Received: 24 February 2018 | Revised: 3 July 2018 | Accepted: 4 July 2018

DOI: 10.1002/jccs.201800071

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

ARTICLE

Green synthesis of novel pyrazolo-fused benzophenazines using $H_3PW_{12}O_{40}$ as efficient and recyclable catalyst under microwave irradiation

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A high-yield, atom-efficient, and green protocol for the synthesis of novel pyrazolo-fused benzophenazines utilizing a multicomponent condensation reaction between 2-hydroxynaphthalene-1,4-dione, *o*-phenylenediamine, aromatic aldehydes, and 4-methylbenzenesulfonohydrazide in the presence of phosphotungstic acid ($H_3PW_{12}O_{40}$) under microwave irradiation (MWI) in EtOH is reported. We provide a novel series of 1*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives interesting for biological screening tests. This protocol offers several advantages satisfying many principles of green chemistry, including atom economy, energy saving, clean reactions, inexpensive reagents, reusability of $H_3PW_{12}O_{40}$, the absence of any tedious work-up or purification, and avoidance of hazardous or toxic reagents/catalysts/solvents.

KEYWORDS

benzophenazine, environmentally friendly, microwave irradiation, multicomponent reaction (MCR), phosphotungstic acid, pyrazole derivative

1 | INTRODUCTION

Phenazine systems comprise a large group of natural and synthetic *N*-containing heterocycles, including more than 100 different compounds of natural origin and over 6000 synthetic compounds. Phenazine natural products are isolated as secondary metabolites primarily from *Pseudomonas*, *Streptomyces*, and a number of other bacterial genera from soil or marine habitats. Phenazine systems are among the important scaffolds and have been proven to possess various biological activities including antibiotic, antimicrobial, antimalarial, antiparasitic, and antitumor activities.[1–4] Synthetic phenazines, such as NC-190, XR-11576, and XR-5944 (Figure 1), were reported to show antiproliferative effects against a variety of human cancer cell lines.[5–7] These reports indicated that benzo[*a*]phenazine derivatives act as dual inhibitors of topoisomerase I and II and in the cell cycle [8,9] topology of DNA affected by key enzymes, while some act as anticancer and antitumor agents. Also, pyridophenazinediones and pyridazinophenazinedione derivatives have shown antitumor activity.[10,11] In addition, fluorescent phenazine derivatives have been applied as photosensitizers in photodynamic therapy (PDT),[12] in which a combination of light and a photosensitizer creates highly reactive oxygen species or hydroxyl radicals near the tumor to selectively destroy the targeted tissue.

Moreover, pyrazoles and their derivatives are a major category of nitrogen-containing heterocyclic compounds that have become increasingly important to the pharmaceutical, chemical, and agricultural industries in recent years.[13–15] These five-membered heterocycles are a key class of bioactive heterocycles because they possess antimicrobial, anticancer, analgesic, anti-inflammatory, anti-tubercular, antidepressant, antihelmintic, anticonvulsant, antipyretic, antioxidant, and herbicidal properties.[16,17]

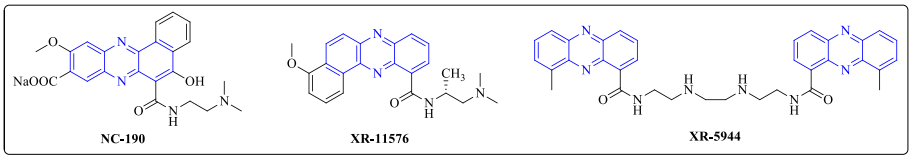


FIGURE 1 Biologically active phenazine derivatives

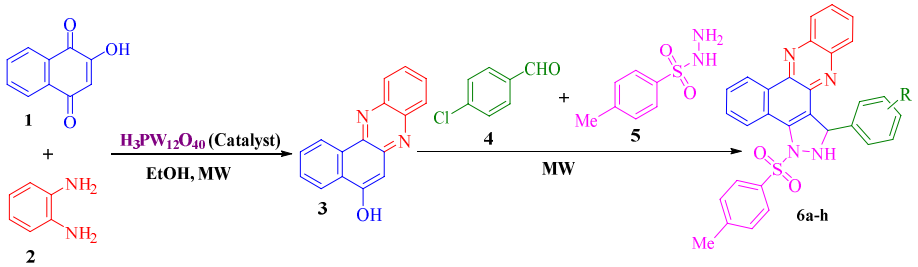
On the other hand, the development of green chemistry techniques has received considerable attention for the synthesis of biologically interesting compounds. Proper choice of the starting materials (use of safe, readily available, cheap, and environmentally benign reagents), atom-economic methodologies with a minimum number of chemical steps, appropriate use of greener reaction conditions such as multicomponent reactions (MCRs), microwave reactions, water solvent medium, PEG-400, reusable heterogeneous catalytic conditions, catalyst- and solvent-free conditions, an ionic liquid, etc., and efficient strategies for product isolation and purification are part of the exploration toward the green chemistry for sustainability.[18–25]

