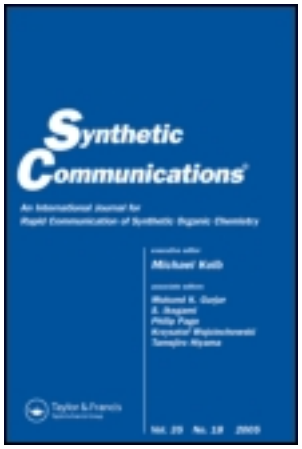

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Novel One-Pot Synthesis for 2,5-Diaryl and 5-Aryl-pyridazin-3(2H)-ones

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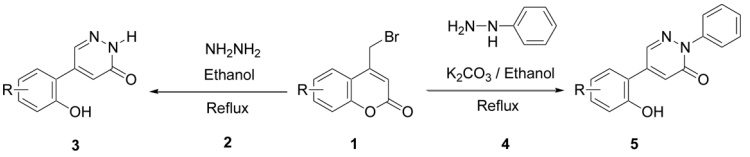
NOVEL ONE-POT SYNTHESIS FOR 2,5-DIARYL AND 5-ARYL-PYRIDAZIN-3(*2H*)-ONES

Mahantesha Basanagouda and Manohar V. Kulkarni
P. G. Department of Chemistry, Karnatak University, Dharwad, Karnataka, India

GRAPHICAL ABSTRACT



Abstract *A novel method for the synthesis of 2-phenyl-5-(*o*-hydroxyphenyl)-pyridazin-3(*2H*)-ones and 5-(*o*-hydroxyphenyl)-pyridazin-3(*2H*)-ones has been found during the reaction of 4-bromomethylcoumarins with phenylhydrazine and hydrazinehydrate, respectively, under controlled alkaline conditions.*

Keywords Coumarin; diphenyl; heterocycle; hydrazinehydrate; phenylhydrazine; pyridazinone

INTRODUCTION

Pyridazine is an electron-deficient heterocyclic system isosteric with benzene and other six-membered heterocycles. Derivatives of pyridazine have gained considerable importance in the fields of medicine and agriculture.[1,2] Among the functionalized pyridazines, the pyridazin-3(*2H*)-one moiety has been found to be a part of clinically accepted cardiovascular[3,4] and anti-inflammatory[5–7] drugs. The importance of pyridazin-3(*2H*)-ones in agriculture is best exemplified by established weedicidal and muticidal agents such as chloridazon and pyridaben (Fig. 1).[8,9]

Earlier approaches to the pyridazine skeleton make use of 1,4-diketonyl compounds and derivatives of hydrazine[10] to obtain a variety of functionalized pyridazines. Introduction of the aryl moiety on the carbon skeleton in pyridazine has been a challenge, which has been met by a variety of coupling reactions involving the use of arylboronic acids, palladium complexes, and organotin compounds. It has been the subject of an extensive review.[9,11] In addition to the stringent experimental

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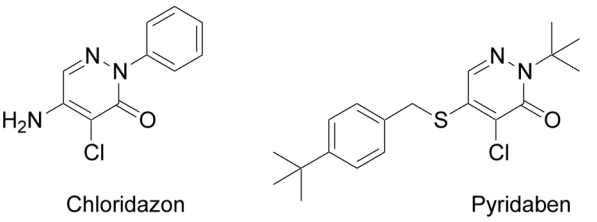


Figure 1. Structures of chloridazon and pyridaben.

conditions, all these methods of introduction of the aryl moiety require a preformed pyridazine, preferentially a chloro pyridazine.

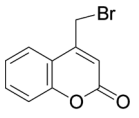
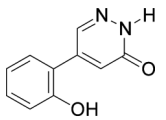
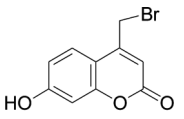
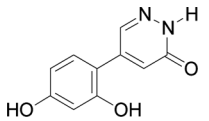
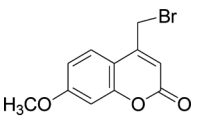
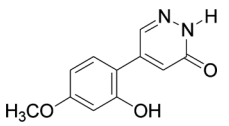
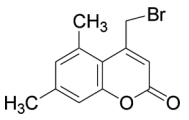
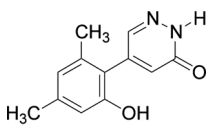
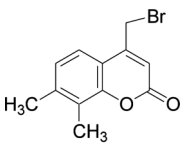
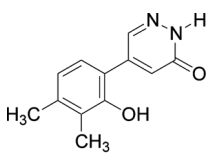
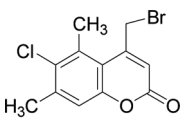
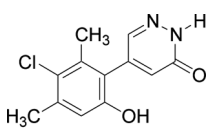
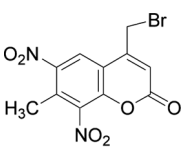
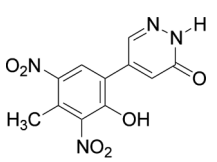
Recently we have reported the formation of 5-(*o*-hydroxyphenyl)-pyridazin-3(*2H*)-ones from 4-bromomethylcoumarins, facilitating the introduction of a functionalized aryl moiety at C-5 position in a single step.[12] In the present article, we have found that in the presence of anhydrous potassium carbonate, phenylhydrazine also reacts with 4-bromomethylcoumarins to yield 2,5-diaryl-pyridazin-3(*2H*)-ones. Our earlier methodology of using hydrazinehydrate has been extended to other functionalized bromomethylcoumarins, showing that 4-bromomethylcoumarins are good synthons to introduce aryl groups on the pyridazine ring.

