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An Efficient and Environmentally Friendly Procedure for the Synthesis of Some Novel 8-Benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones using Tetrabutylammonium Hexatungstate as a Reusable Heterogeneous Catalyst under Solvent-Free Conditions

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An efficient method for the preparation of 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones from the reaction of aromatic aldehydes with cyclohexanone and urea or thiourea in the presence of Tetrabutylammonium hexatungstate, $[TBA]_2[W_6O_{19}]$, as an efficient, inexpensive catalyst under thermal and solvent-free conditions has been developed. Good yields, short reaction times, straightforward workup, reusability of the catalyst, and green conditions are the most obvious advantages of this procedure.

Key Words : Tetrabutylammonium hexatungstate, Benzylidene, Pyrimidinone, Quinazolin-2-ones, Quinazolin-2-thiones

Introduction

In recent decades, multi-component reactions (MCR's) have gained wide applicability in the field of synthetic organic chemistry as they increase the efficiency of the reaction and decrease the number of laboratory operations along with quantities of solvent and chemicals used. The development of new and efficient synthetic methodologies for the rapid construction of potentially bioactive compounds constitutes a major challenge for chemists in organic synthesis. MCRs are very useful to generate diverse combinatorial libraries for drug discovery.[1-4]

Pyrimidinone and its derivatives constitute an important class of natural and synthetic products that possess significant biological and pharmaceutical properties.[5,6] In particular, functionalized pyrimidinones such as fused pyrimidinones with an arylidene part are essential heterocyclic motifs in antitumor agents.[7] These compounds are employed for the preparation of many biologically active products.[8-10]

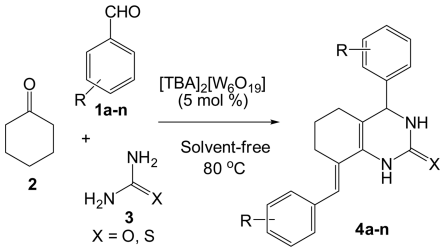
The common procedure for the construction of pyrimidinone scaffolds is Biginelli reaction. The classic version of the Biginelli three-component condensation reaction,[11] has seen widespread use for generating large collections of molecules in combinatorial synthesis.[12] Very recently, for novel Biginelli-like scaffold synthesis, the use of the common open-chain β-dicarbonyl compounds in Biginelli reactions has been extended to the use of cyclic β-diketones,[13] β-ketolactones[14] and cyclic β-diesters.[15] Arylidene heterobicyclic pyrimidinones or quinazolin-2-ones/thiones are samples of these generations. Because of the potential of arylidene heterobicyclic pyrimidinones, numerous methods including the reaction of α,α'-bis(arylidene)cycloalkanones with urea or thiourea catalyzed by strong bases such as sodium ethoxide[7] or strong acids such as HCl have been developed for their synthesis.[16]

The newly method for the preparation of arylidene heterobicyclic pyrimidinones is the condensation reaction of cycloalkanones, urea/thiourea, and aldehydes named as Biginelli-type reactions. These reactions are proceeded using various acidic catalysts including TMSCl,[17] ytterbium chloride,[18] vitamin B1, [19] and *N*-(4-sulfonic acid) butyl triethylammonium hydrogen sulfate ($[TEBSA][HSO_4]$).[20]

Regarding the importance of arylidene heterobicyclic pyrimidinones and the great need for environmentally benign chemical productions, the development of suitable green synthetic methods for these compounds has attracted considerable interest.

Tetrabutylammonium hexatungstate $[TBA]_2[W_6O_{19}]$ has recently emerged as a promising heterogeneous catalyst for a series of organic transformations, such as Knoevenagel condensation,[21] Biginelli reaction,[22] synthesis of bis-coumarins,[23] synthesis of 1,8-dioxodecahydroacridines,[24] Hantzsch reaction[25,26] and one-pot synthesis of 2,4,5-trisubstituted imidazoles.[27]

During the course of our studies toward the development of new routes to the synthesis of heterocyclic compounds,[28-32] we herein disclose for the first time, a valid and an efficient procedure for the synthesis of 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones from the reaction of aromatic aldehydes with cyclohexanone and urea or thiourea in the presence of Tetrabutylammonium hexatungstate, $[TBA]_2[W_6O_{19}]$, as an efficient, inexpensive catalyst under thermal and solvent-free conditions (Scheme 1).



