Received: 16 January 2018 | Revised: 7 May 2018 | Accepted: 16 May 2018

DOI: 10.1002/jccs.201700470

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

ARTICLE

A green and practical one-pot two-step strategy for the synthesis of symmetric 3,6-diarylpyridazines

Mehdi Rimaz[1] | Hossein Mousavi[1] | Behzad Khalili[2] | Farkhondeh Aali[1]

[1]Department of Chemistry, Payame Noor University, Tehran, Iran

[2]Department of Chemistry, Faculty of Science, University of Guilan, Rasht, Iran

Correspondence
Mehdi Rimaz, Department of Chemistry, Payame Noor University, PO Box 19395-3697, Tehran, Iran.
Email: rimaz.mehdi@gmail.com

Funding information
Research Council of Payame Noor University, Grant/Award Number: 68424

A simple, mild, and efficient synthesis of symmetric 3,6-diarylpyridazine derivatives using a green catalytic one-pot two-step reaction of aryl methyl ketones, arylglyoxal monohydrates, and hydrazine hydrate was developed. Environmentally benign nature, high atom-economy, no harmful byproduct, easy workup procedure, no column chromatography steps, and moderate to excellent yields of the products are the salient features of this new multicomponent-based methodology.

KEYWORDS

3,6-Diarylpyridazine, aryl methyl ketone, arylglyoxal monohydrate, DABCO, one-pot, $ZrOCl_2 \cdot 8H_2O$

1 | INTRODUCTION

The field of green chemistry has quickly developed during the new century following the recognition that eco-friendly products and processes represent economically attractive long-term synthetic strategies. The important areas of green chemistry include the development of novel chemical processes that show intrinsically high atom-economies, pronounced energy savings, use of environmentally benign solvents and catalysts, low levels of waste production, and facile workup procedures.[1]

Nowadays, one-pot multicomponent reactions (MCRs) are very useful in organic synthesis, drug, and drug-like molecular discovery owing to their simplicity, flexibility, and efficiency compared with a conventional multistep linear synthetic strategy.[2]

Design and synthesis of symmetric heterocyclic compounds are currently receiving a great deal of attention due to their exclusive specifications and wide applications in organic synthesis, medicinal chemistry, inorganic chemistry, materials science and etc.[3]

Pyridazines belong to a family of six-membered *N*-heterocyclic compounds that exhibit remarkable pharmaceutical activities (Figure 1). For example, several members of this class of heterocyclic scaffolds have been utilized in the development of therapeutic agents that have been employed as antihistaminic,[4] antibacterial,[5] antihypertensive,[6] antidiabetic[7] and anti-inflammatory agents.[8] It is worth noting that, some pyridazine derivatives have been incorporated into semiconductor materials as well as in substances with nonlinear optical properties.[9] On the other hand, some pyridazine scaffolds have been found as promising agrochemical products (Figure 2).

It should be mentioned that literature survey reveals that only a very few articles have been reported for the synthesis of symmetric 3,6-diarylpyridazine derivatives.[10] These reported methods suffer from one or more disadvantages such as harsh reaction conditions, unsatisfactory yields, multistep synthetic operation, tedious workup and, etc. Therefore, obviation of these limitations is necessary to develop a green, simple, and efficient strategy for the synthesis of symmetric 3,6-diarylpyridazine systems.

As part of our ongoing efforts toward the development of new synthetic methods for important heterocyclic frameworks,[11] herein, we report a one-pot two-step process for the synthesis of symmetric 3,6-diarylpyridazine derivatives using a three-component reaction of aryl methyl ketones, arylglyoxal monohydrates, and hydrazine hydrate. This new method is green, simple, and efficient, which can be extended to the synthesis of many other important symmetric and asymmetric 3,6-diarylpyridazine scaffolds (Scheme 1).

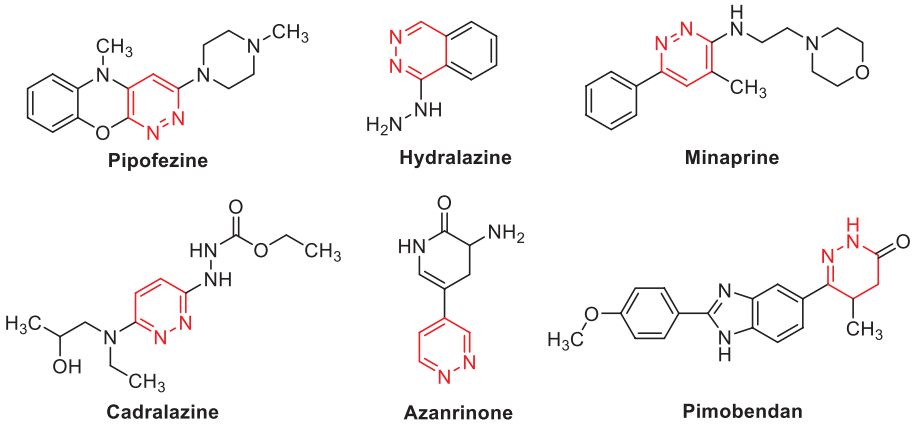


FIGURE 1 Examples of pyridazine-based drugs

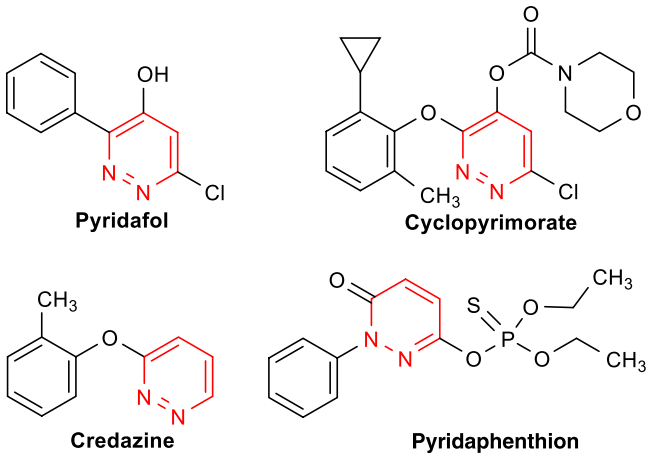
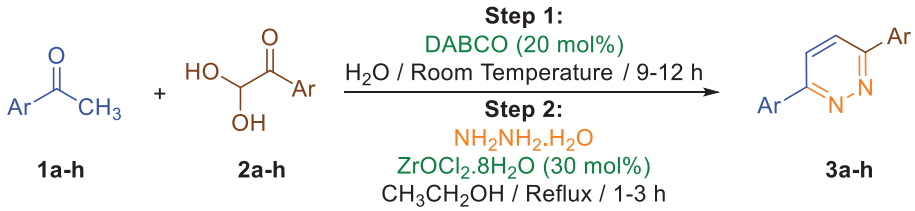