Considering the significant potential of novel pyrazole and benzophenazine derivatives as a source of valuable drug candidates, together with our continued interest on MCRs and our ongoing program for the synthesis of a wide range of complex organic compounds based on green chemistry protocols,[26–30] here we report a green and efficient method for the synthesis of novel 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazines (**6**) through a single-pot multicomponent condensation reaction between 2-hydroxy-1,4-naphthoquinone (**1**), *o*-phenylenediamine (**2**), aromatic aldehydes (**4**), and 4-methylbenzenesulfonohydrazide (**5**) catalyzed by phosphotungstic acid ($H_3PW_{12}O_{40}$) as a highly efficient, eco-friendly, and recyclable solid heteropolyacid catalyst under microwave irradiation (MWI) (180 W, max. 70 °C) in EtOH (Scheme 1).

2 | RESULTS AND DISCUSSION

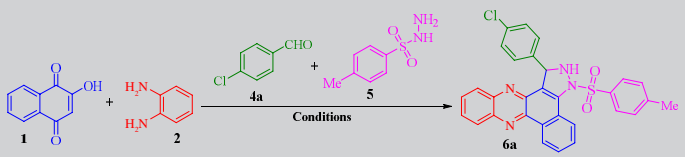
The protocol provided five bonds (one C−C, two C−N, and two C=N) and two new rings in a single operation through condensation/Knoevenagel/Michael/annulation sequences. In order to investigate the reaction conditions for the synthesis of 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives, we carried out the reaction between 2-hydroxynaphthalene-1,-4-dione (**1**) (1 mmol), *o*-phenylenediamine (**2**) (1 mmol), 4-chlorobenzaldehyde (**4a**) (1 mmol), and 4-methylbenzenesulfonohydrazide (**5**) (1 mmol) in EtOH as a model. Initially, to minimize by-product formation, 2-hydroxynaphthalene-1,-4-dione and *o*-phenylenediamine were condensed under MWI at 180 W (max. 70 °C) to form an orange solid of benzo[*a*]phenazin-5-ol (**3**) without using any catalyst, and after approximately 5 min, 4-chlorobenzaldehyde and 4-methylbenzenesulfonohydrazide were added, the mixture was subjected to MWI at 180 W (max. 70 °C), and the progress of the reaction was followed by thin-layer chromatography (TLC). As shown in Table 1, only a trace amount of the product was detected under catalyst-free conditions (entry 1). However, **6a** was obtained in 53% yield when the reaction was conducted in the presence of oxalic acid (10 mol%) in EtOH (entry 2). Several catalysts were evaluated in the reaction, including oxalic acid, PTSA, $H_3PMo_{12}O_{40}$, and $H_3PW_{12}O_{40}$; these were all added in substoichiometric amounts (10 mol%), and the reactions were carried out in ethanol under MWI. The reaction proceeded smoothly in the presence of $H_3PW_{12}O_{40}$, affording higher yield (87%) within 15 min (entry 5). As can be seen, among the tested solvents (EtOH, H_2O, EtOH/H_2O (1:1), and PEG-400; no other organic solvent was tested because of the green chemistry concept) and various amounts of the catalyst, the reaction was more facile and proceeded to give the highest yield using 10 mol% of $H_3PW_{12}O_{40}$ in EtOH under MWI (180 W, max. 70 °C) (entry 5). No significant improvement in yield or reaction time was observed using a higher amount of the catalyst.