Scheme 1. Synthesis of various 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones.

Results and Discussion

To obtain the best reaction conditions, the reaction of benzaldehyde (1 mmol), cyclohexanone (1 mmol), and urea (1.2 mmol), was chosen as a model of the reaction (Table 1). Among various solvent (reflux condition) and solvent-free (thermal, 80 °C) condition screened (Table 1, Entries 1-6), solvent-free was showed higher produced yield of product and the reaction was completed in lower reaction time (Table 1, Entry 6). Solvent-free condition is more demandable in view of the current interest in environmentally benign catalytic processes.

To investigate the effect of reaction temperature on the catalyst reactivity and product yield, the reaction was performed under different temperatures including room temperature and 50, 60, 70, 80 and 90 °C (Table 1, Entries 6-11). The greatest yield in the shortest reaction time was obtained under solvent-free conditions at 80 °C.

On changing the catalyst loading from 1 to 5 mol %, the yield of product was found to changed, however on further increasing the catalyst loading no effective increase in the yield was observed (Table 1, Entry 6 & Entries 12-18). It was observed that 5 mol % of $[TBA]_2[W_6O_{19}]$ gave the product in higher yield (Table 1, Entry 6).

The formation of the product 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones (Scheme 1) indicates that the product is formed by the condensation of benzaldehyde, cyclohexanone, and urea at a 2:1:1 ratio. But the reaction at this ratio of substrate gave the yield lower than that obtained at a 1:1:1.2 ratios (Table 2, Entry 2). This means that excessively used cyclohexanone and urea played important roles in promoting the conversion of benzaldehyde to the product. Corresponding contrastive reactions were performed and the results indicated that whichever of the cyclohexanone or urea was used at double the equivalent, respectively, the yields were appreciably improved (Table 2, Entries 3 and 4). Although the reasons for this conversion are not clear but in confirmation of reported literatures [18] and according to our experimentally observations, the best yield in the shortest reaction time was obtained using the molar ratio of 1:1:1.2 of benzaldehyde, cyclohexanone and urea respectively.

Using these optimized conditions, various pyrimidinone derivatives were prepared by the reaction of various aryl aldehydes with urea or thiourea and cyclohexanone under solvent-free conditions (Table 3, Entries 1-14). In general, aromatic aldehydes bearing functional groups (for example -H, $-CH_3$, $-OCH_3$, -Cl, -F, $-NO_2$, and -Br) react smoothly to give the corresponding products in good yields in short reaction times. As shown in Table 3, a variety of aldehydes bearing either electron-donating or electron-withdrawing groups on the aromatic ring were investigated. However, when aromatic aldehydes with electron-withdrawing groups (Table 3, Entries 2-6) are reactants, the reaction time is shorter than that with electron-donating groups (Table 1, Entries 7-8). Replacement of urea with thiourea results in the high yields of the related products (Table 3, Entries 9-14).

It is noteworthy that the reaction times are very short and workup of products is very convenient. All of the products were isolated by adding water to the reaction mixture, and the solid compounds were filtered off as pure products.

The possibility of recycling the catalyst was examined using the model reaction under the optimized conditions. Upon completion of the reaction, the mixture was dissolved in hot ethanol and filtered. The recovered catalyst was wash-

Table 1. Synthesis of 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one in the presence of $[TBA]_2[W_6O_{19}]$ as catalyst in different reaction conditions[a]

