Research Article

Microwave-Assisted Synthesis of Spirofused Heterocycles Using Decatungstodivanadogermanic Heteropoly Acid as a Novel and Reusable Heterogeneous Catalyst under Solvent-Free Conditions

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Decatungstodivanadogermanic acid ($\text{HH}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$) was synthesized and used as a novel, green heterogeneous catalyst for the synthesis of spirofused heterocycles from one-pot three-component cyclocondensation reaction of a cyclic ketone, aldehyde, and urea in high yields under solvent-free condition in microwave irradiation at 80°C . This catalyst is efficient not only for cyclic ketones, but also for cyclic β -diketones, β -diester, and β -diamide derivatives such as cyclohexanone, dimedone, and Meldrum's acid, or barbituric acid derivatives.

1. Introduction

Dihydropyrimidinones and their derivatives have attracted great attention recently in synthetic organic chemistry due to their pharmacological and therapeutic properties such as antibacterial and antihypertensive activity as well as behaving as calcium channel blockers, α -1a-antagonists [1], and neuropeptide Y (NPY) antagonists [2]. The biological activity of some alkaloids isolated recently has been attributed to a dihydropyrimidinone moiety [3]. The first procedure to these compounds reported by Biginelli [4] more than a century ago makes use of the three-component, one-pot condensation of a β -ketoester, an aldehyde, and a urea under strongly acidic conditions [4]. However this method suffers from low yields in the case of substituted aromatic and aliphatic aldehydes [5]. Owing to the versatile biological activity of dihydropyrimidinones, development of an alternative synthetic methodology is of paramount importance.

Recently, many reviews [8, 9] and papers for preparing these compounds have been reported including classical conditions, with microwave and ultrasound irradiation and by using some other different catalysts such as phosphorus pentoxide-methanesulfonic acid [10], potassium *tert*butoxide

(*t*-BuOK) [11], ammonium dihydrogen phosphate [12], silica-gel [13], mesoporous molecular sieve MCM-41 [14], cyanuric chloride [15], nano- $\text{BF}_3 \cdot \text{SiO}_2$ [16], silica gel-supported polyphosphoric Acid [17], zirconium(IV) chloride [18], indium(III) bromide [19], ytterbium(III)-resin [20], 1-*n*-butyl-3-methylimidazolium tetrafluoroborate (BMImBF_4) or hexafluorophosphate (BMImPF_6) [21], ceric ammonium nitrate (CAN) [22], $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$ [23], lanthanide triflate [24], indium(III) chloride [25], lanthanum chloride [26], H_2SO_4 [27], montmorillonite KSF [28], polyphosphate ester (PPE) [29], $\text{BF}_3 \cdot \text{OEt}_2/\text{CuCl}/\text{HOAc}$ [30], and conc. HCl [31, 32].

However, in spite of their potential utility, many of these methods involve expensive reagents, strongly acidic conditions, long reaction times, high temperatures, and stoichiometric amounts of catalysts and give unsatisfactory yields. Therefore, the discovery of a new catalyst for the preparation of pyrimidinones under neutral and mild conditions is of prime importance. Heterogeneous acid catalysis by heteropoly acids (HPAs) has attracted much interest because of its potential of great economic rewards and green benefits [33–35]. Unlike metal oxides and zeolites, HPAs possess very strong Bronsted acidity, and their acid sites are more uniform

and easier to control than those in other solid acid catalysts. These catalysts make them suitable solid heterogeneous catalysts for organic transformations.

Microwave reaction under solvent-free conditions and/or in the presence of a catalyst, resulting in shorter reaction time and higher product yields than those obtained by using conventional heating, offer low cost together with simplicity in processing and handling [36]. In connection with our previous works on synthesis of pyrimidinones derivatives [37–39] and Meldrum's acid and barbituric acid derivatives [40], we wish to report the results obtained from a study of the reaction of aldehydes, urea, cyclohexanone, and Meldrum's acid or barbituric acid derivatives as a CH-acid, instead of open-chain cyclic β -dicarbonyl compounds, in microwave irradiation under solvent-free conditions. The procedure not only gives products in good yields but also avoids problems connected with solvent use (cost, handling, safety, and pollution), and the reaction times.