Using these optimized conditions, the reaction scope was evaluated by using different benzaldehydes (*ortho*-, *meta*-, and *para*-substituted benzene rings). Commercially available aromatic aldehydes bearing either electron-withdrawing or electron-donating functional groups were all found to be



SCHEME 1 $H_3PW_{12}O_{40}$-catalyzed synthesis of 1-aryl-3-tosyl-2,3-dihydro-1*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazines (**6a–h**) under microwave irradiation in EtOH

TABLE 1 Optimization of reaction conditions of compound **6a**[a]



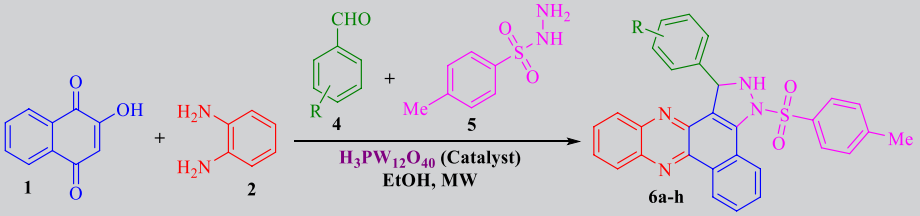
Entry	Catalyst	Reaction conditions	Time (min)	Yield (%)[b]
1	None	EtOH, 180 W	60	Trace
2	Oxalic acid (10 mol%)	EtOH, 180 W	15	53
3	PTSA (10 mol%)	EtOH, 180 W	15	82
4	$H_3PMo_{12}O_{40}$ (10 mol%)	EtOH, 180 W	15	79
5	$H_3PW_{12}O_{40}$ (10 mol%)	EtOH, 180 W	15	87
6	$H_3PW_{12}O_{40}$ (10 mol%)	H_2O, 180 W	15	66
7	$H_3PW_{12}O_{40}$ (10 mol%)	EtOH/H_2O (1:1), 180 W	15	75
8	$H_3PW_{12}O_{40}$ (10 mol%)	PEG-400, 180 W	15	71
9	$H_3PW_{12}O_{40}$ (20 mol%)	EtOH, 180 W	15	88
10	$H_3PW_{12}O_{40}$ (5 mol%)	EtOH, 180 W	20	70
11	$H_3PW_{12}O_{40}$ (10 mol%)	EtOH, 100 W	20	48
12	$H_3PW_{12}O_{40}$ (10 mol%)	EtOH, 300 W	10	85
13	$H_3PW_{12}O_{40}$ (10 mol%)	EtOH, rt	120	Trace

[a] *Reaction conditions*: 2-hydroxynaphthalene-1,4-dione (1 mmol), *o*-phenylenediamine (1 mmol), 4-chlorobenzaldehyde (1 mmol), and 4-methylbenzenesulfonohydrazide (1 mmol) in the presence of different catalytic systems under various conditions.
[b] Isolated yields.

suitable for this one-pot, two-step, four-component, microwave-assisted synthesis of 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives, providing good yields of 78–87% (Table 2, entries 1–8). Structural assignments were made on the basis of IR, ^{1}H NMR, ^{13}C NMR, and elemental analysis. The mass spectra of these compounds displayed molecular ion peaks at the appropriate *m/z* values.

Since the recovery of the catalyst is important in green organic synthesis, we also used our optimized reaction conditions to evaluate the reusability of the catalyst ($H_3PW_{12}O_{40}$). After the completion of the reaction, the reaction mixture was cooled to room temperature. Then, 5 mL of water was added to the mixture, and the crude solid product was filtered and washed repeatedly with water. $H_3PW_{12}O_{40}$ was removed from the reaction medium by washing with H_2O. Since the catalyst is soluble in water, the catalyst was recovered by evaporation of the aqueous solution and washed with diethyl ether and reused for the same

TABLE 2 One-pot, four-component synthesis of 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives[a]



Entry	R	Product	Time (min)	Yield (%)[b]
1	4-Cl	**6a**	15	87
2	4-NO_2	**6b**	15	85
3	4-Br	**6c**	15	81
4	3-NO_2	**6d**	15	83
5	2-NO_2	**6e**	15	80
6	H	**6f**	20	82
7	4-Me	**6g**	20	81
8	4-OMe	**6h**	20	78

[a] *Reaction conditions*: 2-hydroxynaphthalene-1,4-dione (1 mmol), *o*-phenylenediamine (1 mmol), aromatic aldehyde (1 mmol), 4-methylbenzenesulfonohydrazide (1 mmol), and $H_3PW_{12}O_{40}$ (10 mol%) under microwave irradiation (180 W, max. 70 °C) in EtOH (10 mL).
[b] Isolated yields.