FIGURE 2 Selected pyridazine-based agrochemical products

2 | RESULTS AND DISCUSSION

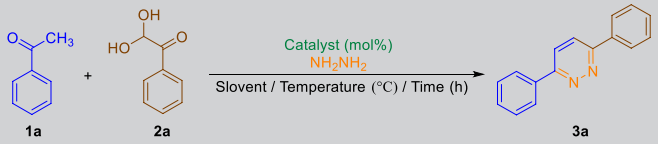
Initially, we selected acetophenone (**1a**), phenylglyoxal monohydrate (**2a**), and hydrazine as model substrates to establish optimum reaction conditions for the synthesis of symmetric 3,6-diphenylpyridazine (**3a**). To maintain green chemistry factors, nonhazardous solvents (water, ethanol, and H_2O–EtOH) are used as the preferred solvents for all of the optimization experiments. It should be noted that, all of our efforts for one-pot single-step synthesis of **3a** using different catalysts were unsuccessful (Table 1). Therefore, we changed our three-component single-step strategy to a combinatorial one-pot two-step protocol. In the step 1, we tested the reaction of **1a** and **2a** for the preparation of a suitable intermediate in the presence of various molar ratios of 1,4-diazabicyclo[2.2.2]octane (DABCO) as a cheap and eco-friendly base-organocatalyst under different temperature conditions in green solvents. In the presence of 20 mol% of DABCO, when water was used as a solvent at room temperature, the reaction proceeded well and the best mass of the desired intermediate obtained within 11 hr. It should be mentioned that, in the step 1, the reaction mixture gave an adhesive material, which stuck to the magnetic stir bar and precipitation of the obtained product (intermediate) was not occurred. Then, material obtained from step 1 was easily filtered from the reaction flask. Subsequently, we have started our study on the step 2 with the condensation of obtained intermediate and hydrazine hydrate in the presence of



Compounds			Aryl
1a	**2a**	**3a**	Ph
1b	**2b**	**3b**	4-BrC_6H_4
1c	**2c**	**3c**	4-ClC_6H_4
1d	**2d**	**3d**	4-$CH_3OC_6H_4$
1e	**2e**	**3e**	3,4-$(CH_3O)_2C_6H_3$
1f	**2f**	**3f**	3,4-$(OCH_2O)C_6H_3$
1g	**2g**	**3g**	3-BrC_6H_4
1h	**2h**	**3h**	3-$CH_3OC_6H_4$

SCHEME 1 One-pot two-step synthesis of symmetric 3,6-diarylpyridazines

TABLE 1 Investigation of the reaction conditions using a one-pot single-step protocol



Entry	Solvent	Hydrazine	Catalyst (mol%)	Temp. (°C)	Time (hr)	Yield (%) of 3a
1	H_2O	Hydrate	DABCO (20)	rt	48	NR
2	H_2O	Hydrate	DABCO (20)	50	48	NR
3	H_2O	Hydrate	DABCO (50)	rt	48	NR
4	H_2O	Hydrate	$ZrOCl_2{\cdot}8H_2O$ (20)	rt	24	NR
5	H_2O	Hydrate	L-proline (20)	rt	24	NR
6	H_2O	Dihydrochloride	$ZrOCl_2{\cdot}8H_2O$ (20)	50	24	NR
7	EtOH	Hydrate	DABCO (20)	rt	24	NR
8	EtOH	Hydrate	DABCO (20)	Reflux	24	NR
9	EtOH	Hydrate	$ZrOCl_2{\cdot}8H_2O$ (20)	rt	48	NR
10	EtOH	Hydrate	$ZrOCl_2{\cdot}8H_2O$ (20)	Reflux	24	NR
11	EtOH	Dihydrochloride	$ZrOCl_2{\cdot}8H_2O$ (20)	rt	24	NR
12	EtOH	Dihydrochloride	$ZrOCl_2{\cdot}8H_2O$ (20)	Reflux	24	NR
13	EtOH	Hydrate	L-proline (10)	rt	24	NR
15	EtOH	Dihydrochloride	L-proline (10)	rt	24	NR
16	EtOH	Dihydrochloride	L-proline (10)	Reflux	24	NR
17	H_2O–EtOH (1:1)	Hydrate	DABCO (20)	rt	24	NR
18	H_2O–EtOH (1:1)	Hydrate	$ZrOCl_2{\cdot}8H_2O$ (20)	rt	24	NR
19	H_2O–EtOH (1:1)	Dihydrochloride	$ZrOCl_2{\cdot}8H_2O$ (20)	Reflux	24	NR
20	H_2O–EtOH (1:1)	Hydrate	L-proline (10)	rt	24	NR
21	H_2O–EtOH (1:1)	Hydrate	L-proline (10)	Reflux	24	NR
22	H_2O–EtOH (1:1)	Dihydrochloride	L-proline (10)	Rrefux	48	NR

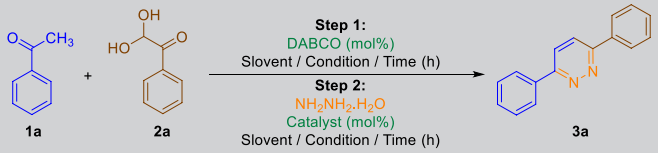
different catalysts such as zirconium (IV) oxydichloride octahydrate ($ZrOCl_2 \cdot 8H_2O$), L-proline, and DABCO for the expected symmetric 3,6-diphenylpyridazine (**3a**). Also, in this step (step 2), the effects of different solvents and temperatures were investigated (Table 2). The best result for step 2 was obtained when we used 30 mol% of $ZrOCl_2 \cdot 8H_2O$ as a green Lewis acid catalyst[12] (LD_{50} [oral rat] = 2,950 mg/kg) in ethanol at reflux under vigorous stirring within 2 hr. It is noticeable that, both steps (step 1 and step 2) of this one-pot reaction were carried out in a flask without purification of the intermediate obtained from the step 1. With optimized reaction conditions in hand, we further carried out the reaction by using various aryl methyl ketones (**1a–h**) and arylglyoxal monohydrate derivatives (**2a–h**) to investigate the scope and generality of this one-pot two-step protocol for the synthesis of symmetric 3,6-diarylpyridazine derivatives (**3a–h**) (Table 3). Pure products (**3a–h**) with moderate to excellent yields were obtained simply by filtration and washing of the solid with hot ethanol (no need of column chromatography stages).

