded that using the current protocol is effective in stabilizing Zr as an active site in the catalyst structure.

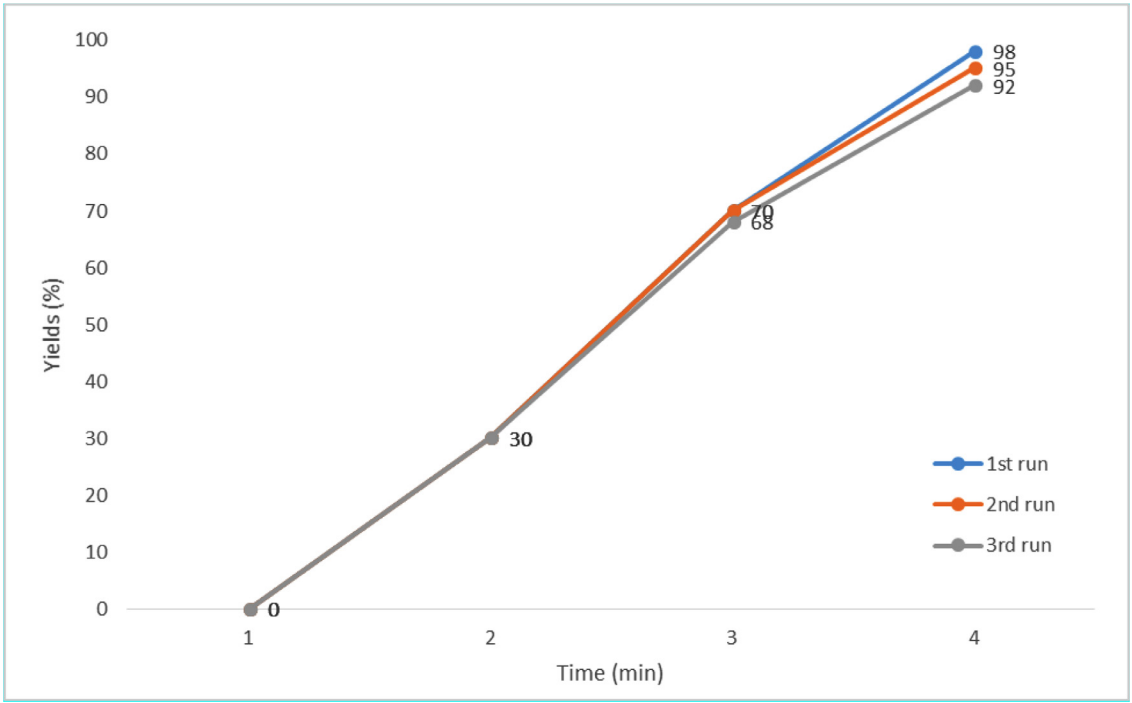


Fig. 7. Reusability of the $Zr(W_5)_2$ catalyst.

Table 2
Preparation of 1,5-Benzodiazepines (4a-12a; R =alkyl, aryl) from 1,2-phenylenediamines (1) and various ketones (2a–j)/various chalcones (6a-i)/ acetoacetate (8a,b) and benzaldehyde (9a-f) catalyzed by $Zr(W_5)_2$[a].

Products	R^1	R^2	Time (min)	Yield (%)[b]	M.p. (°C)[Ref.]
4a	C_6H_5	H	20	98	150-15[35]
4b	*p*-ClC_6H_4	H	63	80	142-144[6]
4c	*p*-BrC_6H_4	H	50	90	146-148[36]
4d	*p*-$O_2NC_6H_4$	H	40	87	154-156[38]
4e	*p*-HOC_6H_4	H	30	95	218-220[36]
4f	*p*-$CH_3OC_6H_4$	H	35	96	116-117[38]
4g	*p*-$CH_3C_6H_4$	H	60	83	98-100[38]
4h	*m*-$O_2NC_6H_4$	H	60	90	86-88[39]
4i	CH_3	CH_3	70	77	136-138[35]
4j	CH_3	H	65	82	137-139[35]
5a	$-(CH_2)_4-$		80	88	136-138[36]
5b	$-(CH_2)_3-$		70	90	138-140[38]

Product	**R^3**	**R^4**	**Time (min)**	**Yield (%)[b]**	**M.p. (°C)[Ref.]**
7a	H	H	25	93	126-128[39]
7b	H	*p*-Cl	60	95	113-115[40]
7c	H	*p*-Me	80	80	125-127[39]
7d	*o*-Cl	H	85	84	130-132[41]
7e	*p*-OH	H	50	88	120-122[42]
7f	*p*-NO_2	H	35	96	103-105[40]
7g	*p*-OMe	H	60	92	144-146[40]
7h	*o*-OH	H	70	90	128-129[42]