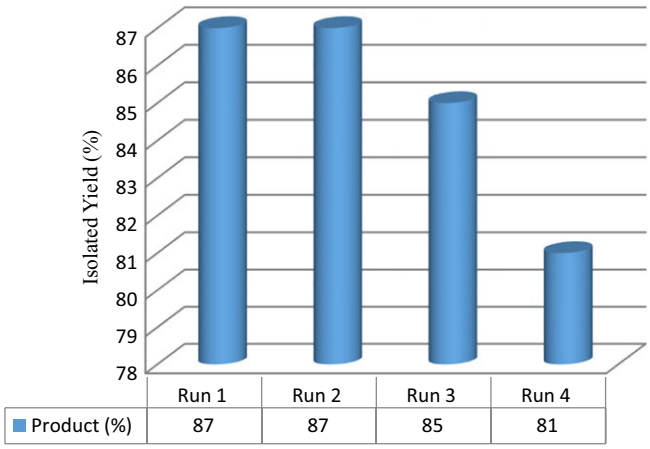
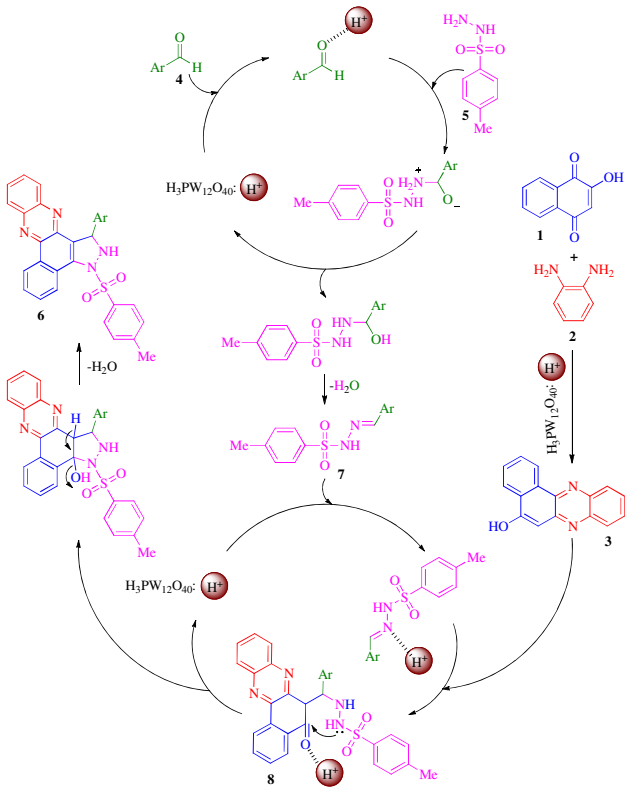


FIGURE 2 Investigation of the recycling of $H_3PW_{12}O_{40}$ (10 mol%) in the synthesis of **6a** from 2-hydroxynaphthalene-1,4-dione (1 mmol), *o*-phenylenediamine (1 mmol), 4-chlorobenzaldehyde (1 mmol), and 4-methylbenzenesulfonohydrazide (1 mmol) under microwave irradiation (180 W, max. 70 °C) in EtOH (15 min)

experiment. We found that the catalyst could be used at least four times with only a slight reduction in activity (Figure 2).

A detailed reaction mechanism for the cyclocondensation of 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazines **6** using $H_3PW_{12}O_{40}$ as the Brønsted acid catalyst is shown in Scheme 2. In this mechanism, the primary condensation of 2-hydroxynaphthalene-1,4-dione (**1**) with *o*-phenylenediamine (**2**) in the presence of $H_3PW_{12}O_{40}$ gives benzo[*a*]phenazin-5-ol **3**. On the other hand, $H_3PW_{12}O_{40}$ is an efficient catalyst to form the hydrazone (**7**), which readily forms *in situ* from the condensation of the aromatic aldehyde (**4**) with 4-methylbenzenesulfonohydrazide (**5**). The Michael addition of benzo[*a*]phenazin-5-ol **3** with hydrazone (**7**) in the presence of $H_3PW_{12}O_{40}$ finally gives the intermediate **8**, which then forms the inner molecular ring after a tautomeric proton shift to produce the corresponding product (**6**).