2. Experimental

2.1. Materials and Methods. All reactions were carried out in an LG domestic unmodified microwave oven model MS-1947C/01. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a BRUKER DRX-500 AVANCE spectrometer at 500.13 and 125.77 MHz, respectively. NMR spectra were obtained on solutions in $\text{DMSO}-d_6$. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) Chemical Company. Decatungstodivanadogermanic acid ($\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$) was prepared according to a reported procedure [41].

2.2. Synthesis of Catalyst. 0.8 g of GeO_2 was dissolved in a hot solution of 10% NaOH, and a solution of 22.8 g of $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$ in 100 mL of hot water was added to get mixture A. The pH of A was adjusted to 6 with HCl (1:1) and heated for 1 h. Then a solution of 7.5 g of Na_2CO_3 dissolved in 25 mL of hot water was added. The mixture was concentrated to 100 mL by heating. 2.4 g of $\text{NaVO}_3 \cdot 2\text{H}_2\text{O}$ and 2.5 g of $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$ were dissolved in 30 mL of hot water, respectively, and the two solutions were mixed to get mixture B. The pH of mixture B was adjusted to 2.5 with H_2SO_4 (1:1). Then A was added dropwise, and the pH was kept at 2.5 while dropping. After stirring for 3 h at 60°C , the solution was cooled to room temperature. The cooled solution was extracted with ether in sulfuric acid medium, and the extractant was dissolved with a small amount of water. After the ether was evaporated, the remaining mixture was placed in the desiccators until orange crystals were separated out. The final yield was about 70%. Anal. Calcd. for $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$: Ge, 2.38; W, 60.18; V, 3.33; H_2O , 12.96. Found: Ge, 2.38; W, 60.06; V, 3.29; H_2O , 12.97% (TG analysis). FT-IR (KBr, cm^{-1}): 3450 ν (O–H); 1620 δ (O–H); 964 ν_{as} (M– O_d); 885 ν_{as} (M– O_b –M); 818 ν_{as} (Ge– O_a); 780 ν_{as} (M– O_c –M); 464 δ (O–Ge–O), (M=W and

V; O_a , inner oxygen; O_b , corner-shared oxygen; O_c , edge-shared oxygen; O_d , terminal oxygen) [41]. UV-Vis spectrum (CH_3CN λ_{max} nm); ($\text{O}_d \rightarrow \text{M}$, CT); 262 ($\text{O}_{b/c} \rightarrow \text{M}$, CT).

The number of hydrogen in the HPA and the states of ionization can be determined by potentiometric titration. The potentiometric titration curve (Figure 1) shows that the six protons of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ are equivalent and they are ionized in one step.

X-ray powder diffraction is widely used to study the structural features of HPA and explain their properties [42]. The data of X-ray powder diffraction are listed in Table 1.

The result of X-ray powder diffraction of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ displays that the diffraction peaks are primarily distributed in four ranges of 2θ which are $7\text{--}10^\circ$, $16\text{--}22^\circ$, $25\text{--}30^\circ$, and $33\text{--}38^\circ$. The positions and intensities of the main peaks are similar to those expected for the Keggin structure. Combined with IR and UV spectra, it is sure that $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ possesses Keggin structure.

HPA consists of protons, HPA anions, and hydration water. Figure 2 is the thermogram of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$. The TG curve shows that the total percent of weight loss is 12.96%, which indicates that each HPA molecule has 22 molecules of water, and there are three steps of weight loss. The first is the loss of 16 molecules of hydration water, the second is the loss of 6 molecules of protonized water and the third is the loss of 3 molecules of structural water. Thus, the accurate molecular formula of the product is (H_5O_2) $3\text{H}_3\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 16\text{H}_2\text{O}$.

In general, we took the temperature of the exothermic peak of DTA curves as a sign of their thermostability [43]. In the DTA curve, there was an exothermic peak at 481.6°C .

2.3. General Procedure for the Reaction of Benzaldehyde Meldrum's Acid and Urea. An intimate mixture of benzaldehyde (0.30 g, 2 mmol), Meldrum's acid (0.144 g, 1 mmol), urea (0.06 g, 1 mmol), and decatungstodivanadogermanic acid (0.03 g 3 mmol) was subjected to microwave irradiation for appropriate time in 600 W microwave oven for 6–7 min (successive irradiation of 30–40 sec with cooling intervals of time as the temperature being 80°C) as indicated by TLC. After cooling, $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ was separated by simple filtration due to its heterogeneous nature, and the reaction mixture was poured onto crushed ice (40 g) and stirred for 5–10 min. The precipitate was filtered under suction, washed with cold water (40 mL) and ethyl acetate (5 mL) to afford the pure product **1a**.

