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ARTICLE

A green one-pot pseudo-five-component sequential protocol for the synthesis of novel 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives

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Abstract

A simple and efficient synthesis of novel 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives has been developed via a sequential one-pot, two-step, pseudo-five-component tandem reaction starting from 2-hydroxynaphthalene-1,4-dione, *o*-phenylenediamine, and aromatic aldehydes in the presence of 2-aminopyridine as co-catalyst and *p*-TsOH as catalyst at 90°C under solvent-free conditions. This sequential green process offers several advantages, such as operational simplicity, high yield, low cost, easy handling, clean reactions, absence of any tedious work-up, and purification of products by non-chromatographic methods.

KEYWORDS

benzo[*a*]phenazin-5-ol, lawsone, methylenebis(benzo[*a*]phenazin-5-ol), polycycles, quinones

1 | INTRODUCTION

Phenazine derivatives as nitrogen-containing heterocycles are of the main building blocks of different compounds of natural origin and synthetic organic molecules. Phenazine systems are among the important scaffolds and show various pharmaceutical activities such as trypanocidal,[1] antiplatet,[2] fungicidal,[3] antitumor, antimalarial, and antiphrastic.[4] Moreover, fluorescent phenazine derivatives are also of interest because of their applications such as electrochemical and biosensors,[5] organic semiconductors,[6] electroluminescence devices,[7] and photosensitizers in photodynamic therapy.[8]

Benzo[*a*]phenazines are structural subunits in a variety of important natural products and exhibit a variety of pharmaceutical activities, such as anticancer, antimalarial activities, and are also applied as useful substrates to prepare pesticides, antibiotics, dyestuffs, dual inhibitors of topoisomerase I and II, and are useful as antitumor agents.[9]

Recently, some synthetic routes to benzo[*a*]phenazine derivatives such as pyrazolo/pyrimido/pyrano/chromeno/furo/oxazino-fused benzophenazines, benzo[*a*]indenopyrano[2,3-*c*]phenazines, benzo[*a*]phthalazino-pyrazolo[3,4-*c*]phenazines under various conditions have been reported in the literature. A sequential one-pot, two-step tandem reaction starting from 2-hydroxy-1,-4-naphthoquinone and *o*-phenylenediamines with aldehydes, malononitrile, lawsone, ketons, 1,3-dicarbonyl compounds, cyanoalkyl acetate, tetracyanoethylene, acetylenic esters, pyrazolone, amines, isocyanide, phthalhydrazide, and others proceeded in the presence of various catalysts such as L-proline, $H_3PW_{12}O_{40}$, La@guanine@SBA-15, DABCO, *p*-TsOH, ionic liquids, H_2SO_4 or phosphotungestic acid, Fe_3O_4 (MNPs), $H_3PW_{12}O_{40}$@nano-ZnO, and nano-γ-Fe_2O_3@SiO_2-SCH_2CO_2H.[10]

Considering the importance of benzo[*a*]phenazine derivatives and in continuation of our ongoing program for the synthesis of heterocyclic compounds,[11] herein we wish to describe, for the *first* time, a new general

synthetic pathway for the *synthesis* of novel 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives via a domino, one-pot, two-step pseudo-five-component condensation reaction between 2-hydroxynaphthalene-1,-4-dione, *o*-phenylenediamine, and aromatic aldehydes in the presence of *p*-TsOH as catalyst and 2-aminopyridine as co-catalyst under solvent-free condition.

2 | RESULTS AND DISCUSSION

Initially, benzo[*a*]phenazine (**3**) was synthesized in 85% yield from the reaction of 2-hydroxynaphthalene-1,-4-dione (**1**) (1.0 mmol) and *o*-phenylenediamine (**2**) (1.0 mmol) at 90°C under solvent-free condition for 30 min. In addition, the reaction was accomplished in the presence of *p*-TsOH (20 mol%) for 15 min in the same reaction conditions and the desired product **3** was obtained in 89% yield (Scheme 1).

In order to investigate the reaction conditions for the synthesis of 6-((4-nitrophenyl)(pyridin-2-ylamino) methyl)benzo[a]phenazin-5-ol (**6a**), we carried out the reaction between benzo[*a*]phenazine (**3**) (1.0 mmol), 4-nitrobenzaldehyde (1.0 mmol), and 2-aminopyridine (1.0 mmol) as a model. We began this domino one-pot three-component reaction in the absence of a catalyst in EtOH under reflux and the product was obtained in 42% yield after 6.0 hr. Interestingly, analysis of the obtained product indicated that product 6,6′-((4-nitrophenyl) methylene)bis(benzo[*a*]phenazin-5-ol) (**5a**) has been formed instead of compound **6a** (Scheme 2).