SCHEME 2 Proposed mechanism for the synthesis of 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives

3 | EXPERIMENTAL

3.1 | General procedures

The chemicals used in this work were purchased from Merck and Aldrich and used without further purification. All melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-470 spectrometer. Elemental analyses for C, H, and N were performed using a Costech ECS 4010 CHNS-O analyzer at the analytical laboratory of Islamic Azad University Yazd branch. Mass spectra were recorded on an Agilent Technology (HP) spectrometer operating at an ionization potential of 70 eV. NMR spectra were obtained on a Bruker DRX-400 Avance spectrometer (^{1}H NMR at 400 Hz, ^{13}C NMR at 100 Hz) in $CDCl_3$ using TMS as the internal standard. Chemical shifts (δ) are given in ppm and coupling constants (J) in hertz. All reactions were carried out using a laboratory microwave oven (MicroSYNTH, Milestone Co., Italy). TLC was performed on silica gel Polygram SILG/UV 254 plates. The required starting material 4-methylbenzenesulfonohydrazide (**5**) was prepared by the reaction of 4-methylbenzene-1-sulfonyl chloride (tosyl chloride) with hydrazine hydrate at 0 °C in THF.[31]

3.2 | General procedure for the synthesis of novel 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives (6a–h)

$H_3PW_{12}O_{40}$ (10 mol%) was added to a mixture of 2-hydroxynaphthalene-1,4-dione (**1**) (1 mmol) and *o*-phenylenediamine (**2**) (1 mmol) in EtOH (10 mL), and this mixture was irradiated in a microwave oven at 180 W until (in less than 5 min) an orange solid of benzo[*a*]phenazin-5-ol (**3**) was formed. The microwave was programmed to give a maximum internal temperature of 70 °C. Then, aryl aldehydes (**4**) (1 mmol) and 4-methylbenzenesulfonohydrazide (1 mmol) (**5**) were added to the above reaction mixture, which was irradiated further at the same temperature (180 W, max. 70 °C) for an appropriate time as shown in Table 2. Upon completion of the reaction (monitored by TLC), the reaction mixture was allowed to cool to room temperature. Then, 5 mL of water was added to the mixture and filtered for separation of the crude product. The separated product was washed twice with water (2 × 5 mL). The solid crude product was subsequently recrystallized from hot

ethanol to give the pure product **6**. The spectral and analytical data are presented below:

3.2.1 | 1-(4-Chlorophenyl)-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6a)

Brown powder; yield 0.467 g (87%), mp 261–263 °C; IR (KBr): ν_{max} = 3285, 3115, 2920, 1636, 1585, 1535, 1465, 1403, 1337, 1315, 1282, 1161, 1024, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, CH_3), 5.29 (s, 1H, CH), 6.93 (d, 1H, J = 8.4 Hz, Ar-H), 7.03–7.58 (m, 5H, Ar-H), 7.62 (d, 2H, J = 8.8 Hz, Ar-H), 7.76 (d, 2H, J = 8.0 Hz, Ar-H), 7.86 (d, 2H, J = 8.0 Hz, Ar-H), 7.88–8.18 (m, 2H, Ar-H), 8.24 (d, 1H, J = 8.0 Hz, Ar-H), 8.33–8.47 (m, 1H, Ar-H), 8.54 (d, 1H, J = 8.0 Hz, Ar-H), 9.22 (d, 1H, J = 7.6 Hz, Ar-H), 9.97 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.2 (CH_3), 64.8 (CH), 116.2, 120.7, 123.8, 124.1, 125.7, 127.5, 128.3, 128.4, 129.1, 129.4, 129.9, 130.0, 130.2, 130.9, 131.1, 131.6, 132.2, 137.5, 138.4, 140.5, 141.6, 142.1, 146.0, 146.8 and 148.5 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 537 (M^+, 4); Anal. Calcd for $C_{30}H_{21}ClN_4O_2S$: C, 67.09; H, 3.94; N, 10.43; S, 5.97%. Found: C, 67.34; H, 4.12; N, 10.72; S, 6.15%.

