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FULL PAPER

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Studying catalytic activity of ternary mixed-metal Keggin $H_7SiV_3W_9O_{40}$ as a versatile acid catalyst for the synthesis of β-acetamido ketones

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One-pot four-component condensation of an aromatic aldehyde with an enolisable ketone and acetyl chloride is investigated in the presence of $H_7SiV_3W_9O_{40}$ in acetonitrile. The prepared catalyst was characterized by standard techniques such as XRD, SEM, and FT-IR to verify the Keggin structure of nanocatalyst. Furthermore, findings revealed a very good catalytic activity for the applied vanadium substituted heteropolyacid in this acid catalyzed condensation reaction. A series of Keggin Si and V-substituted heteropolyacids were compared for the synthesis of β-acetamido-β-(4-chlorophenyl)propiophenone, which showed a better catalytic activity for $H_7SiV_3W_9O_{40}$ and $H_4SiW_{12}O_{40}$ than the lacunary and mixed metal Keggin $H_4SiW_9Mo_3O_{40}$ and $H_5SiW_9Mo_2VO_{40}$. In addition, effect of the nitrilating agent was also demonstrated in this catalytic system and findings show less proficiency for PhCN compared to acetonitrile. Moreover, propiophenone as an α-substituted enolisable ketone was reacted with some aromatic aldehydes and the anti isomer is detected as the major diastereomer. Therefore, $H_7SiV_3W_9O_{40}$ can be introduced as a new effective, inexpensive, and eco-friendly catalyst for the introduced four-component condensation reaction.

KEYWORDS
Acetamido ketone, four-component, $H_7SiV_3W_9O_{40}$, Heteropolyacid, Keggin

1 | INTRODUCTION

Heteropolyoxometalates comprise a wide and well-defined class of early transitionmetal clusters which are constructed from polyoxoanions generated from early transition metals such as tungsten, molybdenum, and vanadium.[1] Although, the chemistry of polyoxometalates is not even new,[2] however, remains as a great and emerging key area in the progress and development of sophisticated molecules.[3] These magic compounds are known with a great variety of structures, applications, properties, and have been considered as intermediate structures between molecules and oxide solids.[4,5] Therefore, various applications like pigments, membranes, and sorbents are extruded from their versatile nature.[6] However, the most important application of these materials remains in the area of catalysis.[7]

Mixed-addenda vanadium substituted polyoxometalates with the general formula of $H_{3\,+\,n}SiM_{12\text{-}n}V_nO_{40}$ (M = Mo and W; n = 1–6) are well known, as an important sub-group of Keggin heteropolyoxometalates, which their catalytic activities remained to be explored. In these compounds one or three addenda units are generally removed from the Keggin-type polyoxometalate to generate the so-called lacunary anions of $XM_{11}O_{39}{}^{n-}$ and $A\text{-}XM_9O_{34}{}^{n-}$. These incomplete species quickly react with an extensive variety of metal ions to refill the vacant sites.[8–11] A tungsten-based Keggin structure $H_4SiW_{12}O_{40}$ is a stable compound which can be prepared in high yield with excellent purity from relatively low-cost precursors. This compound can be subsequently modified to replace three corner-sharing tungsten atoms with vanadium (Scheme 1). The resulting compound $H_7SiV_3W_9O_{40}$ is stable over a wide range of temperatures and pHs.

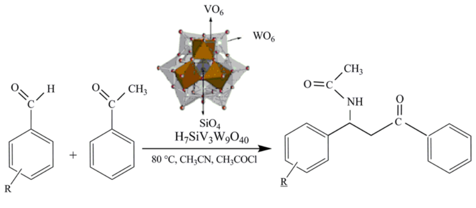
β-Acetamido ketones are versatile mediators in the synthesis of many important biological and pharmacological stuffs such as neopolyoxins, nucleoside antibiotics, nikkomycins, and various antibiotic drugs.[12–15] Aside Dakin–West reaction,[16] one-pot multi-component coupling of an aromatic aldehyde, an enolizable ketone, and acetyl chloride in the presence of acetonitrile is the simplest method for the preparation of *β*-acetamido ketones.[17] A number of catalysts such as montmorillonite K10 clay,[18] silica sulfuric acid,[19] and heteropolyacids[20] have been used to prepare these important organic compounds.

In continuation of our efforts on using heteropolyoxometalates in multi-component condensation reactions,[21–26] we developed the applicability of strong super-acidic vanadium (V) substituted Keggin-type heteropolyacid, $H_7SiV_3W_9O_{40}$, as a nanocatalyst for the efficient and facile synthesis of β-acetamido ketones by one-pot condensation of an aromatic aldehyde, an enolizable ketone, and acetyl chloride in acetonitrile (Scheme 1).

2 | EXPERIMENTAL

2.1 | Materials and methods

All reagents and starting materials were commercially available and used as received. β-Acetamido ketones were characterized by comparison of their physical and spectral data with known reported samples in the literature. Progress of the reactions was monitored by TLC by using Silica gel 60 (70–230 mesh). Infrared spectra were recorded (KBr pellets) on an 8700 Shimadzu Fourier Transform spectrophotometer. X-ray powder diffraction analysis was performed on a BRUKER D8 ADVANCE X-ray diffractometer using a Cu tube operated at 40 kV and 40 mA in the 2θ range of 4–40°. Electron microscopy was performed on a Phillips XL-30 scanning electron microscope (SEM). ^{1}HNMR spectra were recorded on a BrukerAVANCE 200-MHz instrument. All catalysts were prepared and characterized according to literature procedures.[27–30]



SCHEME 1 General formulation for the preparation of substituted *β*-acetamido ketones.

