Scientific paper

Nano-$Rb_2HPW_{12}O_{40}$ as an Efficient and Novel Catalyst for One-Pot Synthesis of β-Amino Ketones

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Abstract

The aim of the research described was to study $Rb_2HPW_{12}O_{40}$ as a green and heterogeneous catalyst for the Mannich reaction. One-pot multi-component condensation of an aldehyde, an amine and a ketone at ambient temperature affords the corresponding β-amino ketones using novel nano-sized $Rb_2HPW_{12}O_{40}$. Simple purification, short reaction time and high yield are some of the advantages of this reaction. Also, the catalyst can be readily isolated. The nano catalyst $Rb_2HPW_{12}O_{40}$ has been characterized by Fourier transform infrared spectroscopy, X-ray powder diffraction and scanning electron microscopy.

Keywords: Mannich reaction, β-amino ketones, hetero poly acid, one-pot reaction

1. Introduction

Mannich reactions are one of the most important carbon-carbon bond forming reactions in synthetic organic chemistry[1,2] because they provide synthetically and biologically important β-amino ketones that are important intermediates. These products can be used for the synthesis of amino alcohols, peptides and lactams, amino acids and various natural products.[3] β-Amino ketones are generally obtained by the condensation of a carbonyl compound with an aldehyde and an amine using various Lewis or Brønsted acid catalysts, such as $HClO_4$–SiO_2,[4] CAN,[5] $CeCl_3 \cdot 7H_2O$,[6] $BiCl_3$,[7] $AuCl_3$–PPh_3,[8] nano-TiO_2,[9] ionic liquids,[10,11] sulphamic acid,[12,13] $Fe(Cp)_2PF_6$,[14] Cu-nanoparticles,[15] $[Re(PFO)_3]$,[16] PEG–SO_3H[17] and ZSM-5-SO_3H,[18] etc.

However, many of these methods have some drawbacks, such as low yields, long reaction times, harsh reaction conditions, toxicity, and difficulties in work-up as well as the problem of catalysts moisture sensitivity. Therefore, there is a further need to find appropriate mild and efficient methods for the preparation of β-amino ketones.

In the recent years, heterogeneous solid catalysts have been used in various organic reactions, as they possess a number of advantages.[19,20] Among the heterogeneous solid acids, heteropoly acids (HPAs) due to their stronger acidity, have been extensively studied as acid catalysts for many reactions, such as the synthesis of trioxanes,[21] alkylation of benzene with olefins,[22] and gas-phase selective oxidation of various organic substrates. Heteropoly acids have many advantages over other acid catalysts, including being non-corrosive, environmentally benign and possessing superacidic properties.

Thus, in this research we have introduced a novel nano-sized $Rb_2HPW_{12}O_{40}$ of the Keggin series which is stable and efficient heterogeneous catalyst in organic synthesis, for example for the described one-pot, three-component reaction of an aldehyde, an amine and a ketone for the preparation of β-amino carbonyl compounds.

2. Experimental

2. 1. General

Chemicals were purchased from Merck and Fluka chemical companies. IR spectra were run on a Shimadzu model 8300 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker Avance DPX-250. The purity of the products and the progress of the reactions were determined by TLC on silica-gel polygram SILG/UV254 plates. Elemental analysis was performed on a Thermo Finnigan (San Jose, CA, USA) Flash EA micro analyzer.

2. 2. Preparation of $Rb_2HPW_{12}O_{40}$

To a solution of $H_3PW_{12}O_{40}$ (1 eq, 5 mmol) in H_2O (20 mL) was added dropwise $RbCl_2$ (2 eq, 10 mmol) in H_2O (20 mL) during stirring for 20 min at room temperature. After completion of the addition, the mixture was stirred for additional 2 h. Finally, the precipitate was filtered, washed with distilled water, and dried to afford nano-sized $Rb_2HPW_{12}O_{40}$.

2. 3. General Procedure for the Synthesis of β-Amino Ketones

To the mixture of the aromatic aldehyde (2 mmol), aromatic amines (2 mmol), and cyclohexanone (2.2 mmol, 0.21 g) was added nano-$Rb_2HPW_{12}O_{40}$ (0.2 g). The reaction mixture was stirred at room temperature for the appropriate time (Table 2). After completion of the reaction, the mixture was diluted with hot ethanol (15 mL) and the catalyst was separated by filtration. Evaporation of the solvent under reduced pressure gave the product.

3. Results and Discussion

As it was already mentioned, the nano-sized $Rb_2HPW_{12}O_{40}$ is a new, highly efficient Lewis acid catalyst which can be used for the Mannich reaction.