RESULTS AND DISCUSSION

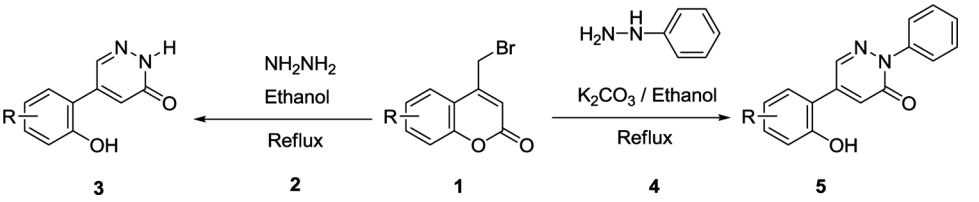
The required substituted 4-bromomethylcoumarins[13] **1** were prepared by the Pechmann cyclization of substituted phenols with 4-bromoethylacetoacetate[14] using sulfuric acid as the condensing agent.

Initially, we extended our earlier method for the synthesis of 5-(*o*-hydroxy phenyl)-pyridazin-3(*2H*)-ones from 4-bromomethylcoumarins by synthesizing newer compounds (Table 1).[12] It was then thought to explore this method to synthesize diaryl-pyridazin-3(*2H*)-ones by modifying the procedure (Scheme 1). We examined the optimum reaction conditions for the reaction with 6-methyl-4-bromomethylcoumarin **1h**, and the results are summarized in Table 2. With 1 equivalent of K_2CO_3, conversion of starting material **1h** was the best (Table 2, entry 6). As a part of ongoing efforts to synthesize 2-phenyl-5-aryl-pyridazin-3(*2H*)-ones, we have attempted the reaction with 6-methyl-4-bromomethylcoumarin **1h** and phenylhydrazine **4** as a model system. We first envisioned reaction conditions without any additives or catalyst; however, refluxing the equimolar amounts of starting materials **1h** and **4** in ethanol did not result in the formation of desired product **5h** as monitored by thin-layer chromatography (TLC) even after 24 h and longer (Table 2, entry 1). Then we increased the amount of **4** in 2 and 5 equivalents refluxed for 8–24 h, which resulted in formation of product **5h** in 5% and 9% respectively (Table 2, entries 2 and 3). Increasing amounts of K_2CO_3 (0.25 equivalent) and (0.50 equivalent) as a base increased the yields of the product **5h** to 12% and 30% respectively (Table 2, entries 4 and 5). With 1 equivalent of K_2CO_3, conversion of starting material **1h** and **4** took place quantitatively within 3 h. Product **5h** was isolated after workup

Table 1. Synthesis of 5-aryl substituted pyridazin-3(2*H*)-ones **3a–g**

Entry	Substrate	Product	Yield (%)	Melting point (°C)
1	 **1a**	 **3a**	71	244
2	 **1b**	 **3b**	69	204
3	 **1c**	 **3c**	72	255
4	 **1d**	 **3d**	68	198
5	 **1e**	 **3e**	71	191
6	 **1f**	 **3f**	65	216
7	 **1g**	 **3g**	63	206

in 75% yield (Table 2, entry 6). This result could not be improved with more K_2CO_3 (2 equivalents gave 74% yield). Having established the optimized reaction conditions, a series of 2,5-diaryl-pyridazin-3(2*H*)-ones **5a–o** were synthesized in good to excellent yields, and the results are shown in Table 3. The electron-donating and



Scheme 1. Synthesis of phenyl pyridazin-3(2*H*)-ones **3** and **5**.

Table 2. Optimization of the reaction conditions for the synthesis of **5h**

Entry	Phenylhydrazine	K_2CO_3	Time (h)	Yield (%)
1	1 equivalent	—	24	—
2	2 equivalents	—	8	5
3	5 equivalents	—	8	9
4	5 equivalents	0.25 equivalent	8	12
5	5 equivalents	0.50 equivalent	8	30
6	5 equivalents	1.00 equivalent	3	75

electron-withdrawing substituents on the coumarin ring did not profoundly affect the efficiency of the reactions. In the case of strong electron-withdrawing groups, such as a nitro group, somewhat lower yields were obtained (Table 3, entry 7).

The plausible mechanism for this conversion resembles that already reported by our laboratory (Scheme 2).[12] The nucleophilic attack of phenyl hydrazine on the lactone carbonyl and the C-4 methylene on 4-bromomethylcoumarins **1** is equally probable, because excess of this reagent is employed and would produce a hydrazino hydrazide **B**. The support for the initial allylic substitution product is from our earlier observation that this reaction in acetic acid leads to the *N*-acetylated product of the intermediate **A**, which has been isolated and characterized.[12] Hydrazine hydrate and other double nucleophiles such as amidines and thiourea are known to bring about similar ring opening of coumarins, which have resulted in the formation of *o*-hydroxyphenyl substituted pyrazoles[15] and pyrimidines.[16] Further, an intramolecular nucleophilic attack of the phenyl hydrazine on the carbonyl group of the hydrazide followed by the expulsion of phenyl hydrazine results in the intermediates **C**, which undergo in situ dehydrogenation to give pyridazinones **5**.