The structures of all the symmetric 3,6-diarylpyridazine derivatives (**3a–i**) were well characterized from their spectral (IR, ^{1}H NMR, and ^{13}C NMR) studies and CHN analysis.

Based on the experimental observation, the plausible stepwise mechanism for the one-pot two-step synthesis of symmetric 3,6-diarylpyridazine derivatives (**3a–h**) is described in Scheme 2. In the first step, aryl methyl ketone (**1a–h**) was converted to the corresponding anionic form (**4a–h**) by DABCO. Subsequently, the aldol reaction of **4a–h** with the formyl group of arylglyoxal (**6a–h**) resulted in the intermediate **7a–h**. In the presence of $ZrOCl_2 \cdot 8H_2O$, intermediate **7a–h** converted the α,β-unsaturated-1,4-dicarbonyl compound (**9a–h**) by elimination of water. Then, **9a–h** that were activated by $ZrOCl_2 \cdot 8H_2O$ facilitate a nucleophilic attack of the hydrazine hydrate (**11**) followed by a dehydration reaction to give the final product (**3a–h**).

It is worthwhile to note that Saraei and coworkers reported a simple method to synthesize 2-hydroxy-1,4-diarylbutane-1,4-diones via the DABCO-catalyzed aldol reaction of acetophenone derivatives and arylglyoxal monohydrates in water at room temperature (Scheme 3).[13] Saraei's work is powerful evidence to verify our mechanism, especially the formation of the aldol adduct in step 1.

TABLE 2 Optimization of the reaction conditions using a one-pot two-step strategy



	Step 1				Step 2				
Entry	Solvent	DABCO (mol%)	Cond.	Time (hr)	Solvent	Catalyst (mol%)	Cond.	Time (hr)	Yield (%) of 3a
1	H_2O	—	rt	48	—	—	—	—	NR
2	H_2O	—	Reflux	48	—	—	—	—	NR
3	EtOH	—	rt	48	—	—	—	—	NR
4	EtOH	—	Reflux	48	—	—	—	—	NR
5	H_2O	(20%)	rt	11	EtOH	—	rt	24	NR
6	H_2O	(50%)	rt	11	EtOH	—	Reflux	24	21
7	H_2O	(60%)	rt	11	EtOH	—	Reflux	24	21
8	H_2O	(20%)	rt	11	EtOH	—	Reflux	24	19
9	H_2O	(20%)	rt	11	EtOH	$ZrOCl_2$ (5%)	Reflux	24	17
10	H_2O	(20%)	rt	11	EtOH	$ZrOCl_2$ (10%)	Reflux	24	18
11	H_2O	(20%)	rt	11	EtOH	$ZrOCl_2$ (15%)	Reflux	24	18
12	H_2O	(20%)	rt	11	EtOH	$ZrOCl_2$ (30%)	Reflux	2	62
13	H_2O	(20%)	rt	11	EtOH	$ZrOCl_2$ (30%)	rt	48	NR
14	H_2O	(20%)	rt	11	H_2O	$ZrOCl_2$ (30%)	rt	48	NR
15	H_2O	(20%)	rt	11	H_2O	$ZrOCl_2$ (30%)	Reflux	48	NR
16	H_2O	(20%)	rt	11	EtOH	DABCO (10%)	Reflux	24	20
17	H_2O	(20%)	rt	11	EtOH	DABCO (20%)	Reflux	24	21
18	H_2O	(20%)	rt	11	EtOH	L-proline (10%)	Reflux	24	21
19	H_2O	(20%)	rt	11	EtOH	L-proline (20%)	Reflux	24	21
20	H_2O	(20%)	rt	11	EtOH	L-proline (30%)	Reflux	24	21

3 | EXPERIMENTAL

3.1 | Materials and techniques

Melting points were determined on an Electrothermal 9200 apparatus. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Bruker DRX-300 AVANCE spectrometer in $CDCl_3$ with tetramethylsilane as the internal standard. Infrared spectra were recorded on a PerkinElmer Spectrum Two FT-infrared spectrophotometer, measured using KBr disks. Microanalyses were performed on a Leco Analyzer 932. All substrates and reagents were commercially available and used without further purification.

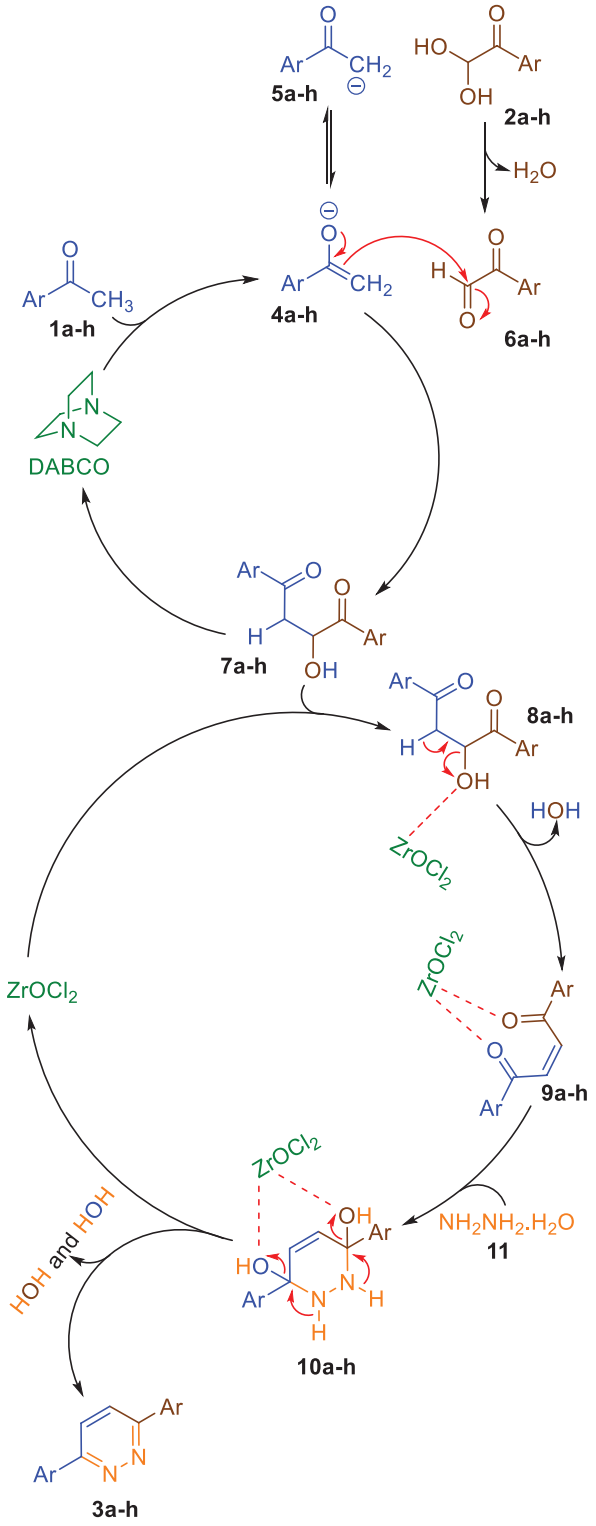
3.2 | General procedure for the one-pot two-step synthesis of symmetric 3,6-diarylpyridazine derivatives (3a–h)