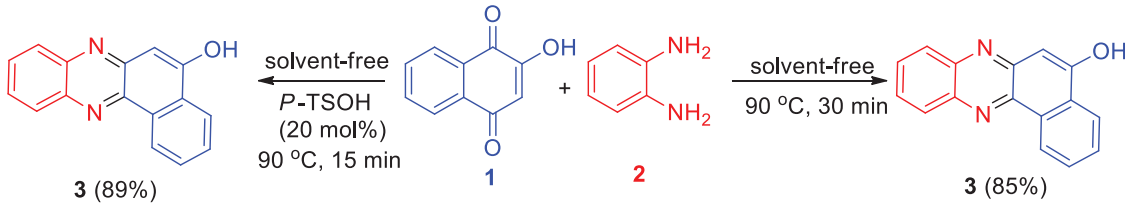
Therefore, it was decided to synthesize bis(benzo[*a*] phenazin-5-ol) derivatives **5**. In order to find optimization conditions, the one-pot reaction of benzo[*a*]phenazine (**3**) (1.0 mmol) and 4-nitrobenzaldehyde (0.5 mmol) was carried out with different amount of *p*-TsOH (5, 10, 15, 20 mol%) as catalyst in EtOH under reflux conditions. The results are summarized in Table 1. As a result, low yields were obtained in the presence of different amount of catalyst after a prolonged time (Table 1, Entries 2–5).

We discovered that addition of 2-aminopyridine to the reaction mixture showed better performance in terms of reaction time as well as yield of the product. However, the effect of amount of amine on the conversion and rate

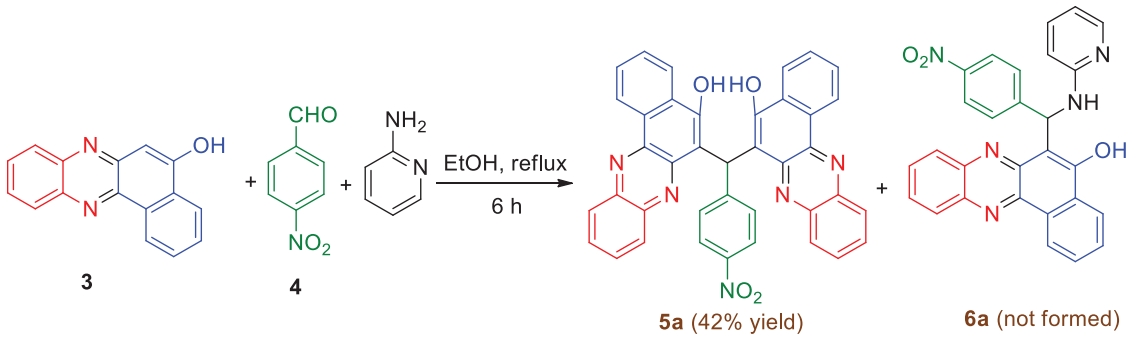
TABLE 1 Optimization of reaction conditions for the synthesis of **5a** in the presence of *p*-TsOH as catalyst[a]

Entry	*p*-TsOH (mol%)	Time (hr)	Yield[b] (%)
1	-	8	10
2	5	8	15
3	10	8	21
4	15	8	25
5	20	8	30

[a]All reactions were carried out using benzo[*a*]phenazine (**3**), (1.0 mmol) and 4- nitrobenzaldehyde (0.5 mmol) in EtOH. (5 ml) under reflux conditions.
[b]Isolated yield.



SCHEME 1 Synthesis of benzo[*a*]phenazine (**3**)



SCHEME 2 One-pot reaction of benzo[*a*]phenazine (**3**), 4-nitrobenzaldehyde and 2-aminopyridine

of the reaction was evaluated by varying the amount of 2-aminopyridine (10, 25, 50, 75 mol%) as co-catalyst (Table 2). As it was shown from Table 2, 50 mol% of 2-aminopyridine (0.5 mmol) as co-catalyst afforded product **5a** in 5.5 hr with 80% yield. Increasing the amount of amine to more than 50 mol%, showed no substantial improvement in the yield (Table 2, Entry 5).