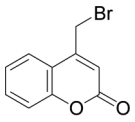
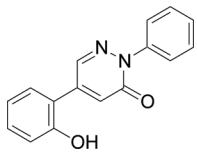
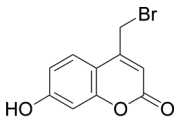
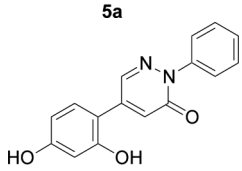
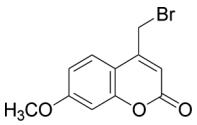
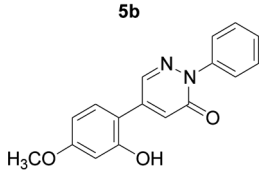
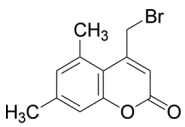
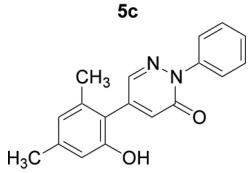
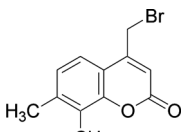
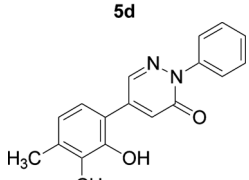
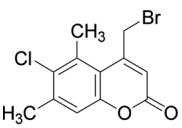
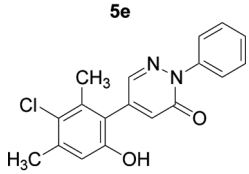
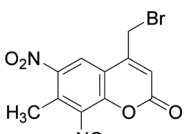
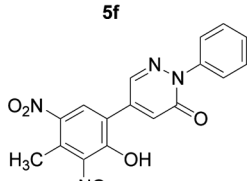
Intramolecular expulsion of acetic acid hydrazide has been proposed in the formation of 3-hydrazinopyridazinones.[17] The driving force for this nucleophilic substitution, followed by ring opening and ring closure (SNRORC), seems to be the stability of the aromatic pyridazinones. Numbering of **3** and **5** are given in Scheme 3.

EXPERIMENTAL

Materials

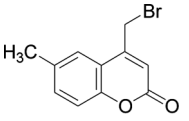
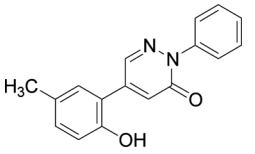
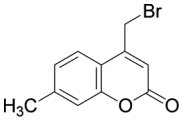
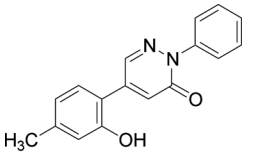
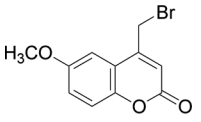
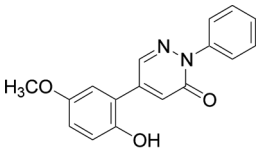
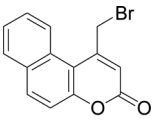
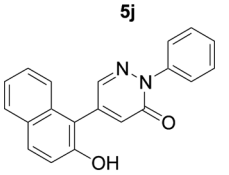
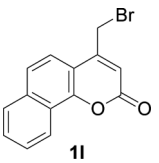
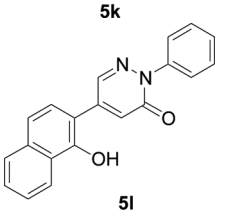
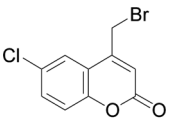
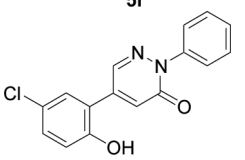
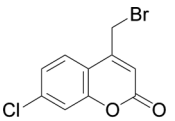
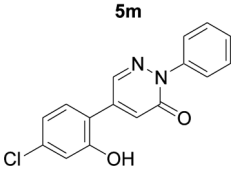
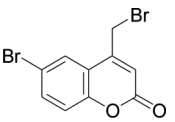
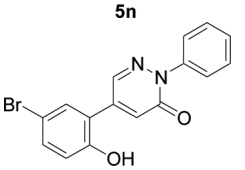
All the starting materials and reagents were purchased from commercial suppliers and used after further purification. Thin-layer chromatography (TLC) was