2.4. General Procedure for the Reaction of Cyclohexanone, Aldehydes, and Urea. The mixture of cyclohexanone (1.0 mmol), aldehyde (2.0 mmol), urea (3.0 mmol), and Decatungstodivanadogermanic acid (3 mmol) was subjected to microwave irradiation for appropriate time in 600 W microwave oven for 6–7 min (successive irradiation of 30–40 sec with cooling intervals of time as the temperature being 80°C) as indicated by TLC. After cooling, $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ was separated by simple filtration due to its heterogeneous nature and the reaction mixture was poured onto crushed ice (40 g) and stirred for 5–10 min. The precipitate was filtered

TABLE 1: Data of X-ray powder diffraction of $H_6GeW_{10}V_2O_{40} \cdot 22H_2O$.

$2\theta/^\circ$	9.27	10.34	16.76	18.75	19.10	20.76	25.52
d/nm	0.954	0.855	0.529	0.473	0.465	0.428	0.349
I	95.8	100.0	14.6	25.0	47.9	41.7	45.8
$2\theta/^\circ$	27.09	28.00	29.57	34.70	35.40	36.72	37.79
d/nm	0.329	0.319	0.302	0.529	0.254	0.245	0.238
I	70.8	60.4	27.1	33.3	22.9	35.4	27.1

FIGURE 1: Potentiometric titration curve of $H_6GeW_{10}V_2O_{40} \cdot 22H_2O$. FIGURE 2: Thermogram of $H_6GeW_{10}V_2O_{40} \cdot 22H_2O$.

under suction, washed with cold water (40 mL) and ethyl acetate (5 mL) to afford the pure product **2a**.

2.5. Spectral Data of Compounds

3,3-Dimethyl-(7S,11R)-diphenyl-2,4-dioxa-8,10-diazaspiro[5.5]undecane-1,5,9-trione (1a). White powder. Mp 223–225°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3195 and 3060 (NH), 1771, 1731 and 1685 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 0.49 (6H, s, CMe_2), 5.29 (2H, s, 2CH), 7.20–7.37 (10H, m, Ar), 7.28 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 27.67 (CMe_2), 57.99 (C_{spiro}), 61.48 (2CH), 105.51 (CMe_2), 127.72, 128.71, 129.26, and 135.54 (Ar), 155.22, 159.69, 165.55 (3C=O). MS (m/z , %) 380 (M^+ , 11), 322 (7), 294 (13), 234 (12), 175 (17), 106 (100), 77 (44), 43 (56).

3,3-Dimethyl-(7S,11R)-bis(4-methylphenyl)-2,4-dioxa-8,10-diazaspiro[5.5]undecane-1,5,9-trione (1b). White powder. Mp 199–200°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3200 and 3060 (NH), 1765, 1730 and 1686 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 0.51 (6H, s, CMe_2), 2.25 (6H, s, 2CH₃), 5.22 (2H, s, 2CH), 7.07–7.2 (8H, m, Ar), 7.17 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 20.62 (2CH₃), 27.73 (CMe_2), 57.99 (C_{spiro}), 61.21 (2CH), 105.44 (CMe_2), 127.56, 129.12, 132.52 and 138.66 (Ar),

155.31, 159.77, 165.64 (3C=O). MS (m/z , %) 408 (M^+ , 14), 350 (7), 322 (11), 189 (27), 173 (36), 120 (100), 91 (69), 75 (14), 43 (59).

3,3-Dimethyl-(7S,11R)-bis(4-chlorophenyl)-2,4-dioxa-8,10-diazaspiro[5.5]undecane-1,5,9-trione (1c). White powder. Mp 204–206°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3205 and 3065 (NH), 1770, 1731 and 1687 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 0.60 (6H, s, CMe_2), 5.32 (2H, s, 2CH), 7.21–7.47 (8H, m, Ar), 7.46 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 27.81 (CMe_2), 57.75 (C_{spiro}), 60.73 (2CH), 105.69 (CMe_2), 128.76, 129.62, 133.92 and 134.33 (Ar), 155.15, 159.63 and 165.32 (3C=O). MS (m/z , %) 449 (M^+ , 16), 390 (7), 209 (22), 173 (36), 166 (57), 140 (98), 75 (14), 43 (100).