Product	**R^5**	**R^6**	**Time (min)**	**Yield (%)[b]**	**M.p. (°C)[Ref.]**
10a	H	Me	53	90	Pale yellow oil
10b	*p*-Cl	Me	50	95	Pale yellow oil
10c	*p*-CN	Me	70	88	153-155[43]
10d	*β*-Naphtalene	Me	100	85	Pale yellow oil
10e	H	Et	40	93	73-77[43]
10f	*p*-Cl	Et	35	95	117-119[43]

[a] Reaction condition: a mixture of *1,2*-phenylenediamine (1mmol) with ketones (2.1 mmol), chalcones or ethyl acetoacetate and benzaldehydes of each (1 mmol) and $Zr(W_5)_2$ (15 mg) without any solvent was heated at 40 and 60 °C.
[b] Isolated yield

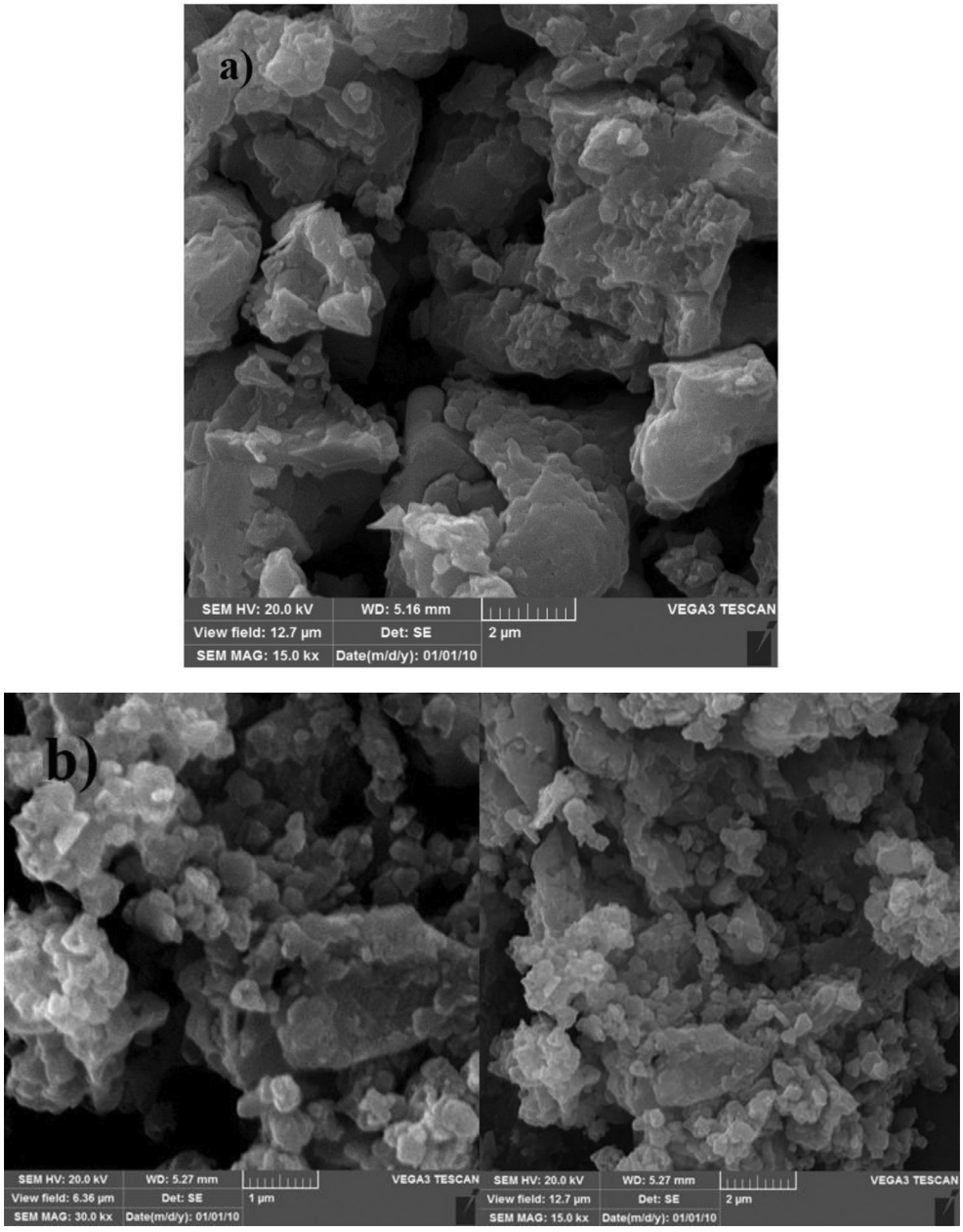


Fig. 8. SEM images of the (a) fresh and (b) reused $Zr(W_5)_2$ catalyst.