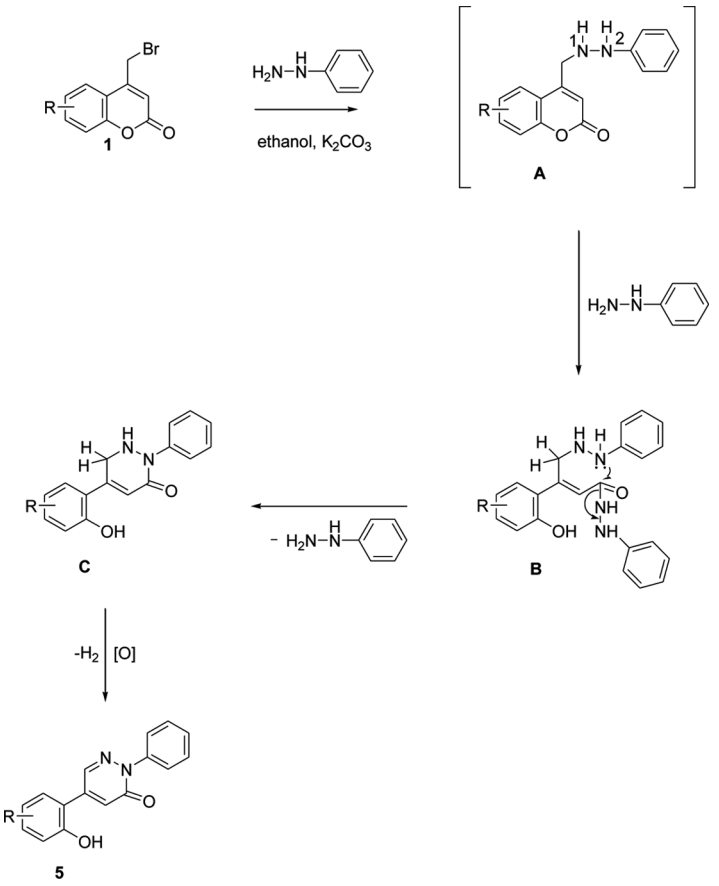
Table 3. Synthesis of 2,5-diaryl substituted pyridazin-3(2*H*)-ones **5a–o**

Entry	Substrate	Product	Yield (%)	Melting point (°C)
1	 **1a**	 **5a**	71	201
2	 **1b**	 **5b**	73	195
3	 **1c**	 **5c**	75	212
4	 **1d**	 **5d**	76	184
5	 **1e**	 **5e**	76	188
6	 **1f**	 **5f**	70	208
7	 **1g**	 **5g**	66	170

(*Continued*)

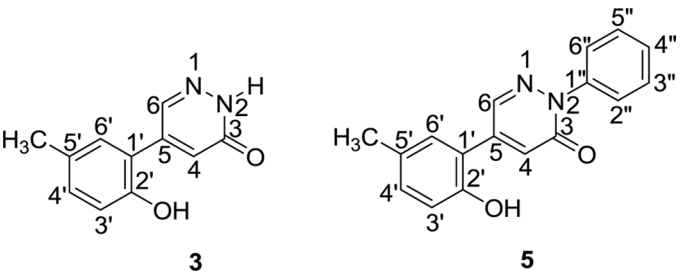
Table 3. Continued

Entry	Substrate	Product	Yield (%)	Melting point (°C)
8	 **1h**	 **5h**	75	226
9	 **1i**	 **5i**	74	244
10	 **1j**	 **5j**	78	224
11	 **1k**	 **5k**	72	169
12	 **1l**	 **5l**	71	270
13	 **1m**	 **5m**	70	237
14	 **1n**	 **5n**	68	192
15	 **1o**	 **5o**	71	258



Scheme 2. Plausible mechanism for the formation of 2,5-diaryl-pyridazin-3(2*H*)ones **5** from coumarins.

carried out on silica-gel plates obtained from Merck (Germany). The melting points were determined by using a Shital melting-point apparatus and are uncorrected. All the compounds were analyzed satisfactorily for C, H, and N. Infrared (IR) spectra (KBr disc) were recorded on a Nicolet-5700 Fourier transform (FT)–IR



Scheme 3. Numbering of **3** and **5**.

spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 300- and 400-MHz spectrometer using $CDCl_3$ as a solvent and tetramethylsilane (TMS) as an internal standard. The chemical shifts are expressed in δ ppm scale downfield from TMS, and proton signals are indicated as *s*, singlet; *d*, doublet; *t*, triplet; and *m*, multiplet. Autospec electron-impact mass spectrometer (70 ev) was used to record mass spectra.

General Procedure for Synthesis of 5-Aryl-pyridazin-3(*2H*)-ones (3a–g)

A mixture of subtituted-4-bromomethylcoumarin **1** (10 mmol) was refluxed with hydrazine hydrate **2** (99%) (50 mmol) in ethanol (10 mL) for 2 h. The reaction mixture was cooled and poured on ice-cold water, and the separated solid **3** was filtered off. It was washed several times with cold ethanol, dried, and recrystallized from a suitable solvent.

Selected Data

5-(2-Hydroxy-phenyl)-pyridazin-3(*2H*)-one (3a). Colorless solid (ethanol), mp 244 °C, yield 71%; IR (KBr, υ in cm^{-1}): 3210 (br), 1655 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.25 (s, 1H, C4-H of pyridazinone), 6.74–7.96 (m, 4H, Ar-H), 8.05 (s, 1H, C6-H of pyridazinone), 10.25 (s, 1H, NH, D_2O exchangeable), 12.60 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.28; N, 14.89. Found: C, 63.71; H, 4.20; N, 14.82.