2.2 | Synthesis of ternary mixed metal $H_7SiV_3W_9O_{40}$

A classic well-known method was performed for the preparation of $H_7SiV_3W_9O_{40}$ from sodium vanadate precursor.[20,29] Sodium vanadate (1.9 g; 15.5 mmol) was dissolved in 300 ml of water. $Na_{10}[\alpha\text{-}SiW_9O_{34}].18H_2O$ (145 g; 52 mmol) was mixed with the stirred solution and 185 ml of 6 M sulfuric acid was subsequently added to this solution under stirring for 45 min. pH was adjusted between 6–7 by solid potassium carbonate. After addition of solid potassium chloride (80 g), an orange potassium salt was precipitated. Further purification was achieved via re-crystallized in water. Calcd (Found): K, 9.34 (9.12); V, 5.16 (5.28); Si, 0.96 (1.12); W, 56.48 (56.73); H_2O, 6.14 (6.32). FT-IR (cm^{-1}): 1003 (w), 960 (s), 902 (vs), 805 (vs), 741 (vs). Then, the potassium salt (15 g; 5 mmol) was dissolved in 65 ml of water in a separatory funnel. Thereafter, diethyl ether was added, followed by slow addition of 100 mL concentrated HCl. The heavy phase was collected and diethyl ether was evaporated under vacuum. The obtained solid was dissolved in a little amount of water. Finally, the heteropolyacid nanoparticles were slowly crystallized at room temperature.

2.3 | General procedure for the preparation of β-acetamido ketones

Aromatic aldehyde (1 mmol), acetyl chloride (2 mmol), and acetophenone (1 mmol) were mixed in 4 ml of acetonitrle in the presence of the desired heteropolyacid (2.5 mol%) at 80 °C. Progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered and the corresponding solid crude product was washed with ice-water and petroleum ether. The pure product could be obtained by re-crystallization from ethanol-water mixture. All products were characterized by FT-IR and ^{1}H NMR spectroscopy and their melting points were compared with those reported in the literature.

2.4 | Spectral data for some selected β-acetamido ketones

2.4.1 | β-Acetamido-β-(phenyl) propiophenone

^{1}H NMR (CDCl$_3$, 200 MHz): δ 2.02 (s, 3H), 3.34 (dd, 1H), 3.66 (dd, 1H), 5.61 (m, 1H), 7.32 (s, 1H), 7.57 (d, J = 9.1 Hz, 5H), 7.76 (d, J = 9.1 Hz, 5H). FT-IR (KBr, cm^{-1}): 3253, 3046, 1666, 1624, 1576, 1288, 1083, 878, 820.

2.4.2 | β-Acetamido-β-(4-chlorophenyl) propiophenone

^{1}H NMR (CDCl$_3$, 200 MHz): δ 2.00 (s, 3H), 3.41 (dd, 1H), 3.71 (dd, 1H), 5.55 (m, 1H), 7.02 (m, 5H), 7.44 (m, 3H), 7.84 (d, 2H). FT-IR (KBr, cm^{-1}): 3265, 3083, 1678, 1641, 1556, 1244, 1104, 887, 824, 683.

2.4.3 | β-Acetamido-β-(3-nitrophenyl) propiophenone

^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.87 (s, 3H), 3.11 (d, 1H), 3.52 (d, 1H), 5.50 (s, 1H), 7.32 (m, 5H), 7.80 (d, 2H), 8.00 (d, 2H). FT-IR (KBr, cm^{-1}): 3290, 3023, 2245, 1681, 1649, 1544, 1440, 1216, 987, 752, 680, 546.

2.4.4 | β-Acetamido-β-(2-hydroxyphenyl) propiophenone

^{1}H NMR (CDCl$_3$, 200 MHz): δ 2.00 (s, 3H), 3.49 (d, 1H), 3.68 (d, 1H), 6.88 (s, 1H), 7.50–7.70 (m, 5H), 7.95 (d, 2H), 8.23 (d, 2H). FT-IR (KBr, cm^{-1}): 3286, 2843, 1679, 1639, 1595, 1502, 1446, 1341, 1288, 851, 748, 681, 587.

2.4.5 | β-Acetamido-β-(4-nitrophenyl) propiophenone

^{1}H NMR (CDCl$_3$, 200 MHz): δ 2.01 (s, 3H, CH$_3$), 3.38 (dd, 1H), 3.85 (dd, 1H), 5.60 (m, 1H), 7.20–7.55 (m,7H), 7.87 (d, 2H), 9.19 (br, 1H, NH). FT-IR (KBr, cm^{-1}): 3285, 1683, 1648, 1522, 1350, 1300, 752.

2.4.6 | β-Acetamido-β-(4-methoxyphenyl) propiophenone

^{1}H NMR (CDCl$_3$, 200 MHz): δ 2.09 (s, 3H), 2.48 (s, 3H), 3.51 (dd, 1H), 3.84 (dd, 1H), 5.59 (m, 1H), 7.39 (s, 1H), 7.54 (m, 5H), 7.97 (m, 4H). FT-IR (KBr, cm^{-1}): 3263, 3054, 1672, 1633, 1581, 1291, 1081, 878, 819.