Entry	Solvent	Catalyst (mol %)	Temperature (°C)	Time (h)	Yield (%)[b]
1	EtOH	5.0	Reflux	3.0	69
2	DMF	5.0	Reflux	3.0	43
3	CH_3CN	5.0	Reflux	3.0	36
4	$CHCl_3$	5.0	Reflux	3.0	42
5	1,4-Dioxane	5.0	Reflux	3.0	44
6	Solvent-free	5.0	80	1.0	91
7	Solvent-free	5.0	RT	3.0	41
8	Solvent-free	5.0	50	3.0	56
9	Solvent-free	5.0	60	2.5	68
10	Solvent-free	5.0	70	2.0	81
11	Solvent-free	5.0	90	1.0	92
12	Solvent-free	0.0	80	1.0	32
13	Solvent-free	1.0	80	1.0	46
14	Solvent-free	2.0	80	1.0	53
15	Solvent-free	3.0	80	1.0	71
16	Solvent-free	4.0	80	1.0	80
17	Solvent-free	6.0	80	1.0	91
18	Solvent-free	7.0	80	1.0	92

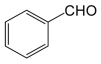
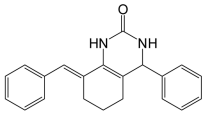
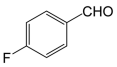
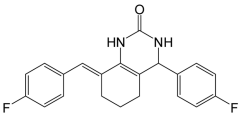
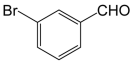
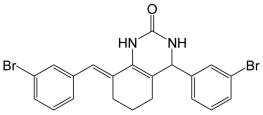
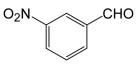
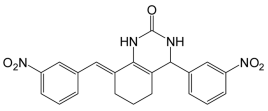
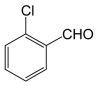
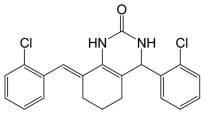
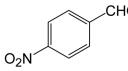
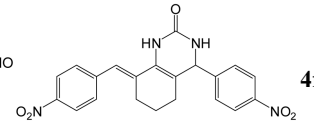
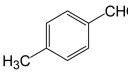
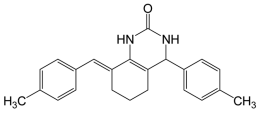
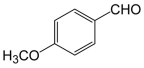
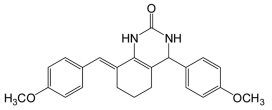
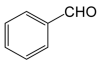
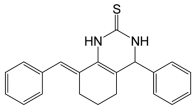
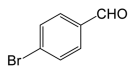
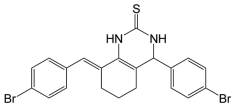
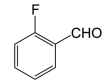
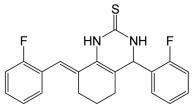
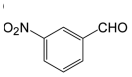
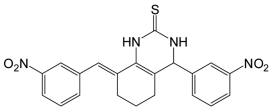
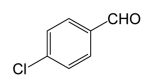
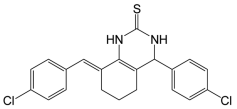
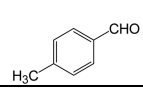
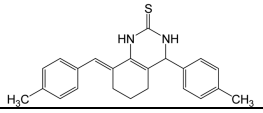
[a]Reaction conditions: benzaldehyde (1 mmol), cyclohexanone (1 mmol) and urea (1.2 mmol). [b]Isolated yield.

Table 2. Effects of ratio of substrates on the synthetic reaction of **4a**[a]

Entry	Time (h)	**1a:2:3a**	Yield (%)[b]
1	1.0	1:1:1.2	91
2	1.0	2:1:1.2	67
3	1.0	1:1:2.4	73
4	1.0	2:2:1.2	79

[a]Reaction conditions: benzaldehyde (**1a**), cyclohexanone (**2**) and urea (**3a**) heating at 80 °C in the presence of $[TBA]_2[W_6O_{19}]$ (5 mol %) under solvent-free condition. [b]Isolated yield.

Table 3. Synthesis of various 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones[a]

Entry	Aldehyde	Product	Compound Number	Time (h)	Yield (%)[b]
1			**4a**	1.0	91
2			**4b**	0.8	93
3			**4c**	0.8	89
4			**4d**	0.8	92
5			**4e**	0.8	91
6			**4f**	0.8	90
7			**4g**	1.2	83
8			**4h**	1.2	84
9			**4i**	0.8	93
10			**4j**	0.8	92
11			**4k**	0.8	95
12			**4l**	0.8	90
13			**4m**	0.8	92
14			**4n**	1.2	86