5-(2,4-Dihydroxy-phenyl)-pyridazin-3(*2H*)-one (3b). Colorless solid (ethanol), mp 204 °C, yield 69%; IR (KBr, υ in cm^{-1}): 3232 (br), 1645 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.49 (s, 1H, C4-H of pyridazinone), 6.80 (s, 1H, C3′-H), 6.94 (d, 1H, $J = 7.34$ Hz, C5′-H), 7.42 (d, 1H, $J = 7.56$ Hz, C6′-H), 8.09 (s, 1H, C6-H of pyridazinone), 10.30 (s, 1H, OH, D_2O exchangeable), 10.92 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72. Found: C, 58.87; H, 4.03; N, 13.81.

5-(2-Hydroxy-4-methoxy-phenyl)-pyridazin-3(*2H*)-one (3c). Colorless solid (ethanol), mp 255 °C, yield 72%; IR (KBr, υ in cm^{-1}): 3129 (br), 1652 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 3.74 (s, 3H, OCH_3), 6.52 (m, 2H, C4-H of pyridazinone and C3′-H), 6.91 (d, 1H, $J = 7.38$ Hz, C5′-H), 7.37 (d, 1H, $J = 7.60$ Hz, C6′-H), 8.11 (s, 1H, C6-H of pyridazinone), 10.27 (s, 1H, NH, D_2O exchangeable), 12.84 (s, 1H, OH, D_2O exchangeable). ^{13}C NMR (100 MHz, DMSO): 55.32, 113.42, 119.34, 121.63, 128.75, 130.21, 132.29, 148.57, 155.63, 156.31, 161.14; LCMS m/z: 219 [M + 1]. Anal. calc. for $C_{11}H_{10}N_2O_3$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.48; H, 4.70; N, 12.78.

5-(2-Hydroxy-4,6-dimethyl-phenyl)-pyridazin-3(*2H*)-one (3d). Colorless solid (ethanol), mp 198 °C, yield 68%; IR (KBr, υ in cm^{-1}): 3188 (br), 1664 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 2.25 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 6.16 (s, 1H, C4-H of pyridazinone), 6.55 (s, 1H, C3′-H), 6.68 (s, 1H, C5′-H), 8.00 (s, 1H, C6-H of pyridazinone), 10.22 (s, 1H, NH, D_2O exchangeable), 12.36 (s, 1H, OH,

D_2O exchangeable). Anal. calc. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.56; H, 5.70; N, 12.79.

5-(2-Hydroxy-3,4-dimethyl-phenyl)-pyridazin-3(*2H*)-one (3e). Colorless solid (ethanol), mp 191 °C, yield 71%; IR (KBr, υ in cm^{-1}): 3185 (br), 1659 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 2.35 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 6.31 (s, 1H, C4-H of pyridazinone), 7.18 (d, 1H, $J = 7.41$ Hz, C5′-H), 7.49 (d, 1H, $J = 7.78$ Hz, C6′-H), 8.12 (s, 1H, C6-H of pyridazinone), 10.24 (s, 1H, NH, D_2O exchangeable), 12.94 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.52; H, 5.71; N, 12.82.

5-(3-Chloro-6-hydroxy-2,4-dimethyl-phenyl)-pyridazin-3(*2H*)-one (3f). Colorless solid (benzene), mp 216 °C, yield 65%; IR (KBr, υ in cm^{-1}): 3232 (br), 1645 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 2.24 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 6.14 (s, 1H, C4-H of pyridazinone), 6.51 (s, 1H, C3′-H), 8.10 (s, 1H, C6-H of pyridazinone), 10.21 (s, 1H, NH, D_2O exchangeable), 12.68 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{12}H_{11}ClN_2O_2$: C, 57.49; H, 4.42; N, 11.17. Found: C, 57.32; H, 4.34; N, 11.10.

5-(2-Hydroxy-4-methyl-3,5-dinitro-phenyl)-pyridazin-3(*2H*)-one (3g). Yellow-colored solid (ethanol), mp 206 °C, yield 65%; IR (KBr, υ in cm^{-1}): 3212 (br), 1651 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 2.41 (s, 3H, CH_3), 6.28 (s, 1H, C4-H of pyridazinone), 7.55 (s, 1H, C6′-H), 8.10 (s, 1H, C6-H of pyridazinone), 10.28 (s, 1H, NH, D_2O exchangeable), 12.62 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{11}H_8N_4O_6$: C, 45.21; H, 2.76; N, 19.17. Found: C, 45.10; H, 2.65; N, 19.06.

General Procedure for Synthesis of 2,5-Diaryl-pyridazin-3(*2H*)-ones (5a–o)

K_2CO_3(10 mmol) was added in ethanol (25 mL) to a mixture of subtituted-4-bromomethylcoumarin **1** (10 mmol) and phenylhydrazine **4** (50 mmol). The reaction mixture was refluxed for 3 h, cooled, and poured on ice-cold water, and the separated solid **5** was filtered off. It was washed several times with aqueous ethanol, dried, and recrystallized from suitable solvent.