3,3-Dimethyl-(7S,11R)-bis(4-fluorophenyl)-2,4-dioxa-8,10-diazaspiro[5.5]undecane-1,5,9-trione (1d). White powder. Mp 216–218°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3205 and 3065 (NH), 1770, 1725 and 1680 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 0.59 (6H, s, CMe_2), 5.32 (2H, s, 2CH), 7.24–7.26 (8H, m, Ar), 7.47 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 27.80 (CMe_2), 58.03 (C_{spiro}), 60.69 (2CH), 105.62 (CMe_2), 115.65, 129.92, 131.64 and 155.27 (Ar), 159.79, 163.45 and 165.48 (3C=O). MS (m/z , %) 417 (M^+ +1, 136), 358 (12), 316 (9), 193 (26), 149 (68), 124 (90), 75 (34), 43 (100).

(7*S*,11*R*)-Diphenyl-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1e**). White powder. Mp 240–242°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3240 and 3065 (NH), 1729 and 1695 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 5.21 (2H, s, 2CH), 7.17–7.31 (10 H, m, Ar), 7.31 (2H, s, 2NH), 11.01 and 11.39 (2H, 2s, NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 57.49 (C_{spiro}), 61.59 (2CH), 127.81, 128.91, 129.36 and 136.12 (Ar), 149.11, 156.05, 165.88 and 170.31 (4C=O). MS (m/z , %) 364 (M^+ , 5), 304 (10), 215 (95), 104 (100), 77 (96), 51 (98).

(7*S*,11*R*)-bis(4-Methylphenyl)-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1f**). White powder. Mp 246–248°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3235 and 2975 (NH), 1724 and 1692 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 2.23 (6H, s, 2CH₃), 5.14 (2H, s, 2CH), 7.03–7.11 (8H, m, Ar), 7.01 (2H, s, 2NH), 10.97 and 11.33 (2H, 2s, NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 20.66 (2CH₃), 57.02 (C_{spiro}), 60.91 (2CH), 127.21, 128.98, 132.66 and 138.11 (Ar), 148.75, 155.66, 165.51 and 169.94 (C=O). MS (m/z , %) 364 (M^+ –CO, 7), 338 (25), 277 (31), 215 (100), 105 (87), 91 (23), 77 (39), 51 (45).

(7*S*,11*R*)-bis(4-Chlorophenyl)-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1g**). Cream powder. Mp 291–293°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3146 and 3065 (NH), 1735 and 1708 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 5.21 (2H, s, 2CH), 7.15–7.41 (8H, m, Ar), 7.20 (2H, s, 2NH), 11.14 and 11.51 (2H, 2s, NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 56.82 (C_{spiro}), 60.33 (2CH), 128.48, 129.23, 133.47 and 134.50 (Ar), 148.58, 155.42, 165.18 and 169.47 (C=O). MS (m/z , %) 432 (M^+ –1, 10), 400 (35), 372 (26), 249 (78), 215 (56), 138 (100), 75 (39), 51 (69).

(7*S*,11*R*)-bis(4-Fluorophenyl)-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1h**). White powder. Mp 213–215°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3195 and 3070 (NH), 1757, 1694 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 5.21 (2H, s, 2CH), 7.11–7.22 (8H, bs, Ar), 7.29 (2H, s, 2NH), 11.15 and 11.49 (2H, 2s, NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 57.05 (C_{spiro}), 60.28 (2CH), 115.27, 129.43, 131.73 and 150.19 (Ar), 155.47, 161.20, 165.35 and 169.62 (C=O). MS (m/z , %) 400 (M^+ , 10), 350 (25), 233 (100), 190 (56), 122 (98), 95 (73), 75 (69), 51 (69).