2.4.7 | [(1*S*, 2*R*)-2-Methyl-1- (2-nitrophenyl) 3-oxo-3-diphenylpropyl] acetamide

^{1}H NMR (CDCl$_3$ + DMSO (d$_6$), 200 MHz): δ 0.87 (d, 3H), 1.56 (s, 3H), 3.99–4.14 (m, 1H), 5.67 (dd, 1H, -CHCO), 7.31–7.82 (m, 7H), 7.98–8.14 (d, 1H), 8.44 (d, 1H). FT-IR (KBr, cm^{-1}): 3263, 3058, 1978, 1646, 1528, 1454, 1355, 1295, 971, 711.

2.4.8 | N-1-[2-Methyl-3-oxo-1-phenylbutyl] acetamide

M. p. 125–128 °C, ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.23–7.31 (m, 5H), 7.12 (d, J = 7.8 Hz, 1H), 5.17 (dd, J = 5.8 and 9.1 Hz, 1H), 3.13 (dd, J = 6.9 and 14.2 Hz, 1H), 2.07 (d, J = 10.2 Hz, 6H), 1.15 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 213.3, 169.9, 140.5, 128.4, 127.3, 126.2, 55.4, 51.2, 29.6, 23.3, 15.3. FT-IR (KBr, cm^{-1}): 3291, 1717, 1653, 1554, 1377, 1305, 1132, 758.

2.4.9 | N-1-[2-Methyl-1-(4-methylphenyl)-3-oxobutyl]acetamide

M. p. 132–134 °C, ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.11 (s, 4H), 6.92 (d, J = 8.3 Hz, 1H), 5.12 (dd, J = 5.8 and 9.1 Hz,1H), 3.09 (dd, J = 6.6 and 13.1 Hz,1H), 2.32 (s, 3H), 2.17–1.94 (m, 6H), 1.15–1.08 (m, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 183.8, 169.5, 137.9, 137.1, 129.4, 126.8, 126.2, 55.2, 51.3, 29.6, 23.3, 21.0, 15.2. FT-IR (KBr, cm^{-1}): 3295, 2987, 1703, 1654, 1556, 1452, 1424, 1375, 1304, 1135, 725, 546.

2.4.10 | N-1-[2-Oxocyclohexyl]-1-phenylmethyl]acetamide

M.p. 219–222 °C, ^{1}H NMR (CDCl$_3$, 200 MHz): δ 8.50 (d, J = 8.3 Hz, 1H), 7.32–7.14 (m, 5H), 6.24 (s, 1H), 5.73 (d, J = 8.25 Hz, 1H), 2.71 (s, 1H), 2.59 (d, J = 5.4 Hz, 2H), 2.41 (d, J = 5.3 Hz, 2H), 2.25 (m, 4H), 2.1 (s, 3H). FT-IR (KBr, cm^{-1}): 3273, 1694, 1636, 1549, 1367, 1232, 694.

2.4.11 | N-1-[(4-Nitrophenyl)-1-[2-oxocyclohexyl]methyl]acetamide

M.p. 193–195 °C, ^{1}H NMR (CDCl$_3$, 200 MHz): δ 8.31–8.23 (m, 2H), 7.75–7.60 (m, 2H), 5.42 (s, 1H), 2.21–2.23 (m, 8H), 1.80 (s, 3H). FT-IR (KBr, cm^{-1}): 3380, 2943, 1656, 1610, 1525, 1341, 1224, 855, 692.

2.4.12 | N-1-[2-Methyl-3-oxo-1,3-diphenylpropyl)]acetamide

M. p. 141–143 °C, ^{1}H NMR (DMSO, 200 MHz): δ 8.41 (d, J = 7 Hz, 1H), 8.1 (s, 1H), 7.75–7.55 (m, 4H), 7.41–7.33 (m, 5H), 5.11 (s, 1H), 1.82 (s, 1H), 1.68 (s, 3H), 0.80 (s, 3H). FT-IR (KBr, cm^{-1}): 2977, 1671, 1657, 1546, 1457, 1369, 975, 707, 609.

anti-Isomer: white crystals, m.p. 165 °C, ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.36–1.39 (d, J = 7.1 Hz,3H), 2.11 (s, 3H), 4.0–4.2 (m, 1H), 5.35–5.42 (dd, J = 3.8 Hz,1H), 7.13–7.50 (m, 9H), 7.73–7.79 (d, J = 7.4 Hz, 2H).

syn-Isomer: white crystals. M.p. 123 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.19–1.22 (d, J = 6.9 Hz, 3H), 2.02 (s, 3H), 4.02–4.12 (m, 1H), 5.46–5.52 (t, J = 7.7 Hz, 1H), 5.95–6.04 (d, J = 5.9 Hz, 1H), 7.21–7.62 (m, 8H), 7.92–8.03 (d, J = 7.2 Hz, 2H).