3. 1. Catalyst Characterization

$Rb_2HPW_{12}O_{40}$ was prepared by using the co-precipitation technique. In order to evaluate the incorporation of $RbCl_2$ and $H_3PW_{12}O_{40}$, the prepared nano-sized $Rb_2HPW_{12}O_{40}$ was characterized by powder X-ray diffraction (XRD), FT-IR spectra and SEM technique. Studies have shown that the absorption bands of Kegging structural type appear in the 700–1000 cm^{-1}. The characteristic absorption bands in the catalyst spectrum appeared at 1080, 985, 890, and 810 cm^{-1} that are assigned to $P–O_i$ (i: internal), $W = O_t$ (t: terminal), interoctahedral $W–O_e–W$ (e: edge-sharing), and $W–O_c–W$ (c: corner-sharing) bands, respectively. The appearance of these vibrational bands in the catalyst confirms Keggin structure of $Rb_2HPW_{12}O_{40}$. In addition, the replacement of the proton with rubidium ions reduced the intensity of the absorption band at 1620 cm^{-1}. These results support the successful preparation of the catalyst.

The XRD spectrum of the $Rb_2HPW_{12}O_{40}$ is shown in Fig. 2. The patterns show the presence of a broad peak around $2\theta = 22°$. Also, the crystal size of the nano-$Rb_2HPW_{12}O_{40}$ was determined from the X-ray patterns using the Debye–Scherrer formula given as $t = 0.9\lambda/B_{1/2}\cos\theta$, where t is the average crystal size, λ the X-ray wavelength used (1.54 Å), $B_{1/2}$ the angular line width at a half maximum intensity and θ the Bragg's angle. The average crystal size of the nano-$Rb_2HPW_{12}O_{40}$ for $2\theta = 26.24°$ is calculated to be around 31.94 nm.