2,4-Dimethyl-(7*S*,11*R*)-diphenyl-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1i**). White powder. Mp 232–234°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3180 and 3060 (NH), 1739 and 1685 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 2.68 and 2.85 (6H, s, 2NMe), 5.28 (2H, s, 2CH), 7.08–7.28 (10H, m, Ar), 7.18 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 27.87 and 28.71 (2NMe), 58.83 (C_{spiro}), 62.04 (2CH), 127.43, 128.84, 129.49, and 135.93 (Ar), 149.44, 155.87, 163.67 and 168.27 (4C=O). MS (m/z , %) 392 (M^+ , 17), 260 (13), 243 (31), 186 (18), 106 (100), 77 (39), 51 (33).

2,4-Dimethyl-(7*S*,11*R*)-bis(4-methylphenyl)-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1j**). White powder. Mp 228–230°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3195 and 3055 (NH), 1738 and 1686 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 2.21 (6H, s, 2CH₃), 2.71 and 2.85 (6H, s, 2NMe), 5.22 (2H, s, 2CH), 6.97–7.09 (8H, m, Ar), 7.08 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 20.64 (2CH₃), 27.42 and 28.72 (2NMe), 58.28

(C_{spiro}), 61.36 (2CH), 126.84, 128.86, 132.51, and 138.21 (Ar), 149.40, 155.35, 163.28 and 167.83 (4C=O). MS (m/z , %) 420 (M^+ , 10), 360 (6), 274 (28), 257 (31), 186 (13), 120 (100), 106 (11), 91 (23), 77 (9).

2,4-Dimethyl-(7*S*,11*R*)-bis(4-chlorophenyl)-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1k**). White powder. Mp 271–273°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3195 and 3060 (NH), 1744 and 1659 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 2.74 and 2.87 (6H, s, 2NMe), 5.30 (2H, s, 2CH), 7.10–7.38 (8H, m, Ar), 7.25 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 27.53 and 28.34 (2NMe), 56.67 (C_{spiro}), 60.82 (2CH), 128.39, 128.97, 129.36, and 133.46 (Ar), 155.14, 156.72, 159.30 and 162.98 (4C=O). MS (m/z , %) 460 (M^+ , 14), 400 (16), 321 (14), 294 (23), 277 (89), 220 (31), 140 (100), 75 (34).

2,4-Dimethyl-(7*S*,11*R*)-bis(4-fluorophenyl)-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5,9-tetraone (**1l**). White powder. Mp 244–246°C dec. IR (KBr) ($\nu_{\max}$, cm^{-1}): 3190 and 3065 (NH), 1740, 1656 (C=O). ^1H NMR (DMSO, Me_4Si): δ_{H} 2.75 and 2.87 (6H, s, 2NMe), 5.30 (2H, s, 2CH), 7.13–7.15 (8H, m, Ar), 7.26 (2H, s, 2NH). ^{13}C NMR (DMSO, Me_4Si): δ_{C} 27.47 and 28.27 (2NMe), 58.28 (C_{spiro}), 60.76 (2CH), 115.21, 129.20, 131.60, and 148.93 (Ar), 155.24, 161.16, 163.12 and 167.53 (4C=O). MS (m/z , %) 428 (M^+ , 10), 385 (6), 305 (17), 278 (33), 261 (69), 204 (31), 124 (100), 95 (35), 75 (34).

4,8-Diphenyloctahydro-1*H*-pyrimido[5,4-*i*]quinazoline-2,10(3*H*,11*H*)-dione (**2a**). Mp 327–329°C; ^1H NMR (DMSO- d_6): δ 7.40–7.19 (m, 10 H), 7.08 (s, 1H), 6.97 (s, 1H), 6.62 (s, 1H), 6.39 (s, 1H), 4.50 (d, 1H), 4.82 (d, 1H), 2.02 (m, 2H), 1.38 (m, 2H), 1.24 (m, 2H), 0.82 (t, 2H); ^{13}C -NMR (DMSO- d_6) δ : 155.9, 140.5, 128.1, 128.6, 126.0, 63.7, 50.2, 49.1, 17.8; ESI-MS 377 ($\text{M}+\text{H}$); $\text{C}_{22}\text{H}_{24}\text{N}_4\text{O}_2$; (376.45); Calcd. C, 70.19; H, 6.43; N, 14.88; O, 8.50. Found. C, 70.03; H, 6.21; N, 14.45; O, 8.23.