2.4.13 | N-1-[2-Methyl-1-(2-nitrophenyl)-3-oxo-3-phenylpropyl]acetamide

M. p. 123–125 °C, ^{1}H NMR (DMSO, 200 MHz): δ 8.54–8.64 (m, 1H), 8.12–7.97 (m, 1H), 7.83–7.34 (m, 8H), 5.67 (dd, J = 7.7 and 13.4 Hz, 1H), 4.11–3.94 (m, 1H), 1.52 (s, 3H), 0.88 (d, J = 7 Hz, 3H). FT-IR (KBr, cm^{-1}): 3268, 3051, 1972, 1641, 1529, 1454, 1351, 1299, 978, 719.

anti-Isomer: off white crystals, m.p. 135–137 °C, ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.41–1.47 (d, J = 7.1 Hz, 3H), 2.11 (s, 3H), 4.11–4.42 (m, 1H), 5.78–5.84 (dd, J = 3.6 Hz, 1H), 7.25–7.97 (m, 10H). syn-Isomer: oily, ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.22–1.28 (d, 3H), 2.05 (s, 3H), 4.41–4.49 (m, 1H), 5.72–5.79 (t, 1H), 6.64–6.67 (d, 1H), 7.34–7.95 (m, 9H).

2.4.14 | N-[2-Methyl-1-(4-methyl-phenyl)-3-oxo-3-phenylpropyl]acetamide

anti-Isomer: white crystals, m.p. 170 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.32–1.37 (d, 3H), 2.11 (s, 3H), 2.23 (s, 3H), 4.02–4.12 (m, 1H), 5.31–5.39 (m, 1H), 7.03–7.07 (d, 2H), 7.13–7.17 (d, 2H), 7.33–7.58 (m, 4H), 7.74–7.81 (d, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.5, 20.8, 23.3, 44.3, 55.5, 126.4, 128.3, 128.5, 129.1, 133.5, 136.5, 136.7, 137.7, 169.9, 204.7. FT-IR (KBr, cm^{-1}): 3311, 2989, 1683, 1648, 1543, 1365, 1141, 972, 702. Anal. Calcd for $C_{19}H_{21}O_2N$: C, 77.25; H, 7.16; N, 4.74; Found: C, 77.22; H, 7.13; N, 4.49.

syn-Isomer: white crystals, m.p. 124 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.21–1.25 (d, J = 6.97 Hz, 3H), 1.98 (s, 3H), 2.27 (s, 3H), 4.02–4.15 (m, 1H), 5.40–5.48 (t, J = 7.62 Hz, 1H), 5.94–6.05 (d, J = 7.68 Hz, 1H), 7.05–7.13 (d, J = 7.82 Hz, 2H), 7.21–7.30 (d, J = 7.96 Hz, 2H), 7.41–7.57 (m, 3H), 7.87–7.91 (d, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 20.8, 23.1, 45.5, 54.8, 126.7, 128.2, 128.6, 129.2, 133.0, 136.4, 136.9, 137.4, 169.7, 201.8. FT-IR (KBr, cm^{-1}): 3242, 3055, 1679, 1637, 1552, 1374, 1291, 973, 712. Anal. Calcd for $C_{19}H_{21}O_2N$: C, 77.25; H, 7.16; N, 4.74; Found: C, 77.22; H, 6.96; N, 4.43.

3 | RESULTS AND DISCUSSION

3.1 | Characterization of Keggin $H_7SiV_3W_9O_{40}$ nanoparticles

FT-IR spectroscopy is a powerful method to investigate structure of heteropoly anions and can detect the hydrogen bond system. The four characteristic vibration modes of Keggin heteropolyacids appear at 1100–800 cm^{-1} which can be used for their identification.[31] Figure 1 shows the FT-IR spectrum of $H_7SiV_3W_9O_{40}$ with three bands at 965, 914 and 785 cm^{-1}, which are ascribed to $\nu_{as}(M–O_d)$, ν_{as} $(Si–O_a)$ and $\nu_{as}(M\text{-}O_c\text{-}M)$ modes, respectively. The $\nu_{as}(M–O_b–M)$ bands are too weak and overlapped with $\nu_{as}(M\text{-}O_c\text{-}M)$. These characteristic peaks indicated that this vanadium-substituted heteropoly acid possesses a Keggin structure.[32] The vibrations around 1620 and 3400 cm^{-1}can be attributed to the bending vibration of H–O–H and stretching vibration of O-H bonds, respectively.[32]

To further investigate the structure and phase of Keggin $H_7SiV_3W_9O_{40}$ nanoparticles, the powder X-ray diffraction (XRD) was measured, as shown in Figure 2. The XRD pattern confirmed four groups of peaks in the