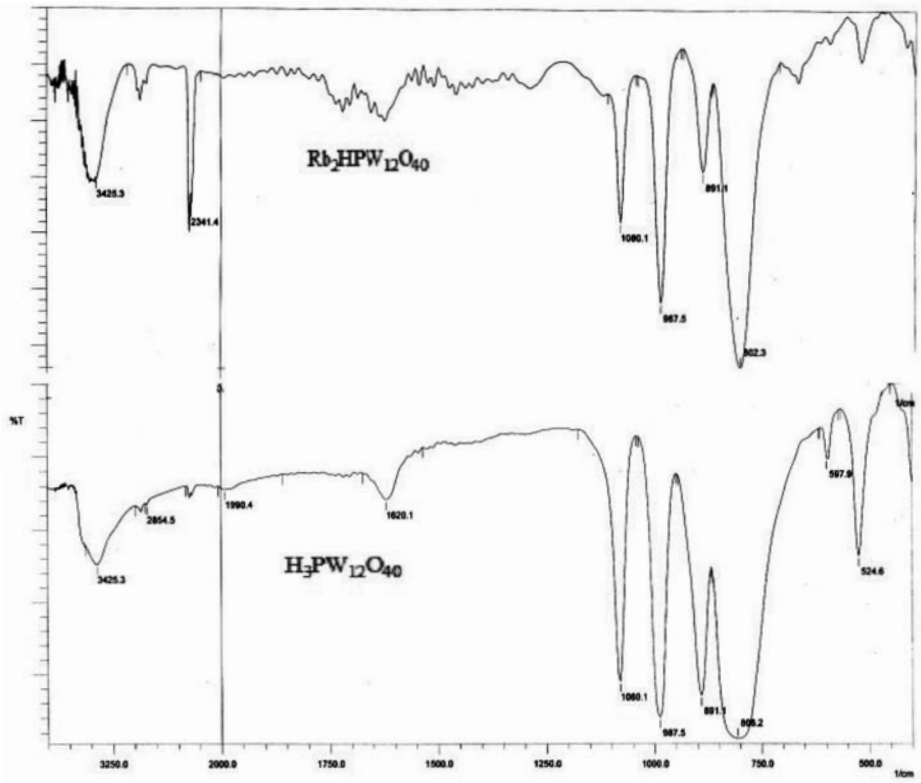


Fig. 1. FT-IR spectrum of $H_3PW_{12}O_{40}$ and $Rb_2HPW_{12}O_{40}$

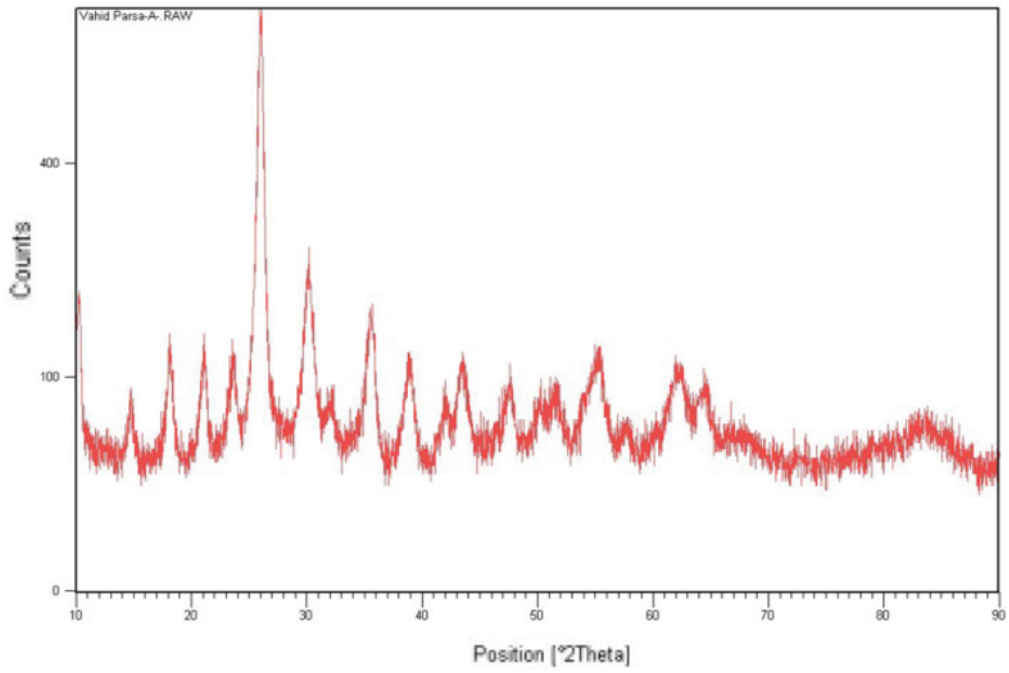


Fig. 2. The XRD of nano-$Rb_2HPW_{12}O_{40}$

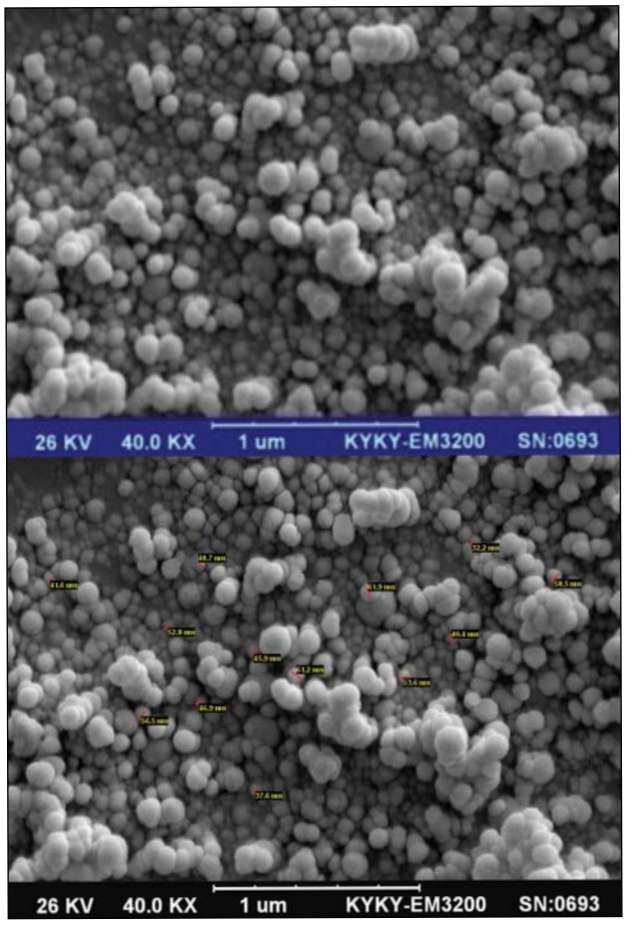


Fig. 3. The SEM image of nano-$Rb_2HPW_{12}O_{40}$

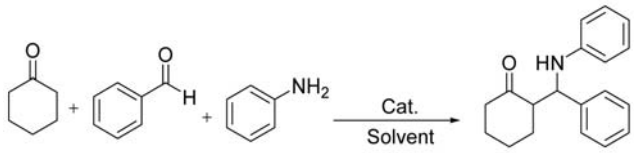
Scanning electron microscopy (SEM) image of the nano-$Rb_2HPW_{12}O_{40}$ catalyst is shown in Fig. 3. SEM analysis of the catalyst reveals the spherical nano-$Rb_2HPW_{12}O_{40}$ with an average size 30–60 nm.

3. 2. Catalytic Studies

In this work, nano-$Rb_2HPW_{12}O_{40}$ has been successfully used as the catalyst for one-pot reaction of substituted anilines and benzaldehydes with cyclohexanone. In order to optimize the reaction conditions, initially we chose the reaction of aniline (2 mmol, 0.18 mL) and benzaldehyde (2 mmol, 0.2 mL) with cyclohexanone (2.2 mmol, 0.23 mL) as a reaction model (Scheme 1). Reaction was screened in different solvents such as CH_3CN, CH_2Cl_2, CH_3Cl and EtOH as well as under solvent-free conditions at room temperature. The results are summarized in Table 1. As shown in Table 1, EtOH provided excellent yield in short time, whereas CH_3CN, CH_3Cl and CH_2Cl_2 afforded lower yields.