[a]Reaction conditions: benzaldehyde (**1a**), cyclohexanone (**2**) and urea (**3a**) heating at 80 °C in the presence of $[TBA]_2[W_6O_{19}]$ (5 mol %) under solvent-free condition. [b]Isolated yields

Table 4. Effect of recycling of $[TBA]_2[W_6O_{19}]$ catalyst on the product of 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one[a]

Entry	Cycle	Time (h)	Yield (%)[b]
1	0	1.0	91
2	1	1.0	90
3	2	1.0	88
4	3	1.0	87

[a]Reaction conditions: benzaldehyde (**1a**), cyclohexanone (**2**) and urea (**3a**) heating at 80 °C in the presence of $[TBA]_2[W_6O_{19}]$ (5 mol %) under solvent-free condition. [b]Isolated yield.

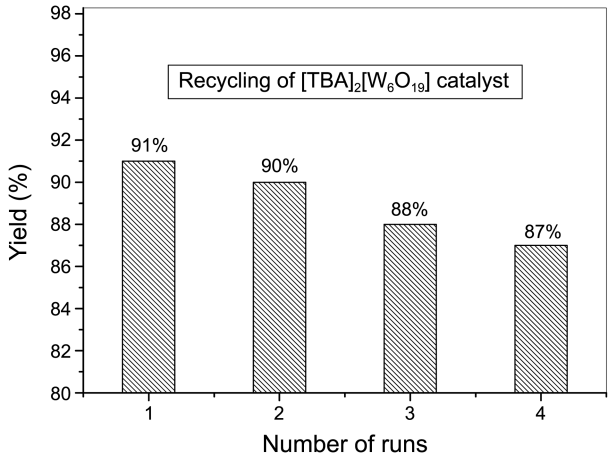
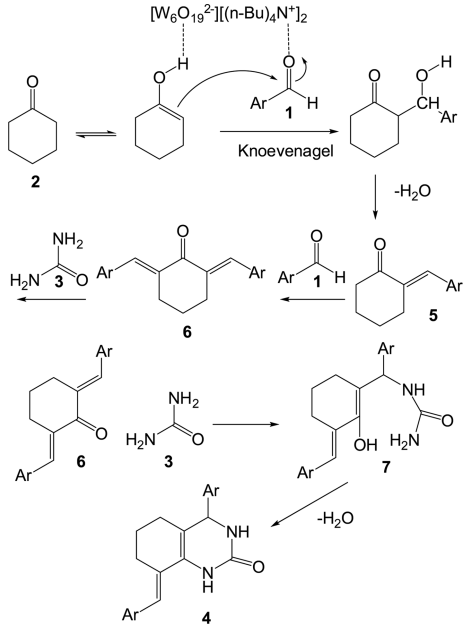


Figure 1. Recycling of $[TBA]_2[W_6O_{19}]$ catalyst on the product of 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one.

ed two times with an aliquot of fresh CH_2Cl_2 (2 × 10 mL), then drying to ready for later run. The recycled catalyst could be reused four times without any additional treatment or appreciable reduction in catalytic activity (Table 4 &



Scheme 2. A plausible mechanism for the formation of the 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones.

Figure 1).

The suggested mechanism of the $[W_6O_{19}^{2-}][(n\text{-}Bu)_4N^+]_2$ catalyzed transformations is shown in Scheme 2. As reported in the literature the Knoevenagel type coupling of benzaldehyde with cyclohexanone gives benzylidene **5**. Further reaction of benzylidene **5** with benzaldehyde to provide α,α'-bis (benzylidene) cyclohexanone **6**. Then compound **6** undergoes intramolecular cyclization to form the intermediate **7**. From intermediate **7**, a water molecule is eliminated to form the product 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones (Scheme 2). Based on the previous report,[23] we can understand that $[W_6O_{19}^{2-}][(n\text{-}Bu)_4N^+]_2$ can play a dual role. Thus, it is proposed that the tetrabutylammonium ion $[(n\text{-}Bu)_4N^+]$ induces the polarization of the carbonyl groups, whereas the terminal oxygen atoms or the bridging oxygen atom in the polyoxometalate anion, $W_6O_{19}^{2-}$, are slightly basic and can promote the necessary reactions. The $[W_6O_{19}^{2-}][(n\text{-}Bu)_4N^+]_2$ can therefore activate the reactants and the intermediates in this reaction.