Selected Data

5-(2-Hydroxy-phenyl)-2-phenyl-pyridazin-3(*2H*)-one (5a). Colorless solid (benzene), mp 201 °C, yield 71%; IR (KBr, υ in cm^{-1}): 3260 (OH), 1664 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 6.61 (s, 1H, C4-H of pyridazinone), 6.92 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.16 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.28–7.33 (m, 2H, Ar-H), 7.38 (d, 1H, $J = 8.60$ Hz, Ar-H), 7.80 (d, 1H, $J = 8.82$ Hz, Ar-H), 8.10 (s, 1H, C6-H of pyridazinone), 8.38 (d, 1H, $J = 9.50$ Hz, Ar-H), 8.53 (d, 1H, $J = 8.90$ Hz, Ar-H), 11.30 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.80; H, 4.64; N, 10.69.

5-(2,4-Dihydroxy-phenyl)-2-phenyl-pyridazin-3(*2H*)-one (5b). Colorless solid (benzene), mp 195 °C, yield 73%; IR (KBr, υ in cm^{-1}): 3240 (OH), 1661

(pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.64 (s, 1H, C4-H of pyridazinone), 6.86 (t, 1H, $J = 7.30$ Hz, C4″-H), 7.17 (d, 2H, $J = 7.56$ Hz, C3″ and C5″-H), 7.26–7.32 (m, 4H, Ar-H), 7.41 (d, 1H, $J = 8.20$ Hz, Ar-H), 8.00 (s, 1H, C6-H of pyridazinone), 11.12 (s, 1H, OH, D_2O exchangeable), 11.31 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99. Found: C, 68.51; H, 4.26; N, 9.87.

5-(2-Hydroxy-4-methoxy-phenyl)-2-phenyl-pyridazin-3(*2H*)-one (5c). Orange-colored solid (benzene), mp 212 °C, yield 75%; IR (KBr, υ in cm^{-1}): 3237 (OH), 1656 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 3.84 (s, 3H, OCH_3), 6.64 (s, 1H, C4-H of pyridazinone), 6.90 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.18 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.22–7.34 (m, 2H, Ar-H), 7.52 (d, 1H, $J = 8.80$ Hz, Ar-H), 7.62 (d, 1H, $J = 8.20$ Hz, Ar-H), 8.01 (s, 1H, C6-H of pyridazinone), 8.33 (s, 1H, C3′-H), 11.31 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{17}H_{14}N_2O_3$: C, 69.38; H, 4.79; N, 9.52. Found: C, 69.28; H, 4.70; N, 9.58.

5-(2-Hydroxy-4,6-dimethyl-phenyl)-2-phenyl-pyridazin-3(*2H*)-one (5d). Colorless solid (benzene), mp 184 °C, yield 76%; IR (KBr, υ in cm^{-1}): 3236 (OH), 1667 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 2.30 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 6.62 (s, 1H, C4-H of pyridazinone), 6.94 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.16 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.26–7.39 (m, 2H, Ar-H), 7.51 (s, 1H, Ar-H), 8.01 (s, 1H, C6-H of pyridazinone), 8.31 (s, 1H, Ar-H), 11.26 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.84; H, 5.39; N, 9.50.

5-(2-Hydroxy-3,4-dimethyl-phenyl)-2-phenyl-pyridazin-3(*2H*)-one (5e). Orange-colored solid (benzene), mp 188 °C, yield 76%; IR (KBr, υ in cm^{-1}): 3240 (OH), 1660 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 2.30 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 6.59 (s, 1H, C4-H of pyridazinone), 6.89 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.16 (d, 2H, $J = 7.14$ Hz, C3″ and C5″-H), 7.26–7.35 (m, 3H, Ar-H), 8.08 (s, 1H, C6-H of pyridazinone), 8.21 (d, 1H, $J = 8.10$ Hz, Ar-H), 11.26 (s, 1H, OH, D_2O exchangeable). ^{13}C NMR (100 MHz, DMSO): δ 20.69, 21.20, 109.20, 113.24, 115.49, 117.64, 121.54, 126.48, 130.24, 131.49, 134.65, 134.99, 143.52, 147.24, 150.32, 161.18; LCMS m/z: 293 [M + 1]. Anal. calc. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.89; H, 5.50; N, 9.49.

5-(3-Chloro-6-hydroxy-2,4-dimethyl-phenyl)-2-phenyl-pyridazin-3(*2H*)-one (5f). Colorless solid (benzene), mp 208 °C, yield 70%; IR (KBr, υ in cm^{-1}): 3231 (OH), 1650 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 2.32 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 6.65 (s, 1H, C4-H of pyridazinone), 6.97 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.19 (d, 2H, $J = 7.52$ Hz, C3″ and C5″-H), 7.31–7.40 (m, 2H, Ar-H), 8.01 (s, 1H, C6-H of pyridazinone), 8.24 (s, 1H, C3′-H), 11.23 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{18}H_{15}ClN_2O_2$: C, 66.16; H, 4.63; N, 8.57. Found: C, 66.05; H, 4.69; N, 8.52.