Furthermore, the reaction was carried out in the presence of various amounts of catalyst (Table 1, entries 5–8). The condensation reaction did not proceed in the absence of the catalyst. However, in the presence of nano-sized $Rb_2HPW_{12}O_{40}$ the reaction is occurring towards the desired product. As the results show, the best outcome was obtained with the use of 0.1 g $Rb_2HPW_{12}O_{40}$ in ethanol at room temperature. Lower amount of the catalyst decreased the yield and increase of the anount of nano-$Rb_2HPW_{12}O_{40}$ did not improve remarkably the results of the reaction.

Table 1. Optimization of the reaction conditions[a]

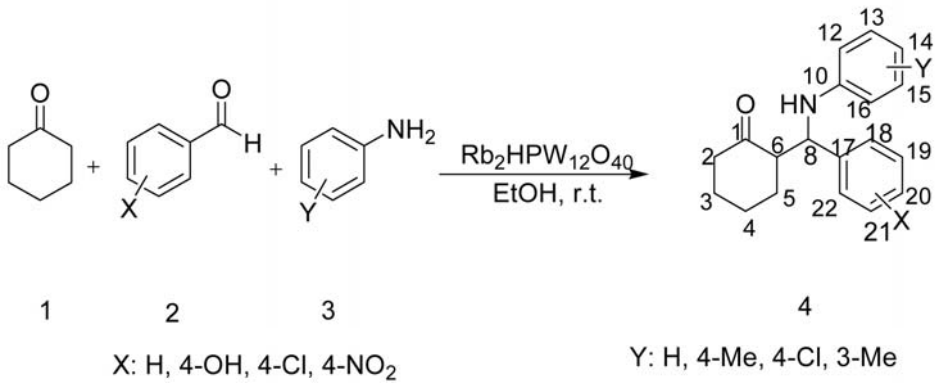


Entry	Solvent	Catalyst (g)	Time [h]	Yield [%]
1	CH_3CN	$Rb_2HPW_{12}O_{40}$ (0.1)	1:10	75
2	CH_2Cl_2	$Rb_2HPW_{12}O_{40}$ (0.1)	1:15	70
3	CH_3Cl	$Rb_2HPW_{12}O_{40}$ (0.1)	1	80
4	solvent-free	$Rb_2HPW_{12}O_{40}$ (0.1)	0.25	90
5	EtOH	$Rb_2HPW_{12}O_{40}$ (0.1)	0.25	97
6	EtOH	$Rb_2HPW_{12}O_{40}$ (0.05)	0.42	95
7	EtOH	$Rb_2HPW_{12}O_{40}$ (0.025)	0.84	90
8	EtOH	$Rb_2HPW_{12}O_{40}$ (0.15)	0.23	97

[a] Reaction conditions: solvent (1 mL), room temperature, benzaldehyde (1 mmol), aniline (1 mmol), cyclohexanone (1.1 mmol).

In order to evaluate the generality of this new protocol, the reactions of different aromatic aldehydes, anilines and cyclohexanone were carried out at room temperature in ethanol as the solvent. The results are summarized in Table 2. In all cases β-amino ketone derivatives were obtained in good yields. Under the optimized reaction conditions the electron-donating groups were observed to accelerate the reaction compared to electron-withdrawing groups (Scheme 1).

The *syn*/*anti* ratio was determined by ^{1}H NMR spectroscopy and by comparing our data with that of known compounds reported in the literature,[23,24] by using the coupling constants of the vicinal protons adjacent to C=O and NH. In general, the coupling constant of the *anti* isomer is higher than that of the *syn* isomer. Data showed that the Mannich reaction exhibited excellent *anti* selectivity in the presence of nano-$Rb_2HPW_{12}O_{40}$ except for the reactions of 4-nitrobenzaldehyde with *m*-toluidin, *p*-toluidin and 4-chloroanilin.



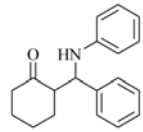
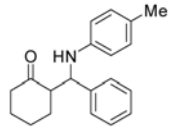
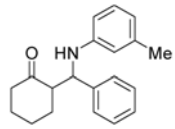
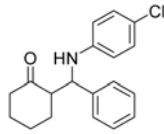
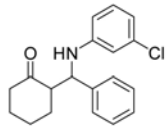
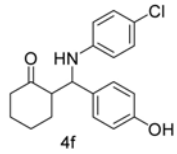
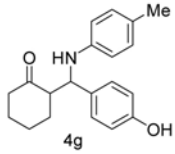
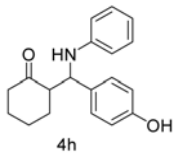
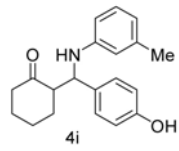
Scheme 1