Experimental

Chemicals and Analysis. All reagents were purchased from Merck, Fluka and Aldrich Chemical Companies and used without further purification. All yields refer to isolated products after purification. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were obtained using Bruker DRX-500 Avance at ambient temperature, using TMS as internal standard. FT-IR spectra were obtained as KBr discs on Shimadzu spectrometer. Mass spectra were determined on a Varion-Saturn 2000 GC/MS instrument. Elemental analysis was measured by means of Perkin Elmer 2400 CHN elemental analyzer flowchart.

Synthesis of Tetrabutylammonium Hexatungstate $[TBA]_2$ $[W_6O_{19}]$. A mixture of sodium tungstate dihydrate, $Na_2WO_4{\cdot}2H_2O$ (99%, 33 g, 0.1 mol), acetic anhydride (40 mL), and *N*,*N*-dimethylformamide (DMF, 30 mL) was heated at 100 °C for 3 h to obtain a white cream. A solution of acetic anhydride (20 mL) and 12 M HCl (18 mL) in DMF (50 mL) was then added in a drop-wise manner over a period of time with stirring, and the resulting mixture was filtered to remove the un-dissolved white solids. A solution of tetrabutylammonium bromide (15.1 g, 0.047 mol) in methanol (50 mL) was then added to the filtrate with rapid stirring to give a white precipitate, and the resulting suspension was stirred for 5 min and the product subsequently collected by filtration. Recrystallization from a minimum amount of hot dimethyl sulfoxide (DMSO) gave the product as colorless diamond-shaped crystals.[33]

General Procedure for the Preparation of Pyrimidinone Derivatives. A mixture of aldehyde (1 mmol), cyclohexanone (1 mmol), urea (1.2 mmol) or thiourea (1.2 mmol), and $[TBA]_2[W_6O_{19}]$ (5 mol %) was stirred at 80 °C. The completion of the reaction was monitored with thin-layer chromatography (TLC; ethyl acetate:cyclohexane, 1:1). After the completion of the reaction, water (10 mL) was added, and the product was filtered. Then, it was recrystallized from ethyl alcohol. The products were characterized by spectral data (IR, ^{1}H NMR, ^{13}C NMR and mass) and comparison of their physical data with the literature data. The spectral data of some synthesized compounds are given.

Spectral Data of the Synthesized Compounds (4a-n).

8-Benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4a): White solid; IR (KBr, cm^{-1}): 3377 and 3216 (N–H str.), 1674 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.16–2.28 (m, 2H, CH_2), 2.45–2.57 (m, 2H, CH_2), 2.70–2.85 (m, 2H, CH_2), 5.47 (s, 1H, CH), 6.82 (s, 1H, CH), 7.29 (s, 1H, NH-3), 7.39-7.77 (m, 10H, Ar-H), 9.33 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.1, 27.0, 28.4, 55.0, 113.6, 127.1, 128.2, 128.5, 129.3, 129.6, 130.5, 131.5, 132.7, 133.6, 135.0, 137.1, 142.6, 156.2; MS (ESI): *m/z* 317 $(M+H)^+$; Anal. Calcd for $C_{21}H_{20}N_2O$: C, 79.75; H, 6.33; N, 8.86%. Found: C, 79.66; H, 6.24; N, 8.82%.

8-(4-Fluorobenzylidene)-4-(4-fluorophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4b): White solid; IR (KBr, cm^{-1}): 3366 and 3211 (N–H str.), 1655 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.08–2.22 (m, 2H, CH_2), 2.32–2.44 (m, 2H, CH_2), 2.67–2.79 (m, 2H, CH_2), 5.55 (s, 1H, CH), 6.70 (s, 1H, CH), 7.22 (s, 1H, NH-3), 7.30-7.63 (m, 8H, Ar-H), 9.27 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.2, 26.9, 28.0, 54.6, 113.7, 127.0, 128.0, 128.3, 129.1, 129.5, 130.1, 131.0, 132.6, 133.6, 134.4, 136.8, 142.6, 154.7; MS (ESI): *m/z* 353 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}F_2N_2O$: C, 71.59; H, 5.11; N, 7.95%. Found: C, 71.55; H, 5.01; N, 7.88%.