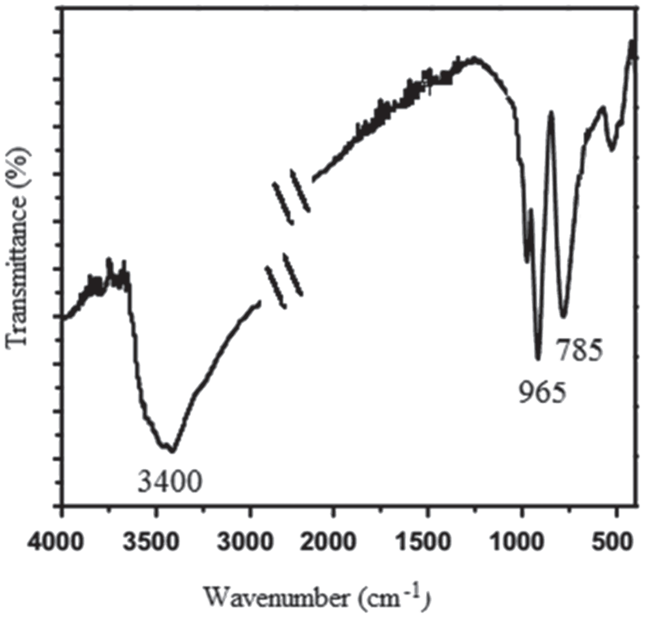


FIGURE 1 FT-IR spectrum of Keggin $H_7SiV_3W_9O_{40}$ nanoparticles

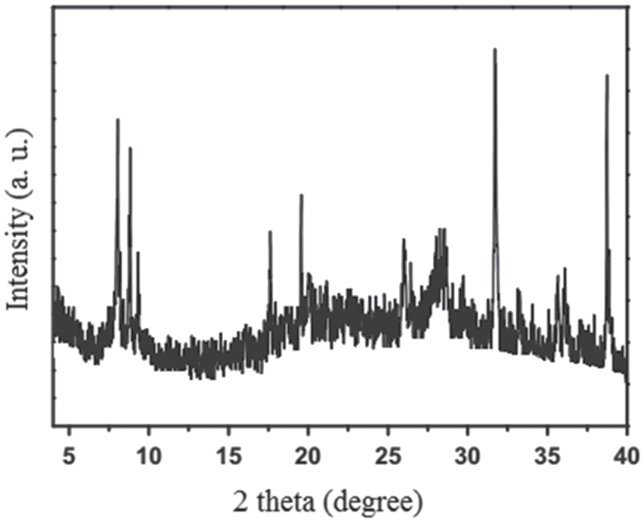


FIGURE 2 XRD pattern of Keggin $H_7SiV_3W_9O_{40}$ nanoparticles

ranges of 2θ, 7–10°, 16–20°, 25–35°, and 35–40°, which are in agreement with the characteristic diffractions of Keggin structure.[33] This result indicated that the nanomaterial had a high crystallinity. Size and morphology of nanoparticles were further studied with FESEM. Figure 3 describes that the Keggin $H_7SiV_3W_9O_{40}$ nanoparticles were semi-spherical in shape in the nano range with a uniform size and good dispersibility.

3.2 | Catalytic tests

TABLE 1 Comparing catalytic activity of some heteropolyacids in the synthesis of β-acetamido-β-(4-chlorophenyl)propiophenone

Heteropolyacid	Structure	Catalyst (mol%)	Time (hr)	Yield (%)
$H_7SiV_3W_9O_{40}$	V substituted Keggin	10	0.5	98
$H_5SiVW_9Mo_2O_{40}$	mixed metal Keggin	10	1	75
$H_4SiW_{12}O_{40}$	Keggin	10	0.5	95
$H_4SiW_9Mo_3O_{40}$	mixed metal lacunary Keggin	10	1	67
$H_4SiW_{11}MoO_{40}$	Mo substituted mixed metal Keggin	10	0.5	82

4-chlorobenzaldehyde (1 mmol), acetyl chloride (2 mmol), acetophenone (1 mmol) in acetonitrle (4 ml) were treated with a desired amount of heteropolyacid at 80 °C. Progress of the reaction was monitored by TLC.

In the first attempt we tried to compare reactivity of a range of mixed metal substituted Keggin and lacunary heteropolyacids. Table 1 compares reactivity of some Keggin-type Si and V-substituted single or mixed metal heteropolyacids in the four component condensation of 4-chlorobenzaldehyde, acetophenone, and acetyl chloride in CH_3CN. Obviously, tungsten substituted heteropolyacids are more effective catalysts than Mo-included ones. Moreover, $H_4SiW_{12}O_{40}$ behaved almost similar to $H_7SiV_3W_9O_{40}$. Different observed reactivity patterns would be explained considering various factors which affect Bronsted and Lewis acidity of heteropolyacids. Strong Bronsted acidity of these pseudo liquid phase super-acidic materials originates from good mobility of the dissociated protons on the surface of crystal structure. These protons include both un-hydrated protons localized at the peripheral oxygen atoms and combined hydrogens with the heteropolyanion.[34–36] Therefore, silicon as the heteroatom and transition metals such as vanadium and molybdenum strongly affect crystal structure and mobility of the mentioned protons. Another important aspect of this study refers to comparison of the rarely studied and less effective quaternary heteropolyacid ($H_5SiW_9Mo_2VO_{40}$) with the ternary counterparts. In addition, less catalytic activity of $H_4SiW_9Mo_3O_{40}$ and $H_5SiW_9Mo_2VO_{40}$ would be explained considering coordination of CH_3CN to the Lewis acid sites of Mo containing heteropolyacids, which may reduce Lewis/Bronstead acidity and, therefore, catalytic activity of these compounds toward the condensation reaction.

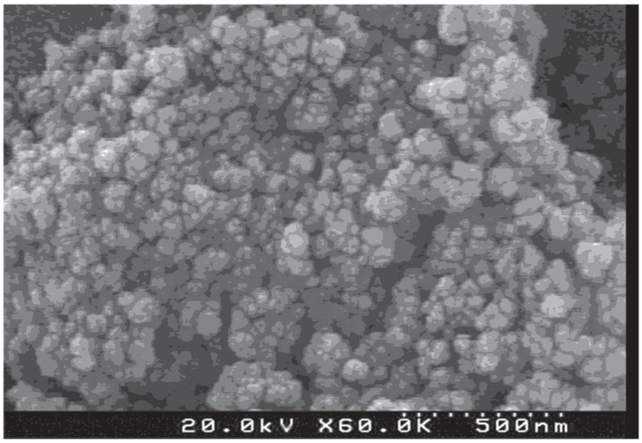


FIGURE 3 FESEM image and size distribution of Keggin $H_7SiV_3W_9O_{40}$ nanoparticles