Next, we examined the effect of different protic and aprotic solvents and solvent-free conditions on the model reaction. As Table 3 indicates, the best result was obtained by heating the reaction mixture under solvent-free conditions at 90°C (Table 3, Entry 7). So, a domino one-pot reaction of benzo[*a*]phenazine (**3**) (1.0 mmol), 4-nitrobenzaldehyde (0.5 mmol) using 20 mol% of *p*-TsOH as catalyst, and 2-aminopyridine (0.5 mmol) as co-catalyst at 90°C under solvent-free condition proved to be the optimum conditions.

Using these optimized reaction conditions, the scope and efficiency of the reaction were explored for the synthesis of a wide variety of substituted 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives **5** via one-pot two-step process. It should be noted that the first step 2-hydroxynaphthalene-1,4-dione (1.0 mmol), *o*-phenylenediamine (1.0 mmol), and *p*-TsOH (20% mol) were mixed at 90°C for 15 min until an orange solid of benzo[*a*]phenazine (**3**) was formed under solvent-free conditions. So, In the next step, aromatic aldehyde (0.5 mmol) and 2-aminopyridine (0.5 mmol) were added to the reaction mixture at 90°C for the synthesis of novel 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives **5a-i** (Scheme 3). The results are summarized in Figure 1. The influence of electron-donating and electron-withdrawing substituents on the aromatic ring of aldehydes upon the reaction yields was investigated. As Figure 1 indicates, aromatic aldehydes containing electron-withdrawing groups increased the rate of reaction and gave higher yields than that with electron-donating groups. After completion of the

TABLE 2 Optimization of reaction conditions for the synthesis of **5a** in the presence of 2-aminopyridine as co-catalyst[a]

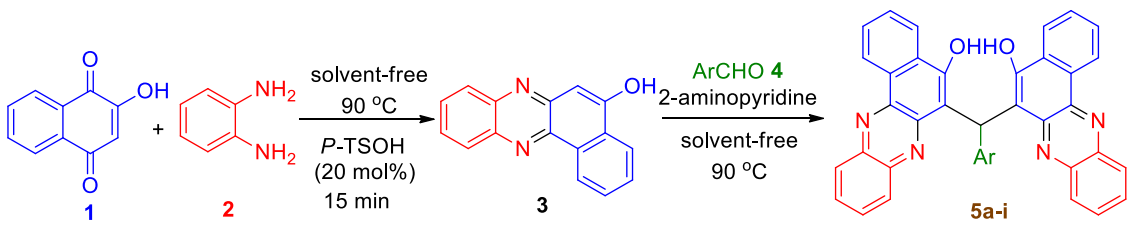
Entry	2-Aminopyridine (mol%)	Time (hr)	Yield[b] (%)
1	-	8	30
2	10	6	50
3	25	6	56
4	50	5.5	80
5	75	5.5	80

[a]All reactions were carried out using benzo[*a*]phenazine (**3**) (1.0 mmol), 4- nitrobenzaldehyde (0.5 mmol) and *p*-TsOH (20 mol%) in EtOH. (5 ml) under reflux conditions.
[b]Isolated yield.

TABLE 3 Optimization of the reaction conditions for the synthesis of **5a**[a] under various conditions

Entry	Solvent	Temperature (°C)	Time (hr)	Yield[b] (%)
1	EtOH	Reflux	5.5	80
2	CH_3CN	Reflux	8	42
3	$CHCl_3$	Reflux	8	40
4	THF	Reflux	8	34
5	H_2O	Reflux	10	25
6	-	90	2	90
7	-	70	2	78

[a]All reactions were carried out using benzo[*a*]phenazine (**3**) (1.0 mmol), 4- nitrobenzaldehyde (0.5 mmol), 2-aminopyridine (0.5 mmol), and *p*-TsOH (20 mol%).
[b]Isolated yield.



SCHEME 3 Synthesis of 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives **5**