8-(3-Bromobenzylidene)-4-(3-bromophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4c): White solid; IR (KBr, cm^{-1}): 3372 and 3216 (N–H str.), 1664 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.16–2.27 (m, 2H, CH_2), 2.36–2.49 (m, 2H, CH_2), 2.69–2.81 (m, 2H, CH_2), 5.60 (s, 1H, CH), 6.72 (s, 1H, CH), 7.17 (s, 1H, NH-3), 7.28-7.55 (m, 8H, Ar-H), 9.32 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.9, 27.4, 28.7, 55.2, 113.8, 127.6, 128.3, 128.8, 129.5, 129.7, 130.7, 131.9, 132.7, 133.2, 135.4, 137.4, 142.5, 154.7; MS (ESI): *m/z* 474 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}Br_2N_2O$: C, 53.19; H, 3.80; N, 5.91%. Found: C, 53.16; H, 3.84; N, 5.95%.

8-(3-Nitrobenzylidene)-4-(3-nitrophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4d): White solid; IR (KBr, cm^{-1}): 3371 and 3222 (N–H str.), 1653 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.05–2.17 (m, 2H, CH_2), 2.27–2.42 (m, 2H, CH_2), 2.60–2.79 (m, 2H, CH_2), 5.60 (s, 1H, CH), 6.66 (s, 1H, CH), 7.24 (s, 1H, NH-3), 7.18-7.34 (m, 8H, Ar-H), 9.45 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.7, 26.5, 28.0, 55.1, 113.6, 127.3, 128.4, 128.9, 129.8, 130.2, 130.6, 131.4, 132.6, 133.2, 135.4, 137.7, 143.1, 156.0; MS (ESI): *m/z* 407 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}N_4O_5$: C, 62.07; H, 4.43; N, 13.79%. Found: C, 62.00; H, 4.33; N, 13.77%.

8-(2-Chlorobenzylidene)-4-(2-chlorophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4e): White solid; IR (KBr, cm^{-1}): 3368 and 3198 (N–H str.), 1662 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.13–2.22 (m, 2H, CH_2), 2.29–2.42 (m, 2H, CH_2), 2.66–2.81 (m, 2H, CH_2), 5.55 (s, 1H,

CH), 6.77 (s, 1H, CH), 7.22 (s, 1H, NH-3), 7.33-7.55 (m, 8H, Ar-H), 9.30 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.2, 27.4, 28.1, 54.8, 113.0, 127.6, 128.4, 128.7, 129.1, 129.6, 130.9, 131.6, 132.3, 133.3, 135.2, 136.7, 142.4, 153.9; MS (ESI): *m/z* 384 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}Cl_2N_2O$: C, 65.47; H, 4.68; N, 7.27%. Found: C, 65.33; H, 4.66; N, 7.22%.

8-(4-Nitrobenzylidene)-4-(4-nitrophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4f): White solid; IR (KBr, cm^{-1}): 3357 and 3233 (N–H str.), 1652 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.10–2.23 (m, 2H, CH_2), 2.31–2.44 (m, 2H, CH_2), 2.66–2.79 (m, 2H, CH_2), 5.64 (s, 1H, CH), 6.69 (s, 1H, CH), 7.15 (s, 1H, NH-3), 7.19-7.40 (m, 8H, Ar-H), 9.37 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.4, 26.7, 27.9, 55.0, 113.5, 127.5, 128.3, 128.8, 129.7, 129.8, 130.4, 131.6, 132.7, 133.2, 135.6, 137.7, 143.2, 154.7; MS (ESI): *m/z* 407 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}N_4O_5$: C, 62.07; H, 4.43; N, 13.79%. Found: C, 62.05; H, 4.42; N, 13.75%.