In a round-bottom flask (25 mL) equipped with a magnetic stirrer, DABCO (20 mol%) was added to a solution of aryl methyl ketone (1 mmol) and arylglyoxal monohydrate (1 mmol) in water (5 mL). The reaction mixture was stirred for appropriate time as mentioned in Table 3 at room temperature. After completion of the reaction (monitored by (TLC) Thin Layer Chromatography), the intermediate obtained was easily filtered from the reaction flask. Then, a mixture of the obtained intermediate and hydrazine hydrate (3 mmol) in the presence of $ZrOCl_2 \cdot 8H_2O$ (30 mol%) as a green Lewis-acid catalyst was stirred in ethanol (7 mL) at reflux. After completion of the reaction, the reaction mixture was cooled to room temperature and filtered to give the crude product, which was purified by recrystallization from boiling ethanol.

3.3 | Physical and spectral data for compounds 3a–h

3.3.1 | 3,6-Biphenylpyridazine (3a)

White solid; mp 224–226 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 8.17 (d, J = 6.9 Hz, 4H, Ar), 7.94 (s, 2H, Ar), and 7.58–7.50 (m, 6H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): 157.6, 136.1, 130.0, 129.0, 126.9, and 124.2; FT-IR (KBr) ν: 3,054, 1,582, 1,448, 1,407, 1,311, 1,154, 1,126, 1,019, 867, 757, 743, 691, and 588 cm^{-1}. Anal. calcd for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; and N, 12.06. Found: C, 82.73; H, 5.21; and N, 12.06.



SCHEME 2 Plausible stepwise mechanism for the green one-pot two-step synthesis of symmetric 3,6-diarylpyridazine derivatives

3.3.2 | 3,6-Bis(4-bromophenyl)pyridazine (3b)

Yellow solid; mp 285–287 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 8.05 (d, J = 8.7 Hz, 4H, Ar), 7.92 (s, 2H, Ar), and 7.70 (d, J = 8.4 Hz, 4H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): 158.0, 137.2, 132.3, 128.4, 125.1, and 124.0; FT-IR (KBr) v: 3,089, 3,048, 1,588, 1,485, 1,420, 1,408, 1,379, 1,328, 1,303, 1,297, 1,074, 1,006, 816, 793, 731, and 577 cm^{-1}. Anal. calcd for $C_{16}H_{10}Br_2N_2$: C, 49.27; H, 2.58; and N, 7.18. Found: C, 49.27; H, 2.58; and N, 7.18.

3.3.3 | 3,6-Bis(4-chlorophenyl)pyridazine (3c)

Yellow solid; mp 260–262 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 8.10 (d, J = 5.4 Hz, 4H, Ar), 7.92 (s, 2H, Ar), and 7.53 (d, J = 6.3 Hz, 4H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): 158.1, 136.5, 129.3, 128.4, 128.1, and 124.0; FT-IR (KBr) v: 3,089, 3,048, 1,597, 1,489, 1,420, 1,410, 1,381, 1,306, 1,297, 1,095, 1,009, 994, 820, 797, 747, and 578 cm^{-1}. Anal. calcd for $C_{16}H_{10}Cl_2N_2$: C, 63.81; H, 3.35; and N, 9.30. Found: C, 63.81; H, 3.35; and N, 9.30.

3.3.4 | 3,6-Bis(4-methoxyphenyl)pyridazine (3d)

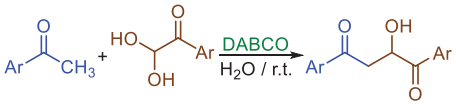
Yellow solid; mp 236–238 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 8.10 (d, J = 5.8 Hz, 4H, Ar), 7.83 (s, 2H, Ar), 7.05 (d, J = 5.7 Hz, 4H, Ar), and 3.89 (s, 6H, 2 × OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): 161.1, 128.6, 128.1, 123.4, 114.3, 113.6, and 55.3; FT-IR (KBr) v: 3,068, 3,048, 2,962, 2,839, 1,606, 1,574, 1,506, 1,426, 1,398, 1,301, 1,252, 1,244, 1,193, 1,032, 1,024, 832, and 821 cm^{-1}. Anal. calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; and N, 9.58. Found: C, 73.95; H, 5.52; and N, 9.58.

3.3.5 | 3,6-Bis(3,4-dimethoxyphenyl)pyridazine (3e)

White solid; mp 201–203 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 8.00 (s, 2H, Ar), 7.85 (s, 2H, Ar), 7.55–7.52 (m, 2H, Ar), 6.99 (d, J = 8.4 Hz, 2H, Ar), 4.02 (s, 6H, 2 × OCH_3), and 3.96 (s, 6H, 2 × OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): 156.4, 150.8, 149.5, 128.7, 123.5, 119.2, 111.0, 109.5, 56.0, and 55.9; FT-IR (KBr) v: 3,003, 2,949, 2,839, 1,600, 1,591, 1,518, 1,464, 1,424, 1,407, 1,274, 1,253, 1,224, 1,146, 1,020, 843, 810, and 801 cm^{-1}. Anal. calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; and N, 7.95. Found: C, 68.17; H, 5.72; and N, 7.95.