3.2.2 | 1-(4-Nitrophenyl)-3-tosyl-2,3-dihydro-1H-benzo[a]pyrazolo[3,4-c]phenazine (6b)

Brown powder; yield 0.465 g (85%), mp 288–290 °C; IR (KBr): ν_{max} = 3310, 3060, 2915, 1644, 1592, 1515, 1469, 1406, 1383, 1340, 1282, 1166, 1048, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3), 5.37 (s, 1H, CH), 7.20 (d, 1H, J = 8.0 Hz, Ar-H), 7.56 (d, 2H, J = 7.6 Hz, Ar-H), 7.59 (d, 2H, J = 8.8 Hz, Ar-H), 7.68 (d, 1H, J = 8.4 Hz, Ar-H), 7.72 (d, 2H, J = 8.0 Hz, Ar-H), 7.76–8.30 (m, 3H, Ar-H), 8.33 (d, 2H, J = 8.8 Hz, Ar-H), 8.42–8.65 (m, 2H, Ar-H), 9.28 (d, 1H, J = 8.0 Hz, Ar-H), 10.02 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3 (CH_3), 65.2 (CH), 115.7, 121.5, 122.3, 124.5, 125.2, 127.3, 128.5, 128.8, 129.0, 129.5, 129.7, 130.1, 130.2, 130.5, 131.3, 131.6, 132.5, 136.8, 138.3, 141.9, 142.8, 145.2, 146.3, 147.4 and 150.1 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 547 (M^+, 1); Anal. Calcd for $C_{30}H_{21}N_5O_4S$: C, 65.80; H, 3.87; N, 12.79; S, 5.86%. Found: C, 65.62; H, 4.07; N, 12.87; S, 5.98%.

3.2.3 | 1-(4-Bromophenyl)-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6c)

Brown powder; yield 0.470 g (81%), mp 250–252 °C; IR (KBr): ν_{max} = 3280, 3025, 2895, 1635, 1586, 1523, 1468, 1397, 1377, 1337, 1279, 1164, 1048, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H, CH_3), 5.32 (s, 1H, CH), 7.19 (d, 2H, J = 8.4 Hz, Ar-H), 7.28–7.34 (m, 1H, Ar-H), 7.36 (d, 1H, J = 8.0 Hz, Ar-H), 7.54–7.57 (m, 1H, Ar-H), 7.59 (d, 2H, J = 8.4 Hz, Ar-H), 7.67–7.72 (m, 1H, Ar-H), 7.78 (d, 2H, J = 8.0 Hz, Ar-H), 7.83 (d, 2H, J = 8.4 Hz, Ar-H), 7.84–8.63 (m, 3H, Ar-H), 9.29 (d, 1H, J = 8.0 Hz, Ar-H), 10.14 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.2 (CH_3), 65.7 (CH), 115.5, 122.0, 122.2, 122.9, 124.5, 125.6, 127.5, 128.5, 128.7, 128.8, 129.1, 129.5, 129.7, 130.1, 130.4, 131.0, 132.3, 134.6, 137.2, 138.5, 140.7, 141.8, 142.5, 146.3, 147.1 and 148.8 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 581 (M^+, 7); Anal. Calcd for $C_{30}H_{21}BrN_4O_2S$: C, 61.97; H, 3.64; N, 9.64; S, 5.51%. Found: C, 62.23; H, 3.51; N, 9.85; S, 5.82%.

3.2.4 | 1-(3-Nitrophenyl)-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6d)

Brown powder; yield 0.454 g (83%), mp 281–283 °C; IR (KBr): ν_{max} = 3230, 3045, 2900, 1634, 1586, 1516, 1452, 1403, 1373, 1333, 1282, 1161, 1046, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, CH_3), 5.31 (s, 1H, CH), 7.23 (d, 1H, J = 8.0 Hz, Ar-H), 7.30 (d, 1H, J = 8.4 Hz, Ar-H), 7.33–7.37 (m, 1H, Ar-H), 7.41 (d, 2H, J = 8.0 Hz, Ar-H), 7.46 (d, 1H, J = 8.4 Hz, Ar-H), 7.56 (d, 1H, J = 8.8 Hz, Ar-H), 7.64 (d, 1H, J = 8.0 Hz, Ar-H), 7.68–8.08 (m, 2H, Ar-H), 8.10 (d, 2H, J = 8.4 Hz, Ar-H), 8.12–8.18 (m, 1H, Ar-H), 8.36 (d, 1H, J = 8.4 Hz, Ar-H), 8.72 (s, 1H, Ar-H), 9.28–9.42 (m, 1H, Ar-H), 10.11 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.8 (CH_3), 65.7 (CH), 116.5, 121.6, 122.7, 124.3, 126.1, 127.5, 128.6, 129.1, 129.4, 129.9, 130.1, 130.4, 130.6, 131.5, 132.7, 135.8, 137.2, 138.1, 142.0, 142.6, 144.1, 146.3, 147.2, 148.2 and 148.8 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 547 (M^+, 3); Anal. Calcd for $C_{30}H_{21}N_5O_4S$: C, 65.80; H, 3.87; N, 12.79; S, 5.86%. Found: C, 66.03; H, 4.11; N, 12.62; S, 6.04%.