4,8-bis(2-Chlorophenyl)octahydro-1*H*-pyrimido[5,4-*i*]quinazoline-2,10(3*H*,11*H*)-dione (**2d**). Mp 321–323°C; ^1H NMR (DMSO- d_6): δ 7.42 (s, 1H), 7.35–7.10 (m, 9H), 6.75 (s, 1H), 5.32 (s, 1H), 5.32 (s, 1H), 3.91 (m, 3H), 3.69 (m, 3H), 2.30 (m, 2H), 2.01 (m, 1H), 1.84 (m, 1H), 1.32 (m, 1H), 1.19 (m, 1H), 0.89 (m, 1H); ^{13}C -NMR (DMSO- d_6) δ : 155.9, 140.5, 133.4, 129.5, 128.6, 127.4, 63.7, 48.6, 45.1, 23.6, 17.8; ESI-MS 445 ($\text{M}+\text{H}$); $\text{C}_{22}\text{H}_{22}\text{Cl}_2\text{N}_4\text{O}_2$ (445.34); Calcd. C, 59.33; H, 4.98; Cl, 15.92; N, 12.58; O, 7.19. Found. C, 59.12; H, 4.56; Cl, 15.74; N, 12.28; O, 7.02.

3. Results and Discussion

The reaction of cyclic β -ketoesters [44] and β -diamides, Meldrum's acid, or barbituric acid derivatives with 1 equivalent of urea and 2 equivalents of aldehydes gives a family of σ symmetric spiroheterobicyclic compounds in good yields in the presence of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ as a catalyst under solvent-free conditions at 80°C (Scheme 1 and Table 2).

To explore the scope and limitations of this reaction further, we have extended it to various *para*-substituted benzald-

TABLE 2: $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ catalyzed synthesis of spiroheterobicyclic rings **1(a-l)**.

Entry	X-Z-X	G	Product	Yield (%)	M.P. (°C)
1	O-C(Me) ₂ -O	H	1a	80	223–225
2	O-C(Me) ₂ -O	Me	1b	68	199–200
3	O-C(Me) ₂ -O	Cl	1c	66	204–206
4	O-C(Me) ₂ -O	F	1d	67	216–218
5	HN-CO-NH	H	1e	87	240–242
6	HN-CO-NH	Me	1f	84	246–248
7	HN-CO-NH	Cl	1g	82	291–293
8	HN-CO-NH	F	1h	77	213–215
9	MeN-CO-NMe	H	1i	83	232–234
10	MeN-CO-NMe	Me	1j	85	228–230
11	MeN-CO-NMe	Cl	1k	77	271–273
12	MeN-CO-NMe	F	1l	75	244–246

SCHEME 1

SCHEME 2

ehydes in the presence of Meldrum's acid and barbituric acid (Scheme 1). We have found that the reaction proceeds very efficiently with benzaldehyde and electron withdrawing *para*-substituted benzaldehydes, but it proceeded only up to Knoevenagel adducts, when electron releasing *para*-substituted benzaldehydes were used (X = OMe, NMe₂).

This investigation has been extended to cyclic ketones like cyclohexanone (Scheme 2). The products formed **2(a-d)** are listed in Table 3.

It was shown that no desirable product could be detected when a mixture react in the absence of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$, which indicated that the catalyst should be necessary. Then the model reaction to synthesize **1a** by the reaction of Meldrum's acid, benzaldehyde, and urea was investigated

with different amounts of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ (0–5 mol%). Yields of the reaction in different conditions were shown in Table 4.

We found that most of the Lewis acids could promote the reaction, but the yields were not so high. In comparison with other catalysts, the use of 3 mol% of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ could make the yield 80% under the microwave power of 600 W and the irradiation time of 7 min. It could be seen that 3 mol% of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ gave the best result of this reaction, although other factors could not yet be optimized.

Based on the above optimized results, that is, 3 mol% amount of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ as a catalyst, we further examined the effects of the microwave power and the irradiation time on the same model reaction to afford **1a**, as shown

TABLE 3: $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ catalyzed reaction of cyclohexanone, aldehyde, and urea.

Entry	R	Products ^a	Yield ^b (%)	M.P (°C)
1	C_6H_5	2a	87	327–329
2	$4\text{-(NO}_2\text{)C}_6\text{H}_4$	2b	79	341–343
3	$4\text{-(CH}_3\text{)C}_6\text{H}_4$	2c	83	348–351
4	$2\text{-(Cl)-C}_6\text{H}_4$	2d	82	321–323

^aReaction conditions: cyclohexanone (1.0 mmol), aldehyde (2.0 mmol), urea (3.0 mmol), and decatungstodivanadogermanic acid (3 mmol) irradiated at 80 °C under solvent-free condition.