3.3.6 | 3,6-Bis(3,4-Methylenedioxyphenyl)pyridazine (3f)

White solid; mp 245–248 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.80 (s, 2H, Ar), 7.41 (s, 2H, Ar), 7.60 (d, J = 7.2 Hz, 2H, Ar), 6.96 (d, J = 7.8 Hz, 2H, Ar), and 6.07 (s, 4H, 2 × OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$): 167.4, 164.5, 157.3, 131.3, 123.6, 121.0, 108.6, 107.1, and 101.5; FT-IR (KBr) v: 3,080, 2,990, 2,904, 1,606, 1,501, 1,489, 1,447, 1,410, 1,373, 1,275, 1,240, 1,140, 1,111, 1,102, 1,036, 931, 895, 847, and 822 cm^{-1}. Anal. calcd for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; and N, 8.75. Found: C, 67.50; H, 3.78; and N, 8.75.

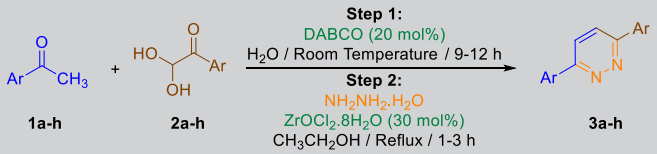


SCHEME 3 Aldol reaction reported by Saraei and coworkers

3.3.7 | 3,6-Bis(3-bromophenyl)pyridazine (3g)

White solid; mp 185–188 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 8.33 (s, 2H, Ar), 8.10 (d, J = 7.8 Hz, 2H, Ar), 7.94 (s, 2H, Ar), 7.66 (d, J = 6.9 Hz, 2H, Ar), and 7.43 (t, J = 8.1 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): 156.6, 137.8, 133.1, 130.6, 130.0, 125.4, 124.2, and 123.3; FT-IR (KBr) ν:

TABLE 3 Regioselective one-pot two-step synthesis of symmetric 3,6-diarylpyridazine derivatives



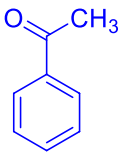
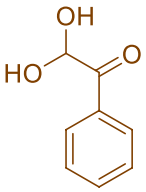
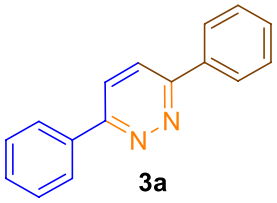
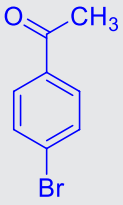
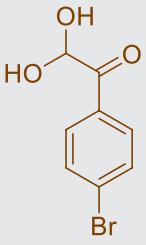
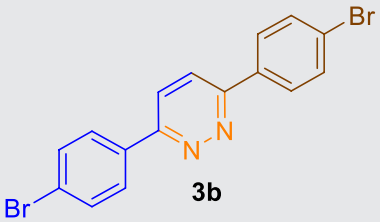
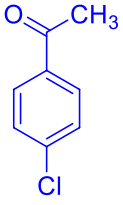
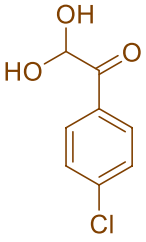
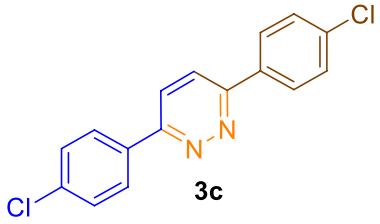
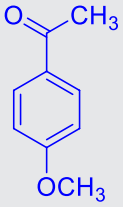
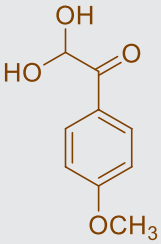
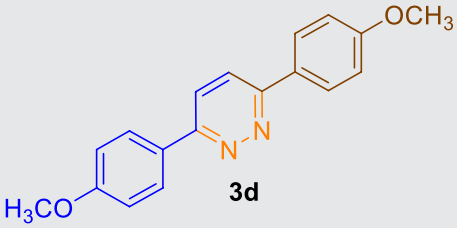
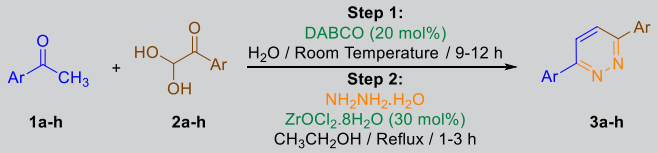
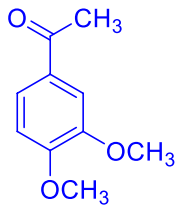
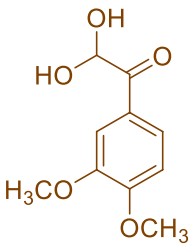
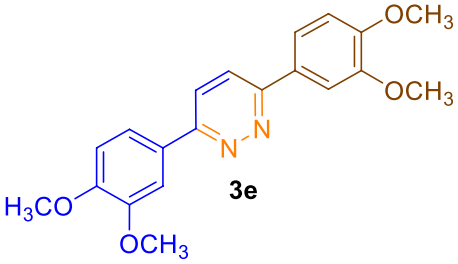
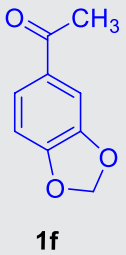
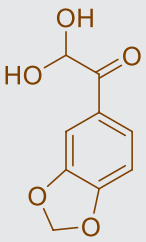
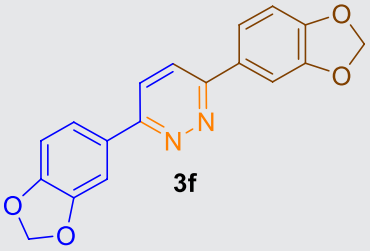
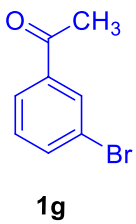
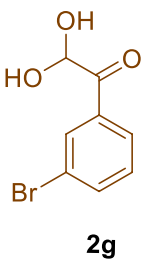
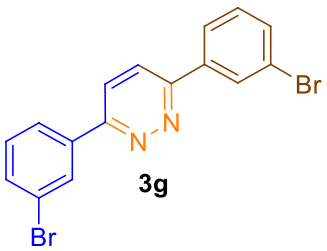
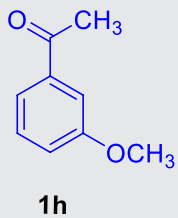
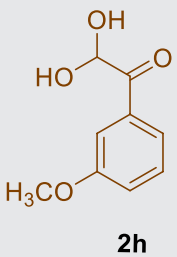
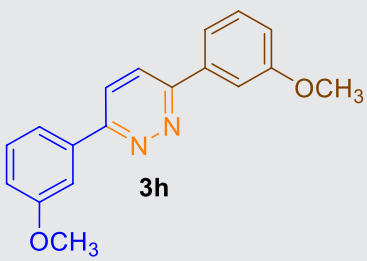
Entry	Aryl methyl ketone	Arylglyoxal monohydrate	3,6-diarylpyridazine	Time (hr) Step 1	Time (hr) Step 2	Yield (%) of 3
1	 1a	 2a	 3a	11	2	62
2	 1b	 2b	 3b	10	1	90
3	 1c	 2c	 3c	10	1	92
4	 1d	 2d	 3d	9	2	79