8-(4-Methylbenzylidene)-4-(4-methylphenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4g): White solid; IR (KBr, cm^{-1}): 3369 and 3207 (N–H str.), 1654 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.06 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 2.23–2.33 (m, 2H, CH_2), 2.42–2.54 (m, 2H, CH_2), 2.67–2.76 (m, 2H, CH_2), 5.44 (s, 1H, CH), 6.74 (s, 1H, CH), 7.19 (s, 1H, NH-3), 7.28-7.45 (m, 8H, Ar-H), 9.29 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.9, 25.9, 27.2, 55.2, 113.6, 127.8, 128.6, 128.9, 129.6, 129.9, 130.7, 131.3, 132.0, 133.4, 134.9, 136.3, 143.0, 155.7; MS (ESI): *m/z* 345 $(M+H)^+$; Anal. Calcd for $C_{23}H_{24}N_2O$: C, 80.23; H, 6.98; N, 8.14%. Found: C, 80.11; H, 6.89; N, 8.12%.

8-(4-Methoxybenzylidene)-4-(4-methoxyphenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-one (4h): White solid; IR (KBr, cm^{-1}): 3362 and 3203 (N–H str.), 1669 (C = O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.17–2.27 (m, 2H, CH_2), 2.35–2.47 (m, 2H, CH_2), 2.70–2.83 (m, 2H, CH_2), 3.66 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 5.55 (s, 1H, CH), 6.88 (s, 1H, CH), 7.22 (s, 1H, NH-3), 7.30-7.60 (m, 8H, Ar-H), 9.34 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.0, 27.3, 28.1, 54.4, 113.3, 127.7, 128.2, 128.5, 129.0, 129.7, 130.7, 131.6, 132.4, 133.8, 134.7, 136.7, 142.7, 153.9; MS (ESI): *m/z* 377 $(M+H)^+$; Anal. Calcd for $C_{23}H_{24}N_2O_3$: C, 73.40; H, 6.38; N, 7.45%. Found: C, 73.33; H, 6.39; N, 7.49%.

8-Benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-thione (4i): White solid; IR (KBr, cm^{-1}): 3315 and 3219 (N–H str.), 1208 (C = S str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.09–2.19 (m, 2H, CH_2), 2.32–2.44 (m, 2H, CH_2), 2.74–2.83 (m, 2H, CH_2), 5.33 (s, 1H, CH), 6.73 (s, 1H, CH), 7.28 (s, 1H, NH-3), 7.20-7.50 (m, 10H, Ar-H), 9.21 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.7, 27.7, 28.5, 55.1, 113.4, 127.4, 128.3, 128.8, 129.6, 130.3, 131.2, 131.9, 132.9, 133.8, 135.2, 137.2, 143.0, 156.1; MS (ESI): *m/z* 333 $(M+H)^+$; Anal. Calcd for $C_{21}H_{20}N_2S$: C, 75.90; H, 6.02; N, 8.43%. Found: C, 75.94; H, 6.06; N, 8.38%.

8-(4-Bromobenzylidene)-4-(4-bromophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-thione (4j): White solid; IR (KBr, cm^{-1}): 3318 and 3221 (N–H str.), 1222 (C = S str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.13–2.29 (m, 2H, CH_2), 2.34–2.47 (m, 2H, CH_2), 2.74–2.82 (m, 2H, CH_2), 5.55 (s, 1H, CH), 6.80 (s, 1H, CH), 7.20 (s, 1H, NH-3), 7.40-7.57 (m, 8H, Ar-H), 9.36 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.3, 27.3, 28.2, 54.2, 113.2, 127.2, 128.2, 128.5, 129.2, 129.5, 130.7, 131.5, 132.1, 133.1, 134.7, 137.6, 143.4, 157.4; MS (ESI): *m/z* 490 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}Br_2N_2S$: C, 51.45; H, 3.67; N, 5.72%. Found: C, 51.33; H, 3.66; N, 5.77%.