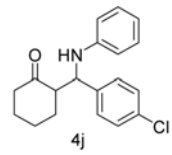
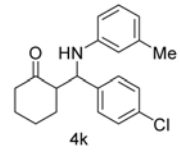
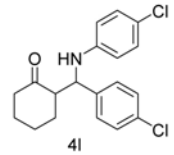
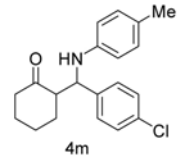
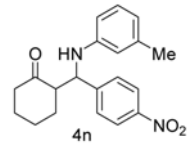
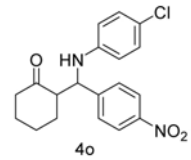
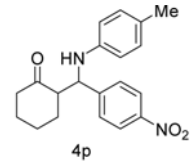
3. 2. 1. Physical and spectroscopic data of selected compounds

2-(Phenyl(phenylamino)methyl)cyclohexanone (Table 2, **4a**): Yield: 97%, white solid, *syn*/*anti*:1/99, FT-IR: ν_{max} (KBr): 3329 (NH stretch), 1701 (C=O stretch) cm^{-1}, ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.55–1.92 (m, 6H, $3CH_2$), 2.25–2.44 (m, 2H, 2-CH), 2.7–2.8 (m, 1H, 6-CH), 4.67 (d, *J* = 7.0 Hz, 0.99H, 8-CH), 4.81 (d, *J* = 4.38 Hz, 0.01H, 8-CH), 7.07–7.21 (m, 5H, CH Ar), 7.23–7.55 (m, 5H, CH Ar) ppm; ^{13}C NMR ($CDCl_3$): δ 23.67, 27.92,31.31, 41.79 (2-C), 57.5 (8-C), 57.97 (6-C), 113.63, 117.51, 127.18, 128.49, 129.08, 130.41, 141.76, 141.29, 212.83 (1-C) ppm. Anal. Calcd for $C_{19}H_{21}NO$ (279.36): C, 81.68; H, 7.58; N, 5.01. Found: C, 81.49; H, 7.69; N, 4.95.

2-((*p*-Toluidino)(phenyl)methyl)cyclohexanone (Table 2, **4b**): Yield: 92%, white solid, *syn*/*anti*: 7/93, FT-IR: ν_{max} (KBr): 3332 (NH stretch), 1708 (C=O stretch) cm^{-1}, ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.62–1.90 (m, 6H, $3CH_2$), 2.23–2.41 (m, 2H, 2-CH_2), 2.45 (s, 3H, CH_3), 2.7–2.8 (m, 1H, 6-CH), 4.63 (d, *J* = 5.0 Hz, 0.93H, 8-CH), 4.79 (d, *J* = 3.5 Hz, 0.07 H, 8-CH), 6.40–6.53 (m, 2H, 12,16-CH Ar),

Table 2: Synthesis of β-amino carbonyl derivatives with nano-$Rb_2HPW_{12}O_{40}$

Entry	X	Y	Product	Time (min)	Yield (%)	m.p. (ref.)
1	H	H	 4a	15	97	126–128 [18]
2	H	4-Me	 4b	90	92	119–120 [25]
3	H	3-Me	 4c	10	93	125–127 [27]
4	H	4-Cl	 4d	10	94	134–136 [18]
5	H	3-Cl	 4e	50	91	129–131 [18]
6	4-OH	4-Cl	 4f	105	90	195–197
7	4-OH	4-Me	 4g	45	89	200–201
8	4-OH	H	 4h	105	88	177–179
9	4-OH	3-Me	 4i	105	90	181–183

Entry	X	Y	Product	Time (min)	Yield (%)	m.p. (ref.)
10	4-Cl	H	 4j	50	95	133–135 [28]
11	4-Cl	3-Me	 4k	360	96	125–127 [29]
12	4-Cl	4-Cl	 4l	90	90	135–137 [30]
13	4-Cl	4-Me	 4m	60	93	122–124 [4]
14	4-NO_2	3-Me	 4n	30	70	165–167 [29]
15	4-NO_2	4-Cl	 4o	75	75	165–167 [26]
16	4-NO_2	4-Me	 4p	100	71	165–167 [30]

6.82–6.97 (m, 2H, 13,15-CH Ar), 7.18–7.45 (m, 5H, CH Ar) ppm. Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77. Found: C, 81.33; H, 8.13; N, 4.61.

2-((*m*-Toluidino)(phenyl)methyl)cyclohexanone (Table 2, entry **4c**): Yield: 93%, Cream solid; *syn*/*anti*: 0/100, FT-IR: ν_{max} (KBr): 3382 (NH stretch), 1693 (C=O stretch) cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.61–2.08 (m, 6H, $3CH_2$), 2.21 (s, 3H, CH_3), 2.23–2.48 (m, 2H, 2-CH_2), 2.79–2.86 (m, 1H, 6-CH), 4.84 (d, *J* = 6.0 Hz, 1H, 8-CH), 6.36–6.52 (m, 3H, CH Ar), 6.97–7.02 (m, 1H, 13-CH Ar), 7.21–7.40 (m, 5H, CH Ar) ppm. Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77. Found: C, 80.98; H, 8.19; N, 4.52. MS (EI) *m/z* 293 (M^+).