TABLE 3 (Continued)



Entry	Aryl methyl ketone	Arylglyoxal monohydrate	3,6-diarylpyridazine	Time (hr) Step 1	Time (hr) Step 2	Yield (%) of 3
5	 1e	 2e	 3e	9	2	86
6	 1f	 2f	 3f	9	2	96
7	 1g	 2g	 3g	12	3	60
8	 1h	 2h	 3h	12	3	65

3,064, 1,581, 1,562, 1,432, 1,419, 1,391, 1,284, 1,078, 1,061, 996, 847, 789, 757, 685, and 656 cm^{-1}. Anal. calcd for $C_{16}H_{10}Br_2N_2$: C, 49.27; H, 2.58; and N, 7.18. Found: C, 49.27; H, 2.58; and N, 7.18.

3.3.8 | 3,6-Bis(3-methoxyphenyl)pyridazine (3h)

White solid; mp 186–189 °C. ^{1}H NMR (300 MHz, $CDCl_3$):) 7.93 (s, 2H, Ar), 7.87 (s, 2H, Ar), 7.65 (d, J = 7.5 Hz, 2H, Ar), 7.45 (t, J = 8.1 Hz, 2H, Ar), 7.07 (dd, J = 6 Hz,

J = 2.1 Hz, 2H, Ar), and 3.93 (s, 6H, 2 × OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): 160.2, 157.4, 137.4, 130.0, 124.3, 119.1, 116.5, and 111.6; FT-IR (KBr) v: 3,048, 2,970, 2,839, 1,592, 1,549, 1,456, 1,429, 1,417, 1,324, 1,310, 1,223, 1,186, 1,038, 1,026, 863, 795, 781, and 699 cm^{-1}. Anal. calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; and N, 9.58. Found: C, 73.95; H, 5.52; and N, 9.58.

4 | CONCLUSIONS

In summary, we have developed a novel, simple, and efficient method for the synthesis of symmetric 3,6-diarylpyridazine derivatives using a green catalytic one-pot two-step reaction of aryl methyl ketones, arylglyoxal monohydrates, and hydrazine hydrate. Mild reaction conditions, operational simplicity, clean reaction profiles, the absence of a tedious separation procedure, high atom-economy, moderate to excellent yields, and easy workup, as well as the use of inexpensive and environmentally benign catalysts and solvents are the key advantages of this multicomponent method.

ACKNOWLEDGMENTS

This work was partially supported by the Research Council of Payame Noor University.

ORCID

Mehdi Rimaz http://orcid.org/0000-0002-5175-0894

Hossein Mousavi http://orcid.org/0000-0003-4292-3762

REFERENCES

[1] (a) A. Yaghoubi, M. G. Dekamin, *ChemistrySelect* **2017**, *2*, 9236. (b) V. B. Yadav, P. Rai, H. Sagir, A. Kumar, I. R. Siddiqui, *ChemistrySelect* **2017**, *2*, 8320. (c) S. J. Kalita, B. Das, D. C. Deka, *ChemistrySelect* **2017**, *2*, 5701. (d) K. J. Tamuli, D. Dutta, S. Nath, M. Bordoli, *ChemistrySelect* **2017**, *2*, 7787. (e) N. Azizi, M. Shahiri Haghayegh, *ChemistrySelect* **2017**, *2*, 8870. (f) A. R. Sheldon, *Chem. Soc. Rev.* **2012**, *6*, 1437. (g) M. G. Dekamin, M. Azimoshan, L. Ramezani, *Green Chem.* **2013**, *15*, 811. (h) M. Abbasi, *J. Chin. Chem. Soc.* **2017**, *64*, 896. (i) A. Yazdani-Elah-Abadi, R. Mohebat, M. Kangani, *J. Chin. Chem. Soc.* **2017**, *64*, 690. (j) A. Dondoni, A. Massi, *Tetrahedron Lett.* **2001**, *42*, 7975. (k) M. Rimaz, H. Mousavi, P. Keshavarz, B. Khalili, *Curr. Chem. Lett.* **2015**, *4*, 159. (l) N. R. Modugu, P. V. Pittala, *Tetrahedron Lett.* **2017**, *58*, 3859. (m) I. Saikia, M. Hazarika, N. Hussain, M. R. Das, C. Tamuly, *Tetrahedron Lett.* **2017**, *58*, 4255. (n) A. Kumar, Y. E. Jad, A. El-Faham, B. G. de la Torre, F. Albericio, *Tetrahedron Lett.* **2017**, *58*, 2986. (o) A. A. Ali, M. Konwar, M. Chetia, D. Sarma, *Tetrahedron Lett.* **2016**, *57*, 5661. (p) D. Ngo, M. Kalala, V. Hogan, R. Manchanayakage, *Tetrahedron Lett.* **2014**, *55*, 4496. (q) S. Zhaleh, N. Hazeri, M. R. Faghihi, M. T. Maghsoodlou, *Res. Chem. Intermed.* **2016**, *42*, 8069. (r) M. Zakeri, M. M. Nasef, T. Kargaran, A. Ahmad, E. Abouzari-Lotf, J. Asadi, *Res. Chem. Intermed.* **2017**, *43*, 717. (s) J. Ma, X. Zhou, X. Zang, C. Wang, Z. Wang, J. Li, Q. Li, *Aust. J. Chem.* **2007**, *60*, 146. (t) V. T. Kamble, B. S. Davane, S. A. Chavan, R. B. Bhosale, *Aust. J. Chem.* **2007**, *60*, 302. (u) W. Su, J. Li, J. Li, *Aust. J. Chem.* **2008**, *61*, 860. (v) B. Karmakar, *Aust. J. Chem.* **2016**, *69*, 1117. (w) G. Stavber, *Aust. J. Chem.* **2010**, *63*, 849. (x) Y. Zou, Y. Hu, H. Lin, D.-Y. Shi, *J. Heterocyclic Chem.* **2013**, *50*, 1174. (y) F. Shi, Y. Gao, S. Tu, *J. Heterocyclic Chem.* **2011**, *48*, 803. (z) A. Saha, R. Kumar, R. Kumar, C. Devakumar, *J. Heterocyclic Chem.* **2010**, *47*, 838.