3.2.5 | 1-(2-Nitrophenyl)-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6e)

Brown powder; yield 0.438 g (80%), mp 219–221 °C; IR (KBr): ν_{max} = 3265, 3030, 2885, 1635, 1589, 1525, 1490, 1468, 1399, 1337, 1281, 1146, 1050, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, CH_3), 5.31 (s, 1H, CH), 6.91 (d, 1H, J = 8.0 Hz, Ar-H), 7.13 (d, 1H, J = 8.0 Hz, Ar-H), 7.17–7.37 (m, 2H, Ar-H), 7.40 (d, 1H, J = 8.4 Hz, Ar-H), 7.45–7.75 (m, 3H, Ar-H), 7.79 (d, 2H, J = 8.4 Hz, Ar-H), 7.83–7.92 (m, 1H, Ar-H), 7.94 (d, 1H, J = 8.0 Hz, Ar-H), 7.98–8.66 (m, 1H, Ar-H), 9.14 (d, 1H, J = 7.6 Hz, Ar-H), 10.13 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3 (CH_3), 62.6 (CH), 115.6, 121.2, 123.8, 124.2, 125.91, 128.1, 128.5, 129.0, 129.4, 129.6, 130.3, 130.7, 131.0, 131.3, 132.5, 135.5, 137.5, 138.8, 140.7, 142.1, 142.8, 146.2, 146.7, 147.2 and 152.1 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 547 (M^+, 8); Anal. Calcd for $C_{30}H_{21}N_5O_4S$: C, 65.80; H, 3.87; N, 12.79; S, 5.86%. Found: C, 65.98; H, 3.97; N, 12.95; S, 6.12%.

3.2.6 | 1-Phenyl-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6f)

Brown powder; yield 0.412 g (82%), mp 249–250 °C; IR (KBr): ν_{max} = 3290, 3020, 2845, 1628, 1580, 1519, 1458, 1399, 1333, 1283, 1140, 1023, 754 cm^{-1}; ^1H NMR

(400 MHz, $CDCl_3$): δ 2.23 (s, 3H, CH_3), 5.27 (s, 1H, CH), 6.99 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz, Ar-H), 7.02 (d, 1H, J = 7.2 Hz, Ar-H), 7.13 (d, 1H, J = 7.6 Hz, Ar-H), 7.26–7.34 (m, 1H, Ar-H), 7.41 (d, 2H, J = 8.0 Hz, Ar-H), 7.45 (d, 1H, J = 8.0 Hz, Ar-H), 7.47–8.14 (m, 5H, Ar-H), 8.18 (d, 2H, J = 8.4 Hz, Ar-H), 8.25–8.31 (m, 1H, Ar-H), 8.60 (d, 1H, J = 8.0 Hz, Ar-H), 9.28 (d, 1H, J = 8.0 Hz, Ar-H), 9.94 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3 (CH_3), 64.9 (CH), 116.4, 121.5, 122.0, 125.4, 125.9, 127.4, 128.4, 128.5, 129.3, 129.6, 129.7, 129.8, 130.0, 130.3, 130.8, 131.5, 132.0, 137.2, 137.6, 141.8, 142.5, 144.5, 146.0, 146.7 and 147.8 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 502 (M^+, 14); Anal. Calcd for $C_{30}H_{22}N_4O_2S$: C, 71.69; H, 4.41; N, 11.15; S, 6.38%. Found: C, 71.92; H, 4.17; N, 11.43; S, 6.19%.