TABLE 4: Yields of the reaction in different conditions.

Amount of catalyst (% mol)	Reaction time (min)/temperature (°C)	Yields (%)
0	7/80	46
1	7/80	52
2	7/80	63
3	7/80	80
4	7/80	75
5	7/80	73

TABLE 5: Effect of the microwave power and the irradiation time on the formation of **1a**.

Entry	Time (min)	Power (W)	Yields (%)
1	4	250	47
2	4	300	52
3	4	400	55
4	4	500	58
5	4	600	63
6	4	700	69
7	4	750	71
8	4	800	74
9	4	900	80
10	2	900	36
11	3	900	62
12	5	900	88
13	7	900	97
14	8	900	94
15	9	900	92

Reaction conditions: benzaldehyde (0.30 g, 2 mmol), Meldrum's acid (0.144 g, 1 mmol), urea (0.06 g, 1 mmol), and decatungstodivanadogermanic acid (0.03 g, 3 mmol) in microwave irradiation at 80 °C under solvent-free condition.

in Scheme 1. The results are listed in Table 5. It could be found that with the increase of the microwave power from 250 W to 900 W, the yield of **1a** showed a linear increase from 47% to 80% when the irradiation time was 4 min. However, with the microwave power of 900 W, when we increased the microwave irradiation time, the yield of **1a** increased first, but a slight decrease was observed for more than 7 min. So the optimized microwave power and the irradiation time were 900 W and 7 min, respectively.

TABLE 6: Comparison of the results of the present work with those of the earlier works.

Catalyst	Conditions	Yield (%)	Time	Reference
NBS/AIBN	Solvent-free/80 °C	72–74	4 h	[6]
AlCl_3	Ethanol/Reflux	82–84	5 h	[7]
$\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$	MWI/Solvent free	87–90	6–7 min	This work

TABLE 7: Reusability of the catalyst for the synthesis of 3,3-dimethyl-(7S, 11R)-diphenyl-2,4-dioxo-8,10-diazaspiro[5.5]undecane-1,5,9-trione^a.

Cycle	0	1st	2nd	3rd	4th
Time (min)	7	7	8	9	9
Yield (%) ^b	80	78	76	73	71

^aReaction conditions: benzaldehyde (0.30 g, 2 mmol), Meldrum's acid (0.144 g, 1 mmol), urea (0.06 g, 1 mmol), and decatungstodivanadogermanic acid (0.03 g, 3 mmol) in microwave irradiation at 80 °C under solvent-free condition.

^bIsolated yields.

In order to show the merit of the present work in terms of time, yield, and reaction conditions in comparison to the earlier reported works, the results of the present study were compared with those of the earlier studies in Table 6. As it can be seen from Table 6, the present method is simpler, more efficient for the synthesis of dihydropyrimidinone derivatives.

In order to confirm the reusability of $\text{H}_6\text{GeW}_{10}\text{V}_2\text{O}_{40} \cdot 22\text{H}_2\text{O}$ catalyst, after the completion of the reaction it was separated from the reaction mixture and washed with ethyl acetate. The recovered catalyst was found to be reusable for four cycles without significant loss in activity (Table 7). At the same time the concentrations of W and V in the filtrate were determined to be less than 1% by ICP-AES. On the other hand, the IR and UV-Vis spectra of the recovered catalyst were identical with fresh catalyst. All these findings confirm that the leaching of the catalyst did not take place under the reaction conditions.

4. Conclusion

In conclusion we have investigated the application of a V-containing HPA as a green and recyclable heterogeneous catalyst for the synthesis spirofused heterocycles from one-pot three-component cyclocondensation reaction of a cyclic ketone, aldehyde, and urea in high yields under solvent-free condition in microwave irradiation. It is an efficient, mild, and green method for the synthesis of spirofused heterocycles. It is noteworthy that the catalyst can be used for subsequent cycles without appreciable loss of activity. In contrast to many other acids, the storage of this nonhygroscopic and noncorrosive solid heteropoly acid does not require special precautions; for example, it can be stored on a bench top for months without losing its catalytic activity.

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