5-(2-Hydroxy-4-methyl-3,5-dinitro-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5g). Yellow-colored solid (benzene), mp 170 °C, yield 66%; IR (KBr, υ in cm^{-1}): 3230 (OH), 1656 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 2.42 (s, 3H, CH_3), 6.67 (s, 1H, C4-H of pyridazinone), 6.98 (t, 1H, $J = 7.30$ Hz, C4″-H),

7.20 (d, 2H, $J = 7.58$ Hz, C3″ and C5″-H), 7.12–7.40 (m, 2H, Ar-H), 8.04 (s, 1H, C6-H of pyridazinone), 8.20 (s, 1H, C6′-H), 11.31 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{17}H_{12}N_4O_6$: C, 55.44; H, 3.28; N, 15.21. Found: C, 55.39; H, 3.19; N, 15.10.

5-(2-Hydroxy-5-methyl-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5h). Yellow-colored solid (benzene), mp 226 °C, yield 75%; IR (KBr, υ in cm^{-1}): 3237 (OH), 1671 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 2.42 (s, 3H, CH_3), 6.56 (s, 1H, C4-H of pyridazinone), 6.88 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.16 (d, 2H, $J = 7.76$ Hz, C3″ and C5″-H), 7.26–7.35 (m, 4H, Ar-H), 8.03 (s, 1H, C6-H of pyridazinone), 8.43 (s, 1H, C6′-H), 11.23 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 20.69, 110.40, 112.93, 116.53, 116.63, 120.86, 125.88, 129.41, 130.99, 132.59, 133.36, 143.75, 145.57, 151.77, 160.26; LCMS m/z: 279 [M + 1]. Anal. calc. for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.32; H, 5.01; N, 10.05.

5-(2-Hydroxy-4-methyl-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5i). Yellow-colored solid (benzene), mp 244 °C, yield 74%; IR (KBr, υ in cm^{-1}): 3238 (OH), 1665 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 2.42 (s, 3H, CH_3), 6.61 (s, 1H, C4-H of pyridazinone), 6.88 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.16 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.29–7.35 (m, 3H, Ar-H), 7.45 (d, 1H, $J = 8.40$ Hz, Ar-H), 8.03 (s, 1H, C6-H of pyridazinone), 8.43 (s, 1H, C3′-H), 11.23 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 21.21, 110.92, 113.45, 117.05, 117.15, 121.38, 126.41, 129.93, 131.51, 133.11, 133.88, 144.27, 146.09, 152.29, 160.79; LCMS m/z: 279 [M + 1]. Anal. calc. for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.29; H, 4.99; N, 10.01.

5-(2-Hydroxy-5-methoxy-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5j). Orange-colored solid (benzene), mp 224 °C, yield 78%; IR (KBr, υ in cm^{-1}): 3246 (OH), 1661 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 3.87 (s, 3H, OCH_3), 6.62 (s, 1H, C4-H of pyridazinone), 6.88 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.17 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.24–7.32 (m, 3H, Ar-H), 7.37 (d, 1H, $J = 9.04$ Hz, Ar-H), 8.04 (s, 1H, C6-H of pyridazinone), 8.20 (s, 1H, C6′-H), 11.24 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 56.09, 109.46, 112.38, 113.42, 117.57, 118.37, 119.85, 121.38, 129.89, 132.60, 144.25, 145.78, 148.55, 155.89, 160.83; LCMS m/z: 295 [M + 1]. Anal. calc. for $C_{17}H_{14}N_2O_3$: C, 69.38; H, 4.79; N, 9.52. Found: C, 69.32; H, 4.75; N, 9.56.

5-(2-Hydroxy-naphthalen-1-yl)-2-phenyl-*2H*-pyridazin-3-one (5k). Brown-colored solid (benzene), mp 169 °C, yield 72%; IR (KBr, υ in cm^{-1}): 3254 (OH), 1644 (pyridazinone C=O); ^1H NMR (400 MHz, DMSO): δ 6.71 (s, 1H, C4-H of pyridazinone), 6.89 (t, 1H, $J = 7.28$ Hz, C4″-H), 7.18 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.32–7.38 (m, 2H, Ar-H), 7.70–7.74 (m, 2H, Ar-H), 7.91 (d, 1H, $J = 8.90$ Hz, Ar-H), 8.02 (d, 1H, $J = 9.12$ Hz, Ar-H), 8.12 (s, 1H, C6-H of pyridazinone), 8.39 (d, 1H, $J = 9.48$ Hz, Ar-H), 8.51 (d, 1H, $J = 8.90$ Hz, Ar-H), 11.30 (s, 1H, OH, D_2O exchangeable). Anal. calc. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.28; H, 4.40; N, 8.82.