2-((4-Chlorophenylamino)(phenyl)methyl)cyclohexanone (Table 2, **4d**): Yield: 94%, White solid; *syn*/*anti*: 0/100, FT-IR: ν_{max} (KBr): 3379 (NH stretch), 1705 (C=O stretch) cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): 1.71–1.96 (m, 6H, $3CH_2$), 2.36–2.40 (m, 1H, 2-CH_2), 2.54–2.58 (m, 1H, 2-CH_2), 2.84–2.88 (m, 1H, 6-CH), 3.86 (br, NH), 4.23 (m, 1H, 8-CH), 6.93 (d, *J* = 8.4 Hz, 2H, 12,16-CH Ar), 7.16–7.17 (m, 5H, CH Ar), 7.36 (d, *J* = 8.4 Hz, 2H, 13,15-C H Ar) ppm. Anal. Calcd for $C_{19}H_{20}NOCl$: C, 72.72; H, 6.42; N, 4.46. Found: C, 73.98; H, 6.74; N, 4.01.

2-((3-Chlorophenylamino)(phenyl)methyl)cyclohexanone (Table 2, **4e**): Yield: 91%, Cream solid; *syn*/*anti*: 0/100, FT-IR: ν_{max} (KBr): 3340 (NH stretch), 1701 (C=O

stretch) cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): 1.69–2.01 (m, 6H, $3CH_2$), 2.31–2.47 (m, 2H, 2-CH_2), 2.76–2.82 (m, 1H, 6-CH_2), 4.58 (d, *J* = 6.6 Hz, 1H, 8-CH), 4.92 (br, NH), 6.41–6.45 (m, 1H, 12-CH Ar), 6.53–6.56 (m, 1H, 16-CH Ar), 6.53–6.56 (m, 1H, 14-CH Ar), 6.59–6.63 (m, 1H, 13-CH Ar), 6.96–7.01 (m, 1H, 20-CH Ar), 7.24–7.40 (m, 4H, CH Ar) ppm. Anal. Calcd for $C_{19}H_{20}NOCl$: C, 72.72; H, 6.42; N, 4.46. Found: C, 72.65; H, 6.34; N, 4.65.

2-((*p*-Chlorophenylamino)(4-hydroxyphenyl)methyl) cyclohexanone (Table 2, **4f**): Yield: 90%, Yellowish solid; *syn/anti*: 0/100, FT-IR: ν_{max} (KBr): 3328 (NH, OH stretch), 1654 (C=O stretch) cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): 1.69–1.99 (m, 6H, $3CH_2$), 2.49–2.58 (m, 2H, 2-CH_2), 2.84–2.95 (m, 1H, 6-CH), 3.68 (br, NH), 4.24 (s, 1H, 8-CH), 6.64 (d, *J* = 8.7 Hz, 2H, CH Ar), 7.13–7.17 (m, 2H, CH Ar), 7.36 (d, *J* = 8.4 Hz, 2H, CH Ar), 7.80 (d, *J* = 8.4 Hz, 2H, CH Ar), 8.37 (s, OH) ppm. Anal. Calcd for $C_{19}H_{20}NOCl$: C, 69.19; H, 6.11; N, 4.25. Found: C, 68.93; H, 6.33; N, 4.29. MS (EI) *m/z* 329 (M^+).

2-((*p*-Toluidino)(4-hydroxyphenyl)methyl)cyclohexanone (Table 2, **4g**): Yield: 89%, Yellow solid; *syn/anti*: 0/100, FT-IR: ν_{max} (KBr): 3200 (NH, OH stretch), 1705 (C=O stretch) cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): 1.79–1.98 (m, 6H, $3CH_2$), 2.37 (s, 3H, CH_3), 2.48–2.57 (m, 2H, 2-CH), 2.83–2.88 (m, 1H, 6-CH), 4.24 (s, 1H, 8-CH), 6.63 (d, *J* = 8.7 Hz, 2H, 12,16-C H Ar), 6.95 (d, *J* = 8.7 Hz, 2H, 19,21-C H Ar), 7.11–7.16 (m, 2H, 13,15-C H Ar), 7.11–7.16 (m, 2H, 18,22-C H Ar), 8.39 (s, OH) ppm. Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.18; H, 7.31; N, 4.26. MS (EI) *m/z* 309 (M^+).

2-((*m*-Toluidino)(4-hydroxyphenyl)methyl)cyclohexanone (Table 2, **4i**): Yield: 90%, orange solid, *syn/anti*: 0/100, FT-IR: ν_{max} (KBr): 3200 (NH and OH stretch), 1654 (C=O stretch) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.74–1.79 (m, 2H, CH_2), 1.87–1.91 (m, 2H, CH_2), 2.12–2.67 (m, 2H, CH_2), 2.37 (s, 3H, CH_3), 2.54 (t, *J* = 6.75 Hz, 2H, 2-CH), 2.89–2.85 (m, 1H, 6-CH), 4.21 (s, 1H, 8-CH), 6.83–6.89 (m, 2H, 12,16-CH Ar), 7.01–7.05 (m, 1H, 14-CH Ar), 7.20–7.38 (m, 3H, 19,21,13-CH), 7.75 (d, *J* = 8.5 Hz, 2H, 18,21-CH), 8.37 (s, OH) ppm. ^{13}C NMR ($CDCl_3$): δ 21.39, 23.15, 23.74, 28.93, 40.07 (2-C), 55.3 (8-C), 56.7 (6-C), 115.52, 115.99, 117.97, 121.63, 126.64, 129.03, 130.98, 132.58, 136.52, 160.65 (20-C), 220 (1-C) ppm. Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.48; N, 10.34. Found: C, 77.85; H, 7.62; N, 4.52. MS (EI) *m/z* 309 (M^+).