3.2.7 | 1-(p-Tolyl)-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6g)

Brown powder; yield 0.418 g (81%), mp 236–238 °C; IR (KBr): ν_{max} = 3170, 3035, 2900, 1634, 1590, 1542, 1496, 1461, 1406, 1336, 1277, 1150, 1050, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 5.25 (s, 1H, CH), 6.85–7.03 (m, 1H, Ar-H), 7.13 (d, 1H, J = 8.0 Hz, Ar-H), 7.19–7.37 (m, 2H, Ar-H), 7.40 (d, 2H, J = 8.4 Hz, Ar-H), 7.46 (d, 1H, J = 8.0 Hz, Ar-H), 7.55–7.72 (m, 3H, Ar-H), 7.80 (d, 2H, J = 8.0 Hz, Ar-H), 7.93–8.85 (m, 3H, Ar-H), 9.16–9.19 (m, 1H, Ar-H), 10.01 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1 and 21.3 ($2CH_3$), 65.1 (CH), 117.1, 122.9, 124.7, 125.3, 125.9, 127.3, 128.4, 128.8, 129.2, 129.6, 129.8, 130.1, 130.5, 130.8, 131.3, 131.7, 135.4, 136.8, 138.4, 140.5, 141.9, 142.4, 146.4, 146.9 and 149.4 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 516 (M^+, 9); Anal. Calcd for $C_{31}H_{24}N_4O_2S$: C, 72.07; H, 4.68; N, 10.85; S, 6.21%. Found: C, 71.85; H, 4.42; N, 10.99; S, 6.52%.

3.2.8 | 1-(4-Methoxyphenyl)-3-tosyl-2,3-dihydro-1*H*-benzo[a]pyrazolo[3,4-c]phenazine (6h)

Brown powder; yield 0.415 g (78%), mp 233–234 °C; IR (KBr): ν_{max} = 3195, 3030, 2885, 1634, 1587, 1541, 1491, 1451, 1406, 1333, 1278, 1157, 1049, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 5.26 (s, 1H, CH), 7.03 (d, 2H, J = 8.8 Hz, Ar-H), 7.05–7.08 (m, 1H, Ar-H), 7.18 (d, 1H, J = 8.4 Hz, Ar-H), 7.23–7.40 (m, 1H, Ar-H), 7.46 (d, 2H, J = 8.4 Hz, Ar-H), 7.56 (d, 1H, J = 8.0 Hz, Ar-H), 7.74 (d, 1H, J = 8.0 Hz, Ar-H), 7.77 (d, 2H, J = 8.4 Hz, Ar-H), 7.88 (d, 2H, J = 8.4 Hz, Ar-H), 8.15–8.61 (m, 2H, Ar-H), 9.24–9.27 (m, 1H, Ar-H), 10.03 (s, 1H, NH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7 ($2CH_3$), 56.2 (OCH_3), 64.7 (CH), 114.3, 115.8, 121.7, 122.5, 124.5, 125.8, 126.1, 127.5, 128.5, 128.9, 129.1, 129.4, 129.7, 130.3, 130.7, 131.4, 132.0, 136.8, 137.5, 138.9, 141.7, 142.4, 145.8, 146.5, 148.3 and 157.7 ($C_{olefinic}$ and C_{arom}) ppm; MS (*m/z*, %): 532 (M^+, 5); Anal. Calcd for $C_{31}H_{24}N_4O_3S$: C, 69.91; H, 4.54; N, 10.52; S, 6.02%. Found: C, 70.19; H, 4.41; N, 10.84; S, 6.23%.

4 | CONCLUSIONS

In this paper, we reported a green and straightforward procedure for the efficient synthesis of novel 11*H*-benzo[*a*]pyrazolo[3,4-*c*]phenazine derivatives in high yields through a single-pot, multicomponent protocol by using $H_3PW_{12}O_{40}$ as an inexpensive, nontoxic, highly reactive, and recyclable solid heteropolyacid catalyst under MWI in EtOH. Commercial availability of the chemicals, simple experimental procedure, easy work-up, high atom economy, short reaction times, high yields, and excellent chemoselectivity are the main advantages of this protocol. Our work has introduced a green and cost-effective methodology. Moreover, the synthesized chemicals are expected to show attractive pharmacological activities and may act as potential drug candidates, since benzophenazine and pyrazole motifs possess a wide range of biological activities.

ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the Research Council of Islamic Azad University of Yazd.

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How to cite this article: Mohebat R, Dehgan P, Yazdani-Elah-Abadi A. Green synthesis of novel pyrazolo-fused benzophenazines using $H_3PW_{12}O_{40}$ as efficient and recyclable catalyst under microwave irradiation. *J Chin Chem Soc*. 2018;1–7. https://doi.org/10.1002/jccs.201800071