5-(1-Hydroxy-naphthalen-2-yl)-2-phenyl-*2H*-pyridazin-3-one (5l). Orange-colored solid (benzene), mp 270 °C, yield 71%; IR (KBr, υ in cm^{-1}): 3267 (OH), 1650 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.75 (s, 1H, C4-H of pyridazinone), 6.90 (t, 1H, $J = 7.24$ Hz, C4″-H), 7.20 (d, 2H, $J = 7.60$ Hz, C3″ and C5″-H), 7.31–7.35 (m, 2H, Ar-H), 7.72–7.75 (m, 2H, Ar-H), 7.93 (d, 1H, $J = 9.01$ Hz, Ar-H), 8.04 (d, 1H, $J = 9.16$ Hz, Ar-H), 8.17 (s, 1H, C6-H of pyridazinone), 8.40 (d, 1H, $J = 9.52$ Hz, Ar-H), 8.54 (d, 1H, $J = 8.92$ Hz, Ar-H), 11.32 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 110.17, 113.02, 113.57, 121.46, 122.19, 122.30, 123.01, 124.46, 127.86, 128.32, 129.33, 129.95, 131.71, 134.61, 144.22, 147.16, 151.11, 160.53; LCMS m/z: 315 [M + 1]. Anal. calc. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.48; H, 4.54; N, 8.94.

5-(2-Hydroxy-5-chloro-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5m). Orange-colored solid (benzene), mp 237 °C, yield 70%; IR (KBr, υ in cm^{-1}): 3258 (OH), 1678 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.68 (s, 1H, C4-H of pyridazinone), 6.90 (t, 1H, $J = 7.32$ Hz, C4″-H), 7.14 (d, 2H, $J = 7.64$ Hz, C3″ and C5″-H), 7.30–7.35 (m, 2H, Ar-H), 7.45 (d, 1H, $J = 8.84$ Hz, Ar-H), 7.68 (d, 1H, $J = 8.84$ Hz, Ar-H), 8.00 (s, 1H, C6-H of pyridazinone), 8.79 (s, 1H, C6′-H), 11.29 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 112.50, 112.94, 118.02, 118.79, 121.06, 126.13, 128.16, 128.26, 129.44, 131.34, 131.72, 143.63, 144.42, 152.30, 159.73; LCMS m/z: 299 [M + 1]. Anal. calc. for $C_{16}H_{11}ClN_2O_2$: C, 64.33; H, 3.71; N, 9.38. Found: C, 64.28; H, 3.75; N, 9.30.

5-(2-Hydroxy-4-chloro-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5n). Orange-colored solid (benzene), mp 192 °C, yield 68%; IR (KBr, υ in cm^{-1}): 3250 (OH), 1672 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.67 (s, 1H, C4-H of pyridazinone), 6.91 (t, 1H, $J = 7.32$ Hz, C4″-H), 7.18 (d, 2H, $J = 7.82$ Hz, C3″ and C5″-H), 7.31–7.38 (m, 2H, Ar-H), 7.54 (d, 1H, $J = 8.80$ Hz, Ar-H), 7.64 (d, 1H, $J = 8.82$ Hz, Ar-H), 8.03 (s, 1H, C6-H of pyridazinone), 8.66 (s, 1H, C3′-H), 11.32 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 112.46, 112.92, 118.00, 118.75, 121.01, 126.10, 128.13, 128.23, 129.42, 131.31, 131.69, 143.60, 144.41, 152.25, 159.71; LCMS m/z: 299 [M + 1]. Anal. calc. for $C_{16}H_{11}ClN_2O_2$: C, 64.33; H, 3.71; N, 9.38. Found: C, 64.25; H, 3.77; N, 9.28.

5-(2-Hydroxy-5-bromo-phenyl)-2-phenyl-*2H*-pyridazin-3-one (5o). Orange-colored solid (benzene), mp 258 °C, yield 71%; IR (KBr, υ in cm^{-1}): 3227 (OH), 1677 (pyridazinone C=O); ^{1}H NMR (400 MHz, DMSO): δ 6.67 (s, 1H, C4-H of pyridazinone), 6.90 (t, 1H, $J = 7.24$ Hz, C4″-H), 7.14 (d, 2H, $J = 7.64$ Hz, C3″ and C5″-H), 7.30–7.35 (m, 2H, Ar-H), 7.40 (d, 1H, $J = 8.80$ Hz, Ar-H), 7.80 (d, 1H, $J = 8.84$ Hz, Ar-H), 8.00 (s, 1H, C6-H of pyridazinone), 8.96 (s, 1H, C6′-H), 11.30 (s, 1H, OH, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO): δ 112.53, 112.94, 116.03, 118.49, 119.08, 121.06, 129.22, 129.43, 131.75, 134.09, 143.64, 144.34, 152.70, 159.69; LCMS m/z: 345 [M + 1]. Anal. calc. for $C_{16}H_{11}BrN_2O_2$: C, 56.00; H, 3.23; N, 8.16. Found: C, 55.88; H, 3.17; N, 8.09.

CONCLUSION

In conclusion, this article provides an efficient method for the synthesis of mono- and diaryl-pyridazin-3(2*H*)-ones. Different substituents on coumarin and arylhydrazine provide a plethora of substituted 2,5-diaryl-pyridazin-3(2*H*)-ones. The synthetically viable yields (typically 50–80% or moderate to good isolated yield) and straightforward procedure for the preparation make this an attractive route to the diaryl-pyridazin-3(2*H*)-ones. The advantages offered by this method are readily available starting material, simple operation, insensitivity to air and moisture, good yields of products, and cost-effectiveness. Further, the reactivity of the phenolic hydroxyl group of 5-aryl moiety may be extended in the synthesis of biologically active compounds.

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