Then, effect of the presence of catalyst was investigated in the four-component coupling of benzaldehyde, acetophenone, and acetyl chloride in acetonitrile. Findings revealed that Keggin $H_7SiV_3W_9O_{40}$ nanoparticles behaved as an active catalyst, due to its bi-functional nature originating from their strong acidic protons and presence of vanadium (V) transition metal ion, as effective electron acceptor resource.[37] The four-component coupling condensation of 4-chlorobenzaldehyde, acetophenone, and acetyl chloride was performed in acetonitrile in the absence of catalyst. Findings revealed that the reaction could not be productive, and no reaction was happened even after prolonged reaction time (5 hr), indicating that this is a heteropolyacid catalyzed reaction (Table 2). According to the reactivity pattern observed for various heteropolyoxometalates in Table 1, $H_7SiV_3W_9O_{40}$ was selected as the best catalyst and efficiency of the present method was evaluated considering some influencing parameters such as catalyst amount and temperature. Table 2 describes effect of different mol% of $H_7SiV_3W_9O_{40}$. The best result was achieved with 10 mol% of this catalyst. 98% of product was attained with 4-chlorobenzaldehyde after 0.5 hr and higher mol% of catalyst led to a decreased yield.

Table 3 shows effect of temperature on the reaction progress in the presence of 2.5 mol% $H_7SiV_3W_9O_{40}$. As is anticipated, yield% was enhanced with the reaction temperature in the range of 25–80 °C. Therefore, the best temperature was adjusted under refluxing of acetonitril for all subsequent reactions.

Then, effect of various solvents was compared with the solvent-free case (Table 4). It was found that the reaction was almost completed after 30 min in the absence of solvent and indeed CH_3CN acted as both solvent and primary reagent in the four component condensation reaction.

Effect of the nitrilating agent was also demonstrated in this catalytic system. Therefore, the two nitrilatings agents of CH_3CN and PhCN were compared in the presence of 2.5 mol% of $H_7SiV_3W_9O_{40}$ (Scheme 2). Obviously, acetonitrile was more efficient than PhCN and provided 76% of β-acetamido-β-(4-chlorophenyl)propiophenone after 3 hr; while, phenyl cyanide afforded only 28% yield after 6 hr.

TABLE 2 Synthesis of β-acetamido-β-(4-chlorophenyl) propiophenone in the presence of different catalytic amounts of $H_7SiV_3W_9O_{40}$ in refluxing acetonitrile

Catalyst	Catalyst (mol%)	Time (hr)	Yield (%)
-	-	5	-
$H_7SiV_3W_9O_{40}$	0.5	6	53
$H_7SiV_3W_9O_{40}$	2.5	3	76
$H_7SiV_3W_9O_{40}$	5	2	78
$H_7SiV_3W_9O_{40}$	10	0.5	98
$H_7SiV_3W_9O_{40}$	15	0.5	89

Reaction condition is described below Table 1.

TABLE 3 Synthesis of β-acetamido- β-(4-chlorophenyl) propiophenone in acetonitrile at different temperatures

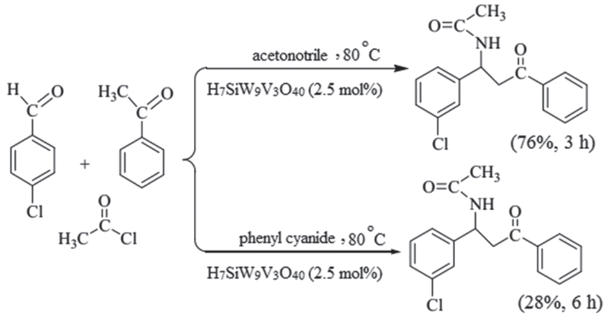
Catalyst	Time (hr)	Yield (%)	Temperature (° C)
$H_7SiV_3W_9O_{40}$ (2.5 mol%)	3	76	80
$H_7SiV_3W_9O_{40}$ (2.5 mol%)	5	48	50
$H_7SiV_3W_9O_{40}$ (2.5 mol%)	6	33	25

Reaction condition is described below Table 1.

TABLE 4 Effect of some solvents on the progress of the condensation reaction

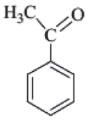
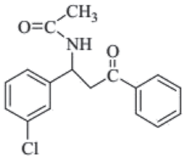
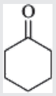
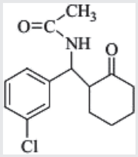
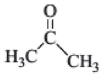
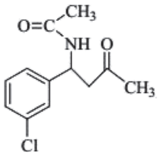
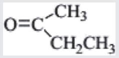
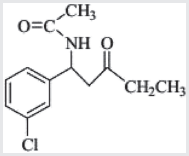
Conditions	Time (hr)	Temperature (°C)	Yield (%)
Solvent-free	0.5	80	98
CH_2Cl_2	1	reflux	<15
H_2O	1	reflux	30
MeOH	1	reflux	55

Reaction condition is described below Table 1. 10 mol% $H_7SiV_3W_9O_{40}$ was used in all cases.



SCHEME 2 Effect of nitrilating agent on the synthesis of β-acetamido-β-(4-chlorophenyl)propiophenone.