8-(2-Fluorobenzylidene)-4-(2-fluorophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-thione (4k): White solid; IR (KBr, cm^{-1}): 3314 and 3208 (N–H str.), 1215 (C = S str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07–2.17 (m, 2H, CH_2), 2.32–2.40 (m, 2H, CH_2), 2.70–2.82 (m, 2H, CH_2), 5.57 (s, 1H, CH), 6.77 (s, 1H, CH), 7.19 (s, 1H, NH-3), 7.38-7.54 (m, 8H, Ar-H), 9.37 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.3, 25.3, 27.9, 54.5, 113.2, 127.2, 128.2, 128.6, 129.2, 129.3, 130.7, 131.7, 132.3, 133.1, 134.7, 136.7, 142.2, 155.0; MS (ESI): *m/z* 369 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}F_2N_2S$: C, 68.48; H, 4.89; N, 7.61%. Found: C, 68.37; H, 4.90; N, 7.65%.

8-(3-Nitrobenzylidene)-4-(3-nitrophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-thione (4l): White solid; IR (KBr, cm^{-1}): 3329 and 3193 (N–H str.), 1209 (C = S str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.10–2.20 (m, 2H, CH_2), 2.27–2.40 (m, 2H, CH_2), 2.66–2.77 (m, 2H, CH_2), 5.44 (s, 1H, CH), 6.77 (s, 1H, CH), 7.13 (s, 1H, NH-3), 7.27-7.47 (m, 8H, Ar-H), 9.27 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.1, 27.2, 28.6, 57.3, 114.7, 128.1, 128.7, 129.0, 129.9, 130.2, 130.5, 131.4, 132.6, 133.6, 136.0, 138.1, 142.5, 153.9; MS (ESI): *m/z* 423 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}N_4SO_4$: C, 58.82; H, 3.92; N, 13.72%. Found: C, 58.77; H, 3.92; N, 13.70%.

8-(4-Chlorobenzylidene)-4-(4-chlorophenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-thione (4m): White solid; IR (KBr, cm^{-1}): 3327 and 3211 (N–H str.), 1216 (C = S str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07–2.16 (m, 2H, CH_2), 2.34–2.47 (m, 2H, CH_2), 2.75–2.87 (m, 2H, CH_2), 5.45 (s, 1H, CH), 6.87 (s, 1H, CH), 7.21 (s, 1H, NH-3), 7.36-7.59 (m, 8H, Ar-H), 9.37 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.5, 26.5, 27.8, 54.7, 113.3, 127.3, 128.2, 128.5, 129.2, 129.3, 130.5, 131.5, 132.1, 133.1, 134.7, 136.7, 142.6, 153.9; MS(ESI): *m/z* 401 $(M+H)^+$; Anal. Calcd for $C_{21}H_{18}Cl_2N_2S$: C, 62.86; H, 4.49; N, 6.98%. Found: C, 62.80; H, 4.39; N, 6.89%.

8-(4-Methylbenzylidene)-4-(4-methylphenyl)-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-thione (4n): White solid; IR (KBr, cm^{-1}): 3320 and 3207 (N–H str.), 1212 (C = S str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.21–2.33 (m, 2H, CH_2), 2.44–2.53 (m, 2H, CH_2), 2.68–2.77 (m, 2H, CH_2), 5.24 (s, 1H, CH), 6.63 (s, 1H, CH), 7.11 (s, 1H, NH-3), 7.30-7.51 (m, 8H, Ar-H), 9.17 (s, 1H, NH-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.1, 26.8, 27.9, 55.4, 113.5, 127.0, 128.2, 128.8, 129.3, 129.5, 131.1, 131.4, 131.9, 134.0, 136.3, 137.1, 142.7, 154.8; MS (ESI): *m/z* 361 $(M+H)^+$; Anal. Calcd for $C_{23}H_{24}N_2S$: C, 76.67; H, 6.67; N, 7.78%. Found: C, 76.62; H, 6.64; N, 7.73%.

Conclusion

In conclusion, we have demonstrated that $[TBA]_2[W_6O_{19}]$ can be used as a highly efficient and recyclable heterogeneous catalyst for the one-pot synthesis of 8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-1*H*-quinazolin-2-ones/thiones by coupling various aromatic aldehydes with cyclohexanone and urea or thiourea under solvent-free conditions at 80 °C. Use of the relatively nontoxic and reusable green catalyst, high catalytic efficiency, good yields, short reaction times, and straightforward workup under green conditions are advantages of this protocol.

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