[2] (a) M. Waheed, N. Ahmed, M. A. Alsharif, M. I. Alahmadi, S. Mukhtar, *ChemistrySelect* **2017**, *2*, 7946. (b) K. A. Grice, R. Patil, A. Ghosh, J. D. Paner, M. A. Guerrero, E. J. M. Camacho, P. S. Cao, A. H. Niyazi, S. Zainab, R. D. Sommer, G. Waris, S. Patil, *New J. Chem.* **2018**, *42*, 1151. (c) V. A. Palchykov, R. M. Chabanenko, V. V. Konshin, V. V. Dotsenko, S. G. Krivokolysko, E. A. Chigorina, Y. I. Horak, R. Z. Lytvyn, A. A. Vakhula, M. D. Obushak, A. V. Mazepa, *New J. Chem.* **2018**, *42*, 1403. (d) X. Gao, Z. Yang, W.-J. Hao, B. Jiang, S. J. Tu, *J. Heterocyclic Chem.* **2017**, *54*, 2434. (e) S. J. Jadhav, R. B. Patil, D. R. Kumbhar, A. A. Patravale, D. R. Chandam, M. B. Deshmukh, *J. Heterocyclic Chem.* **2017**, *54*, 2434. (f) M. Beerappa, K. Shivashankar, *J. Heterocyclic Chem.* **2017**, *54*, 2197. (g) C. Kathing, S. Kumar, S. Tumtin, N. G. Singh, J. W. S. Rani, R. Nongrum, R. Nongkhlaw, *J. Heterocyclic Chem.* **2017**, *54*, 1486. (h) M. Ghandi, S. Rahimi, N. Zarezadeh, *J. Heterocyclic Chem.* **2017**, *54*, 102. (i) G. M. Reddy, J. Raul Garcia, *J. Heterocyclic Chem.* **2017**, *54*, 89. (j) J. Safaei-Ghomi, H. Shahbazi-Alavi, S. H. Nazemzadeh, *J. Chin. Chem. Soc.* **2017**, *64*, 1213. (k) A. R. Moosavi-Zare, H. Goudarziafshar, S. Dastbaz, *J. Chin. Chem. Soc.* **2017**, *64*, 727. (l) H. Alinezhad, V. Alinezhad, S. Mohseni Tavakkoli, *J. Chin. Chem. Soc.* **2017**, *64*, 385. (m) E. Tabrizian, A. Amoozadeh, *J. Chin. Chem. Soc.* **2017**, *64*, 331. (n) A. K. M. Magesh Selva Kumar, P. Dhivya, S. P. Rajendran, *J. Chin. Chem. Soc.* **2017**, *64*, 138. (o) M. Rimaz, H. Mousavi, M. Behnam, L. Sarvari, B. Khalili, *Curr. Chem. Lett.* **2017**, *6*, 55. (p) N. Azizi, M. Edrisi, *Res. Chem. Intermed.* **2017**, *43*, 379. (q) S. Golchin, M. H. Mosslemin, A. Yazdani-Elah-Abadi, N. Shams, *Res. Chem. Intermed.* **2017**, *43*, 1735. (r) S. Kumari, M. Rajeswari, J. M. Khurana, *Aust. J. Chem.* **2016**, *43*, 1735. (s) J. Sindhu, H. Singh, J. M. Khurana, K. R. Aneja, *Aust. J. Chem.* **2013**, *66*, 717. (t) H. Singh, J. Sindhu, J. M. Khurana, C. Sharma, K. R. Aneja, *Aust. J. Chem.* **2013**, *66*, 1088. (u) S. Rostamnia, A. Hasankhani, *Synlett* **2014**, *25*, 2753. (v) E. Doustkhah, S. Rostamnia, A. Hasankhani, *J. Porous Mater.* **2016**, *23*, 549. (w) H. Golchin Hosseini, E. Doustkhah, M. V. Kirillova, S. Rostamnia, G. Mahmoudi, A. M. Kirillov, *Appl. Catal. A Gen.* **2017**, *548*, 96. (x) S. Rostamnia, *RSC Adv.* **2015**, *5*, 97044. (y) S. Rostamnia, E. Doustkhah, A. Baghban, B. Zeynizadeh, *J. Appl. Polym. Sci.* **2016**, *133*, 43190. (z) E. Doustkhah, S. Rostamnia, *J. Colloid Interface Sci.* **2016**, *478*, 280.

[3] (a) F. Wang, X.-C. Li, W.-Y. Lai, Y. Chen, W. Huang, F. Wudl, *Org. Lett.* **2014**, *16*, 2942. (b) N. Zheng, H. Li, G. Sun, K. Zhong, B. Yin, *Org. Biomol. Chem.* **2013**, *11*, 5100. (c) K. A. Nolan, J. R. Doncaster, M. S. Dunstan, K. A. Scott, A. D. Frankel, D. Siegel, R. C. Whitehead, I. J. Startford, R. A. Bryce, *J. Med. Chem.* **2009**, *52*, 7142. (d) J. Mann, A. Baron, Y. Opoku-Boahen, E. Johansson, G. Parkinson, L. R. Kelland, S. Niedle, *J. Med. Chem.* **2001**, *44*, 138. (e) J. R. Price, N. G. White, A. Perez-Velasco, G. B. Jameson, C. A. Hunter, S. Brooker, *Inorg. Chem.* **2008**, *47*, 10729. (f) T. F. Mastropietro, N. Marino, D. Armentano, G. De Munno, C. Yuste, F. Lloret, M. Julve, *Cryst. Growth Des.* **2013**, *13*, 270. (g) L. Resconi, S. Guidotti, I. Camurati, R. Frabetti, F. Focante, I. E. Nifant'ev, I. P. Laishevtsev, *Chem. Phys.* **2005**, *206*, 1405. (h) A. Vembris, E. Zarins, J. Jubels, V. Kokars, I. Muzikante, A. Miasojedovas, S. Jursenas, *Opt. Mater.* **2012**, *34*, 1501. (i) S. E. Bodman, C. M. Fitchet, *Supramol. Chem.* **2015**, *27*, 840. (j) J. G. Yu, S. H. Han, H. R. Jeon, H. K. Chung, J. Y. Lee, *J. Luminesc.* **2018**, *194*, 33. (k) H. A. Hintz, N. J. Sortedahl, S. M. Meyer, D. A. Decato, B. J. Dahl, *Tetrahedron Lett.* **2017**, *58*, 4703. (l) M. P. Algi, Z. Oztas, S. Trikeş, A. Cihaner, F. Algi, *J. Fluoresc.* **2017**, *27*, 509. (m) N. O. Mahmoodi, M. Mohammadi Zeydi, *J. Iran Chem. Soc.* **2018**, *15*, 311. (n) M. T. El Sayed, *J. Heterocyclic Chem* **2018**, *55*, 21. (o) D. D. Zhukovsky, V. V. Sizov, G. L. Starova, S. P. Tunik, E. V. Grachova, *J. Organometal. Chem.* **2018**, *867*, 367.