TABLE 5 Synthesis of β-acetamido-β-(4-chlorophenyl) ketones

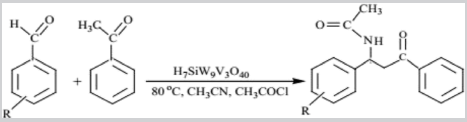
Carbonyl compound	Product	Time (h)	Yield (%)
		0.5	98
		3	27
		5	18
		5	24

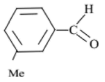
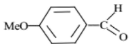
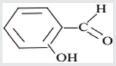
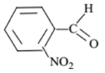
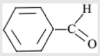
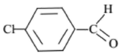
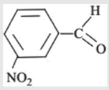
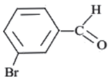
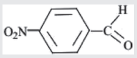
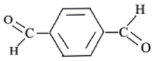
Reaction condition is described below Table 1.

In another attempt to compare reactivity of acetophenone with other carbonyl compounds, acetone, cyclohexanone, and ethyl methyl ketone were substituted with the former.[18,20] Interestingly, in agreement with the literature acetophenone was the best for the condensation with 4-chlorobenzaldehyde and acetyl chloride in acetonitrle (Table 5).

Effect of different electron releasing/withdrawing groups on the phenyl ring of aldehyde moiety was investigated to explore generality and productivity of $H_7SiV_3W_9O_{40}$ and the corresponding results are gathered in Table 6. Thus, applicability and merit of this protocol was ascertained by performing a range of aromatic aldehydes under optimized conditions. Nearly, in all cases, aromatic aldehydes with substituents carrying either electron-withdrawing or electron-donating groups reacted successfully and gave smoothly the expected products in good to excellent yields. However, in some cases it seems that aromatic aldehydes bearing electron-withdrawing groups reacted faster than those involving electron-donating groups.

TABLE 6 Synthesis of different β-acetamido-β-(aryl) propiophenones

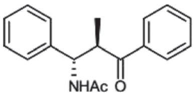
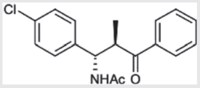
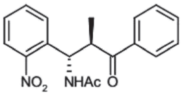
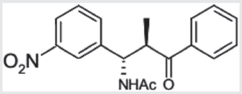
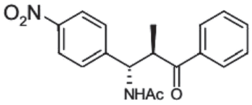
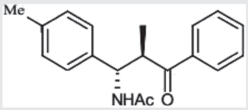
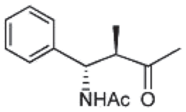
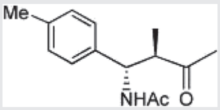
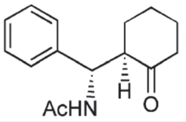
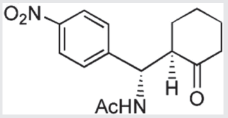


Aldehyde	Time (h)	Yield (%)	M.P. (°C)	Ref.
	1.5	65	80–82	[18]
	1.5	75	108–109	[38]
	1.5	87	114–116	[39]
	2	75	129–131	[40]
	0.5	85	186–188	[41]
	0.6	90	103–105	[40]
	0.5	98	144–146	[40]
	0.5	97	109–111	[40]
	0.6	93	101–103	[42]
	0.5	98	148–150	[41]
	0.6	95	>300	[42]

Aromatic aldehyde (1 mmol), acetyl chloride (2 mmol), acetophenone (1 mmol) in acetonitrle (4 ml) was treated with 10 mol% of $H_7SiV_3W_9O_{40}$ at 80 °C. Progress of the reaction was monitored by TLC. Yields refer to the isolated products.

To demonstrate the versatility of this catalyst, it has been shown that aromatic aldehydes can react with propiophenone and other R-substituted ketones to afford the β-acetamido ketones in a diastereoselective manner. Thus, propiophenone as an α-substituted enolisable ketone was treated with some aromatic aldehydes under the optimum conditions (Table 7). It was found that two

TABLE 7 Reaction of some substituted ketones with some aromatic aldehydes

Entry	β-acetamido ketone	Syn: anti[a]	Yield (%)	Time (h)	M.P. (°C)
1		38:62	88	1	140–141
2		36:64	93	1	151–152
3		39:61	95	0.7	120–122
4		35:65	97	0.5	
5		31:69	92	0.7	133–134
6		30:70	84	0.7	152–154
7		27:73	87	2.5	126–128
8		33:67	81	2.5	135–137
9		36:64	65	2	219–222
10		32:68	69	2	193–195

[a] Ratio of syn:anti isomer was defined based on coupling constants of methine proton with ^1H NMR. 10 mol% of $H_7SiV_3W_9O_{40}$ was used in all cases. Yields refer to the isolated products.

TABLE 8 Comparison of the catalytic efficiency of $H_7SiV_3W_9O_{40}$ with some reported catalysts in the synthesis of β-acetamido- β-(4-chlorophenyl)propiophenone