Table 3
A comparison of catalytic activity of $Zr(W_5)_2$ with different Zr salts and Zr-free POM in the reaction of 1,2-phenylenediamine and acetophenone [a,b].

Entry	Catalysts (amount)	Reaction conditions Solvent/ Temperature (°C)	Time (min)	Yield (%)
1	$ZrCl_4$ (15 mg)	S.F./ 40	20	80
2	$Zr(NO_3)_4.5H_2O$ (15 mg)	S.F./ 40	20	75
3	$Zr(SO_4)_2.4H_2O$ (15 mg)	S.F./ 40	20	75
4	$Zr(CH_3COO)_4$ (15 mg)	S.F./ 40	20	72
5	$(TBA)_7[PW_{11}O_{39}]$ (15 mg)	S.F./ 40	20	45
6	$(TBA)_8[SiW_{11}O_{39}]\cdot 4H_2O$ (15 mg)	S.F./ 40	20	40
7	$(TBA)_9[BW_{11}O_{39}]\cdot 11H_2O$ (15 mg)	S.F./ 40	20	30
8	$Zr(W_5)_2$ (15 mg)	S.F./ 40	20	98

[a] mixture of *1,2*-phenylenediamine (1mmol) with acetophenone (2.1 mmol) and $Zr(W_5)_2$ (15 mg) without any solvent was heated at 40 °C.
[b] Isolated yields.

Regarding the reaction mechanism, according to the literature [41], the reaction of 1,2-phenylenediamine with carbonyl containing starting material, such as chalcones, ketone and ethyl acetoacetate can proceed through activation of the carbonyl group by the catalyst [42]. As an example of the reaction mechanism with carbonyl containing materials, the reaction's mechanism of 1,2-phenylenediamine with chalcones is discussed here (Scheme 2). Initially, **$Zr(W_5)_2$** catalyst as Louis acid sites, activates the carbonyl group of chalcones. Subsequently, the amino group of 1,2-phenylenediamine attacks the C=C bond of the chalcone and leads to the formation of a condensation intermediate. The latter is converted to the seven membered ring of 1,5-BDs *via* Michael type addition followed by cyclization and removal of a molecule of H_2O.

To explore the catalytic reusability of the catalyst, the catalytic activities of the fresh and reused **$Zr(W_5)_2$** catalyst for the synthesis of 1,5-BDs by method **a** were compared (Fig. 7). The results clearly specified that the **$Zr(W_5)_2$** preserved its catalytic performance upon reusing with only a negligible loss of activity.

To elucidate whether the reusing can result in any change in the morphology of the catalyst, the SEM images of the fresh and reused **$Zr(W_5)_2$** catalyst were compared (Fig. 8). Obviously, the reusing of the **$Zr(W_5)_2$** did not cause any morphological change.

4. Concluding remarks

In the present study, one heterogeneous catalyst based on isopolyoxometalate **$Zr(W_5)_2$** was synthesized and characterized using a suite of analytical techniques. Notably, alkylammonium cations (TBA^+) on the surface of POMs provide flexible structures with hydrophobic and polar nature that promote the catalytic performance by trapping organic reactants on the catalyst surface. This catalyst also showed a remarkable ability to develop a wide range of 1,5-BDs under solvent-free conditions. The heterogeneous nature of the **$Zr(W_5)_2$** catalyst makes its separation facile and convenient. Moreover, the recovered **$Zr(W_5)_2$** could be successfully reused for promoting at least 3 runs of the reaction without significant loss of the catalytic activity. In comparison to other reported methods, this protocol takes advantage on shorter reaction time, solvent-free condition, simple work-up and high yield. Also, further studies are underway in our laboratory to extend the application of these family catalysts to other coupling reactions.

Declaration of Competing Interest

The authors declare no conflict of interest

CRediT authorship contribution statement

Masoume Malmir: Methodology, Formal analysis, Investigation, Software, Data curation, Writing – original draft. **Majid M. Heravi:** Conceptualization, Funding acquisition, Supervision, Methodology, Writing – review & editing, Project administration, Visualization. **Zahra Yekke-Ghasemi:** Methodology, Formal analysis, Investigation, Software, Data curation, Writing – original draft. **Satar Saberi:** Software. **Masoud Mirzaei:** Methodology, Conceptualization, Funding acquisition, Supervision, Methodology, Writing – review & editing, Project administration, Visualization.

Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2022.134631

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