[4] M. Gyoten, H. Nagaya, S. Fukuda, Y. Ashida, Y. Kawano, *Chem. Pharm. Bull.* **2003**, *51*, 122.

[5] M. Sönmez, I. Berber, E. Akbas, *Eur. J. Med. Chem.* **2006**, *41*, 101.

[6] S. Demirayak, A. C. Karaburun, R. Beis, *Eur. J. Med. Chem.* **2004**, *39*, 1089.

[7] I. G. Rathish, K. Javed, S. Bano, S. Ahmad, M. S. Alam, K. K. Pillai, *Eur. J. Med. Chem.* **2009**, *44*, 2673.

[8] (a) F. Rohet, C. Coudert, J. Conquelet, *J. Bioorg. Med. Chem.* **1997**, *5*, 655. (b) M. Gökçe, S. Utku, E. Küpelli, *Eur. J. Med. Chem.* **2009**, *44*, 3760. (c) R. K. Tonk, S. Bawa, G. Chawla, G. S. Deora, S. Kumar,

V. Rathore, N. Mulakayala, A. Rajaram, A. M. Kalle, O. Afzal, *Eur. J. Med. Chem.* **2012**, *57*, 176.

[9] Y. Cheng, B. Ma, F. Wudl, *J. Mater. Chem.* **1999**, *9*, 2183.

[10] (a) S. G. Cohen, S.-h. Hsiao, E. Saklad, C. H. Wang, *J. Am. Chem. Soc.* **1957**, *79*, 4400. (b) S. G. Coh, F. G. Baddar, A. El-Habashi, A. K. Fateen, *J. Chem. Soc.* **1965**, *0*, 3342. (c) M. J. Haddadin, B. J. Agha, M. S. Saka, *Tetrahedron Lett.* **1984**, *25*, 2577. (d) F. Barba, M. D. Velasco, A. Guirado, N. Moreno, *Synth. Commun.* **1985**, *15*, 939. (e) J. Nakayama, T. Konishi, A. Ishii, M. Hoshino, *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2608. (f) Y. Chen, Y. Lam, S.-Y. Lee, *Chem. Lett.* **2001**, *3*, 274. (g) Q. Gao, Y. Zhu, M. Lian, M. Liu, J. Yuan, G. Yin, A. Wu, *J. Org. Chem.* **2012**, *77*, 9865.

[11] (a) M. Rimaz, H. Mousavi, *Turk. J. Chem.* **2013**, *37*, 252. (b) M. Rimaz, H. Rabiei, B. Khalili, R. H. Prager, *Aust. J. Chem.* **2014**, *67*, 283. (c) M. Rimaz, *Aust. J. Chem.* **2015**, *68*, 1529. (d) M. Rimaz, Z. Jalalian, H. Mousavi, R. H. Prager, *Tetrahedron Lett.* **2016**, *57*, 105. (e) M. Rimaz, J. Khalafy, H. Mousavi, *Res. Chem. Intermed.* **2016**, *42*, 8185. (f) M. Rimaz, H. Mousavi, M. Behnam, B. Khalili, *Curr. Chem. Lett.* **2016**, *5*, 145. (g) M. Rimaz, H. Mousavi, L. Nikpey, B. Khalili, *Res. Chem. Intermed.* **2017**, *43*, 3925. (h) M. Rimaz, J. Khalafy, H. Mousavi, S. Bohlooli, B. Khalili, *J. Heterocyclic Chem.* **2017**, *54*, 3174. (i) M. Rimaz, B. Khalili, G. Khatyal, H. Mousavi, F. Aali, *Aust. J. Chem.* **2017**, *70*, 1274.

[12] (a) K. Nikoofar, Z. Khademi, *Res. Chem. Intermed.* **2016**, *42*, 3929. (b) G. Brahmachari, B. Banerjee, *Asian J. Org. Chem.* **2012**, *1*, 251. (c) B. Karimi, M. Kiani, *Catal. Commun.* **2011**, *14*, 62. (c) M. Jafarpour, A. Rezaeifard, M. Heidari, *Phosphorus Sulfur Silicon* **2011**, *186*, 1470. (d) S. Khodabakhshi, M. Khaleghi Abbasabadi, M. Baghrnejad, F. Marahel, *J. Chin. Chem. Soc.* **2015**, *62*, 9. (e) G. Brahmachari, S. Das, *J. Heterocyclic Chem.* **2014**, *51*, E140. (f) S. Karami, B. Karimi, S. Khodabakhshi, *J. Chin. Chem. Soc.* **2013**, *60*, 22. (g) S. Mishra, R. Ghosh, *Tetrahedron Lett.* **2011**, *52*, 2857. (h) I. Mohammadpoor-Baltork, A. R. Khosropour, S. H. Hojati, *Catal. Commun.* **2007**, *8*, 1865. (i) H. Firouzabadi, N. Iranpoor, M. Jafarpour, A. Ghaderi, *J. Mol. Catal. A Chem.* **2006**, *253*, 249. (j) Y. Wu, L.-N. He, Y. Du, J.-Q. Wang, C.-X. Miao, W. Li, *Tetrahedron* **2009**, *65*, 6204. (k) H. R. Tavakoli, S. M. Moosavi, A. Bazgir, *Res. Chem. Intermed.* **2015**, *41*, 3041. (l) F. Matloubi Moghaddam, H. Ismaili, G. Rezanejade Bardajee, *Heteroatom Chem.* **2006**, *17*, 136.

[13] M. Saraei, B. Eftekhari-Sis, S. Mozaffarnia, J. Korean, *J. Korean Chem. Soc.* **2013**, *57*, 252.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Rimaz M, Mousavi H, Khalili B, Aali F. A green and practical one-pot two-step strategy for the synthesis of symmetric 3,6-diarylpyridazines. *J Chin Chem Soc*. 2018;1–9. https://doi.org/10.1002/jccs.201700470