2-((*p*-Toluidino)(4-chlorophenyl)methyl)cyclohexanone (Table 2, **4m**): Yield: 93%, orange solid, *syn/anti*: 63/37, FT-IR: ν_{max} (KBr): 3367 (NH stretch), 1697 (C=O stretch) cm^{-1}, ^1H NMR (250 MHz, $CDCl_3$): 1.59–1.92 (m, 3H, CH_2), 1.94–2.05 (m, 3H, CH_2), 2.17 (s, 3H, CH_3), 2.26 (m, 2H, 2-CH), 2.81–2.85 (m, 1H, 6-CH), 4.68 (d, *J* = 4.25 Hz, 0.63H, 8-CH), 4.82 (d, *J* = 5.25 Hz, 0.37H, 8-CH), 6.41 (d, *J* = 8.25 Hz, 2H, 12,16-CH Ar), 6.89 (d, *J* = 8.25 Hz, 2H, 13,15-CH Ar), 7.55 (d, J_1 = 8.75 Hz, J_2 = 4.75 Hz, 18,22-CH Ar), 8.14 (d, *J* = 8.75 Hz, 2H, 10,21-CH Ar) ppm. Anal. Calcd for $C_{20}H_{22}ClNO_2$: C, 73.27; H, 6.76; N, 4.27. Found: C, 73.48; H, 6.43; N, 4.21.

2-((4-Chlorophenyl)(4-chlorophenylamino)methyl) cyclohexanone (Table 2, **4l**): Yield: 90%, White solid, *syn/anti*: 0/100, FT-IR: ν_{max} (KBr): 3409.9 (NH stretch), 1701.1 (C=O stretch) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.70–1.96 (m, 6H, $3CH_2$), 2.31–2.43 (m, 2H, 2-CH), 2.73 (m, 1H, 6-CH), 4.51 (d, *J* = 6.0 Hz, 1H, 8-CH), 6.41 (d, *J* = 8.0 Hz, 2H, 12,16-CH Ar), 7.0 (d, *J* =7.75 Hz, 2H, 18,22-CH Ar), 7.27–7.33 (m, 4H, CH Ar) ppm. Anal. Calcd for $C_{19}H_{19}Cl_2ON$: C, 65.53; H, 5.50; N, 4.02. Found: C, 65.77; H, 5.64; N, 4.13. MS (EI) *m/z* 347 (M^+).

2-((*m*-Toluidino)(4-chlorophenyl)methyl)cyclohexanone (Table 2, **4k**): Yield: 96%, beige solid, *syn/anti*: 0/100, FT-IR: ν_{max} (KBr): 3348 (NH stretch), 1701 (C=O stretch) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.71–1.92 (m, 6H, $3CH_2$), 2.19 (S, 3H, CH_3), 2.31–2.54 (m, 2H, 2-CH), 2.87–2.89 (m, 1H, 6-CH), 4.59 (d, *J* = 6.25 Hz, 1H, 8-CH), 6.28–6.36 (m, 2H, 12,16-CH Ar), 6.47 (d, *J* = 7.25 Hz, 1H, 14-CH Ar), 6.95 (t, *J* = 7.75 Hz, 1H, 13-CH Ar), 7.25–7.38 (m, 4H, CH Ar) ppm; ^{13}C NMR ($CDCl_3$): δ 21.56, 23.92, 27.82, 31.44 (2-C), 41.98 (8-C), 57.33 (6-C), 110.47, 114.50, 118.70, 128.58, 128.99, 132.0, 138.86, 140.48, 146.99 (10-C), 212.43 (1-C) ppm. Anal. Calcd for $C_{20}H_{22}ClNO$ (327.85): C, 73.27; H, 6.76; N, 4.27. Found: C, 73.01; H, 6.81; N, 4.39. MS (EI) *m/z* 327 (M^+).