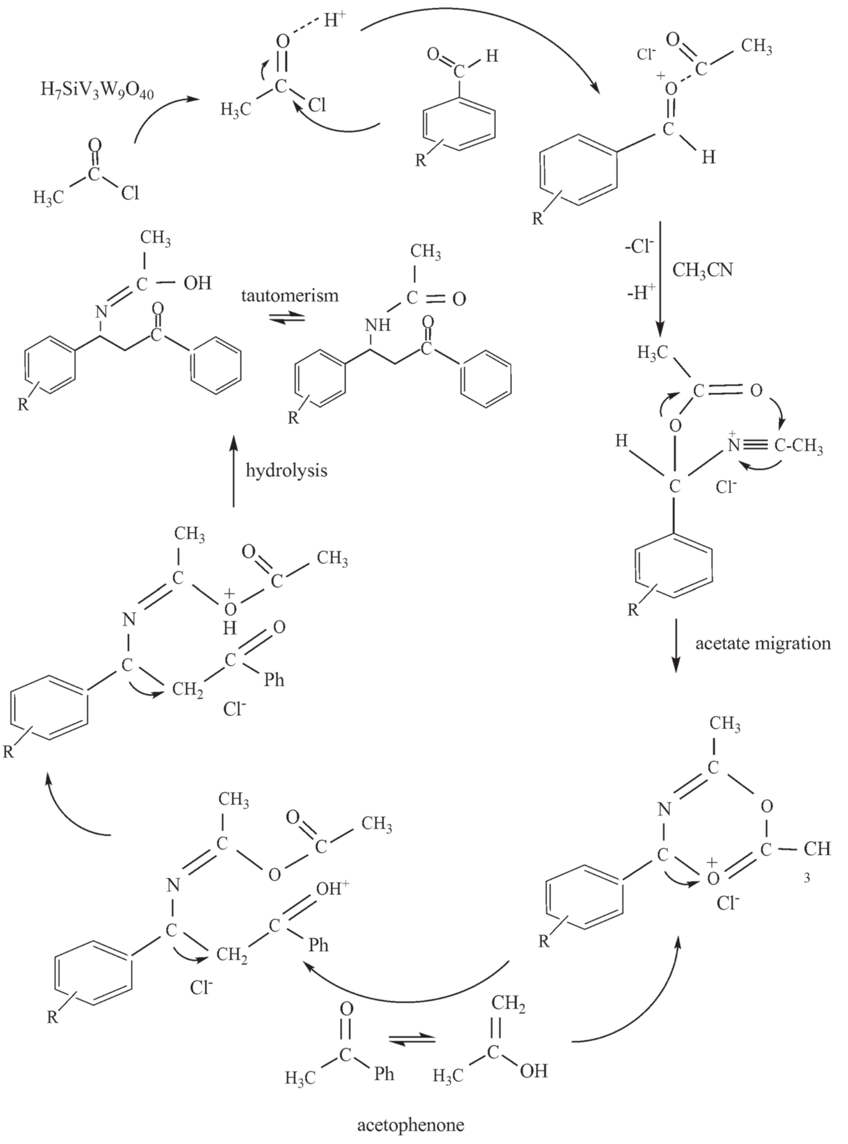
Catalyst	Mol%	Time (hr)	Yield %	Ref.
$H_7SiV_3W_9O_{40}$	10	0.5	98	This work
$ZrOCl_2.8H_2O$	15	12	83	[43]
Zn $(OTf)_2$	10	30	60	[44]
$BF_3.OEt_2$	100	30	78	[44]
$CuCl_2$	100	30	79	[44]

Reaction condition is described below Table 1.

diastereomeric products can be formed in definite proportions, in which the anti isomer was the major product. Noteworthy, the ratio of syn: anti isomers can be evaluated from coupling constant of methine proton (CHCO) by means of 1H NMR. Furthermore, the reaction of some benzaldehyde derivatives with ethyl methyl ketone and cyclohexanone was also investigated. These two ketones were also effective and the anti-diastereomers were obtained as the major products (Table 7, entries 7–10).

Table 8 compares catalytic efficacy and superiority of $H_7SiV_3W_9O_{40}$ with some reported methodologies by consideration of yield%, reaction parameters, catalyst amount, and reaction time. For this purpose, reaction of 4-chlorobenzaldehyde, acetophenone and acetyl chloride was monitored in acetonitril as a model reaction. Clearly, $H_7SiV_3W_9O_{40}$ was among the best catalysts in this series.

Finally, a reaction pathway is disclosed in Scheme 3. The mechanism would be involved acylation of the aromatic aldehyde with acetyl chloride and production of an α-chloroacetate as intermediate (I). Then, this intermediate reacts with acetonitrile to produce the corresponding α-acetoxy amide, which can combine with the enolate form of acetophenone to give a six-membered



SCHEME 3 A plausible reaction pathway for the condensation of aldehyde, acetophenone, acetyl chloride, and acetonitrile.

imidate ester and, thereafter, the amide product. Protonation of aldehyde also can activate the carbony group for the nucleophillic attack.[20]

4 | CONCLUSIONS

In conclusion, the present report introduces catalytic efficacy of $H_7SiV_3W_9O_{40}$ as a new convenient and effective mediator for the preparation of various β-acetamido ketones. The prepared catalyst is characterized by standard techniques such as XRD, SEM, and FT-IR to verify that the Keggin structure of nanocatalyst is formed. A series of Keggin Si and V-substituted heteropolyacids are compared and show a better catalytic activity for $H_7SiV_3W_9O_{40}$ and $H_4SiW_{12}O_{40}$ than the lacunary and mixed metal Keggin $H_4SiW_9Mo_3O_{40}$ and $H_5SiW_9Mo_2VO_{40}$. Another important aspect of this study refers to comparison of the rarely studied and less effective quaternary heteropolyacid ($H_5SiW_9Mo_2VO_{40}$) with the ternary counterparts. Moreover, less proficiency is attained for PhCN compared to acetonitrile and condensation of propiophenone leads to the anti isomer as the major diastereomer.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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