2-((*m*-Toluidino)(4-nitrophenyl)methyl)cyclohexanone (Table 2, **4n**): Yield: 70%, Yellow solid, *syn/anti*: 36/64, FT-IR: ν_{max} (KBr): 3382.9 (NH stretch), 1693.2 (C=O stretch) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.57–1.75 (m, 3H, CH_2), 1.85–2.06 (m, 3H, CH_2), 2.19 (s, 3H), 2.31–2.41 (m, 2H, 2-CH), 2.81–2.85 (m, 1H, 6-CH), 4.69 (d, *J* = 5.0 Hz, 0.64H, 8-CH), 4.84 (d, *J* = 4.25 Hz, 0.36H, 8-CH), 6.27 (d, *J* = 8.0 Hz, 2H, 12,16-CH Ar), 6.49 (d, *J* = 6.5 Hz, 1H, 14-CH Ar), 6.96 (t, *J* = 7.75 Hz, 1H, 13-CH Ar), 7.53–7.58 (m, 2H, 18,22-CH Ar), 8.15 (d, *J* = 8.75 Hz, 2H, 19,21-CH Ar) ppm; ^{13}C NMR ($CDCl_3$): δ 21.54, 24.46, 24.93, 27.03, 27.75, 32.0, 42.39, 42.44, 56.23, 57.06, 57.17, 57.75, 110.37, 110.95, 114.38, 114.96, 119.08, 119.37, 123.66, 128.19, 128.59, 129.03, 129.13, 139.9, 146.65, 150.0, 160.38, 160.48, 211.08 (1-C), 212.36 (1-C) ppm. Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 71.41; H, 5.98; N, 8.32. Found: C, 71.24; H, 5.87; N, 8.04.

2-((4-Chlorophenylamino)(4-nitrophenyl)methyl) cyclohexanone (Table 2, **4o**): Yield: 75%, white solid, *syn/anti*: 42/58, FT-IR: ν_{max} (KBr): 3200 (NH stretch), 1654 (C=O stretch) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.58–1.74 (m, 3H, CH_2), 1.92–2.05 (m, 3H, CH_2), 2.26–2.47 (m, 2H,

2-CH), 2.81–2.85 (m, 1H, 6-CH), 4.62 (d, J = 4.75 Hz, 0.58H, 8-CH), 4.79 (d, J = 3.5 Hz, 0.42H, 8-CH), 6.41 (d, J = 8.75 Hz, 2H, 12,16-CH Ar), 7.02 (d, J = 8.75 Hz, 2H, 13,15-CH Ar), 7.53 (dd, J_1 = 8.75 Hz, J_2 = 3.5 Hz, 2H, 18.22-CH Ar), 8.15 (d, J = 8.75 Hz, 2H, 19,21-CH Ar) ppm. Anal. Calcd for $C_{19}H_{19}ClN_2O_3$: C, 63.60; H, 5.34; N, 7.81. Found: C, 63.98; H, 5.84; N, 7.54.

2-((*p*-Toluidino)(4-nitrophenyl)methyl)cyclohexanone (Table 2, **4p**): Yield: 71%, Yellow solid, *syn*/*anti*: 37/63, FT-IR: ν_{max} (KBr): 3367 (NH stretch), 1697 (C=O stretch) cm^{-1}; ^1H NMR ($CDCl_3$): 1.59–1.92 (m, 3H, CH_2), 1.94–2.05 (m, 3H, CH_2), 2.17 (s, 3H, CH_3), 2.26 (m, 2H, 2-CH), 2.81–2.85 (m, 1H, 6-CH), 4.68 (d, J = 5.25 Hz, 0.63H, 8-CH), 4.82 (d, J = 4.25 Hz, 0.37H, 8-CH), 6.41 (d, J = 8.25 Hz, 2H, 12,16-CH Ar), 6.89 (d, J = 8.25 Hz, 2H, 13,15-CH Ar), 7.55 (d, J_1 = 8.75 Hz, J_2 = 4.75 Hz, 2H, 18,22-CH Ar), 8.14 (d, J = 8.75 Hz, 2H, 19,21-CH Ar) ppm. Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 71.34; H, 6.81; N, 8.59.

4. Conclusion

In conclusion, we have reported a simple and new catalytic method for the synthesis of β-amino carbonyl compounds by one-pot three-component Mannich reaction of cyclohexanone, aromatic aldehydes, and anilines using nano-$Rb_2HPW_{12}O_{40}$ as an efficient and green heterogeneous catalyst. The significant advantages of this method are high yields, simple work-up and easy preparation and handling of the catalyst.

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6. References

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Povzetek

Namen naših raziskav je bil ugotoviti učinkovitost $Rb_2HPW_{12}O_{40}$ kot heterogenega zelenega katalizatorja pri Mannichovi reakciji. Večkomponentna kondenzacija aldehidov, amina in ketona, ki poteka v eni sami posodi pri sobni temperaturi, omogoča ob uporabi ustreznega novega nano-$Rb_2HPW_{12}O_{40}$ kot katalizatorja pripravo ustreznih β-aminoketonov. Enostavno čiščenje, kratki reakcijski časi in visoki izkoristki so le nekatere izmed prednosti tega postopka. Poleg tega lahko katalizator tudi enostavno ponovno izoliramo. Nano-katalizator $Rb_2HPW_{12}O_{40}$ smo karakterizirali z infrardečo spektroskopijo s Fourierjevo transformacijo, rentgensko praškovno difrakcijo in vrstično elektronsko mikroskopijo.