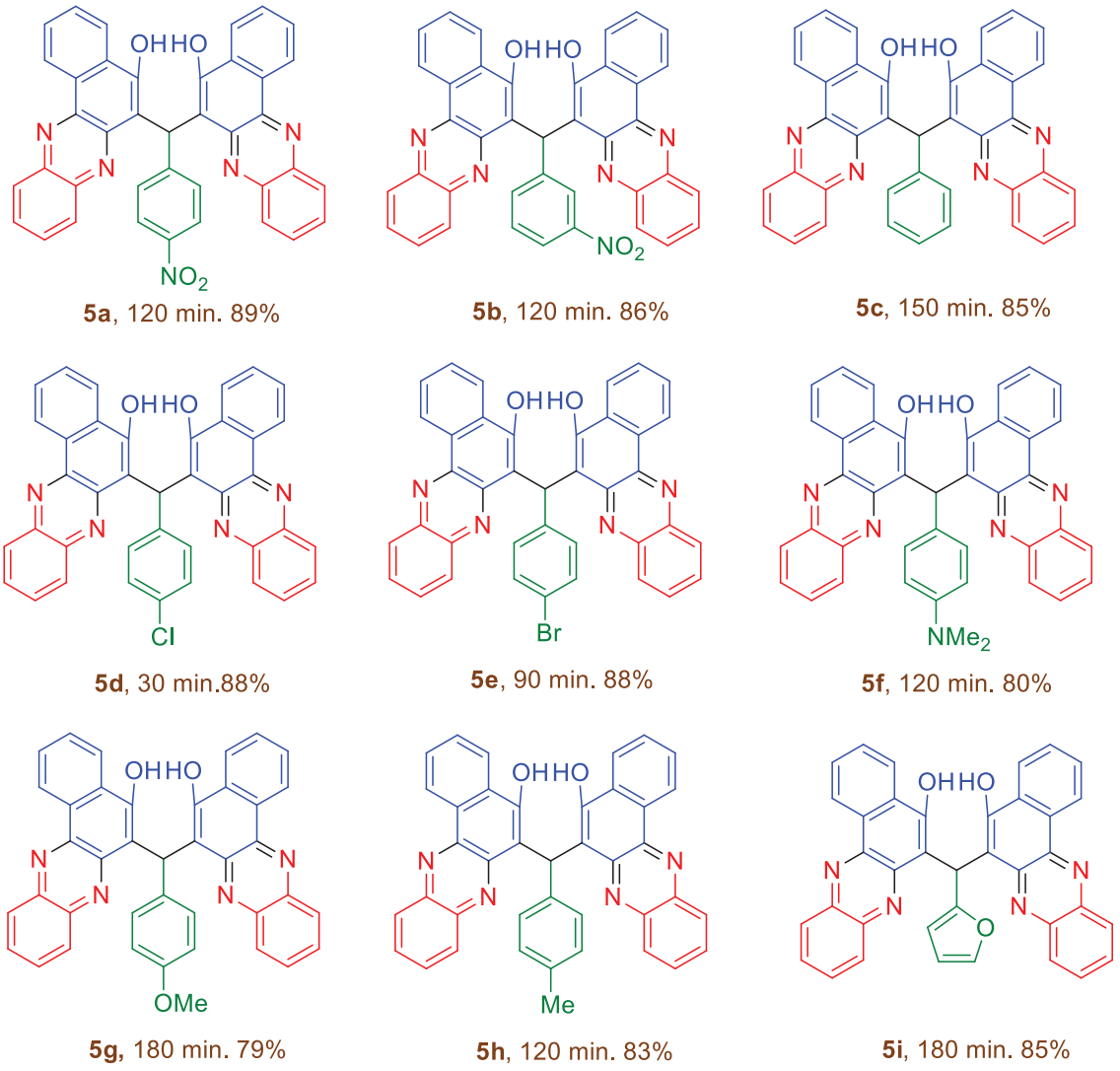
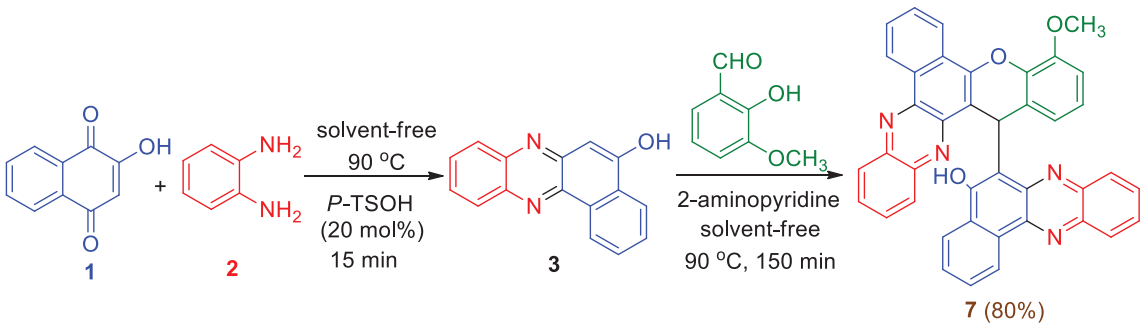


FIGURE 1 Synthesis of compounds **5a-i**

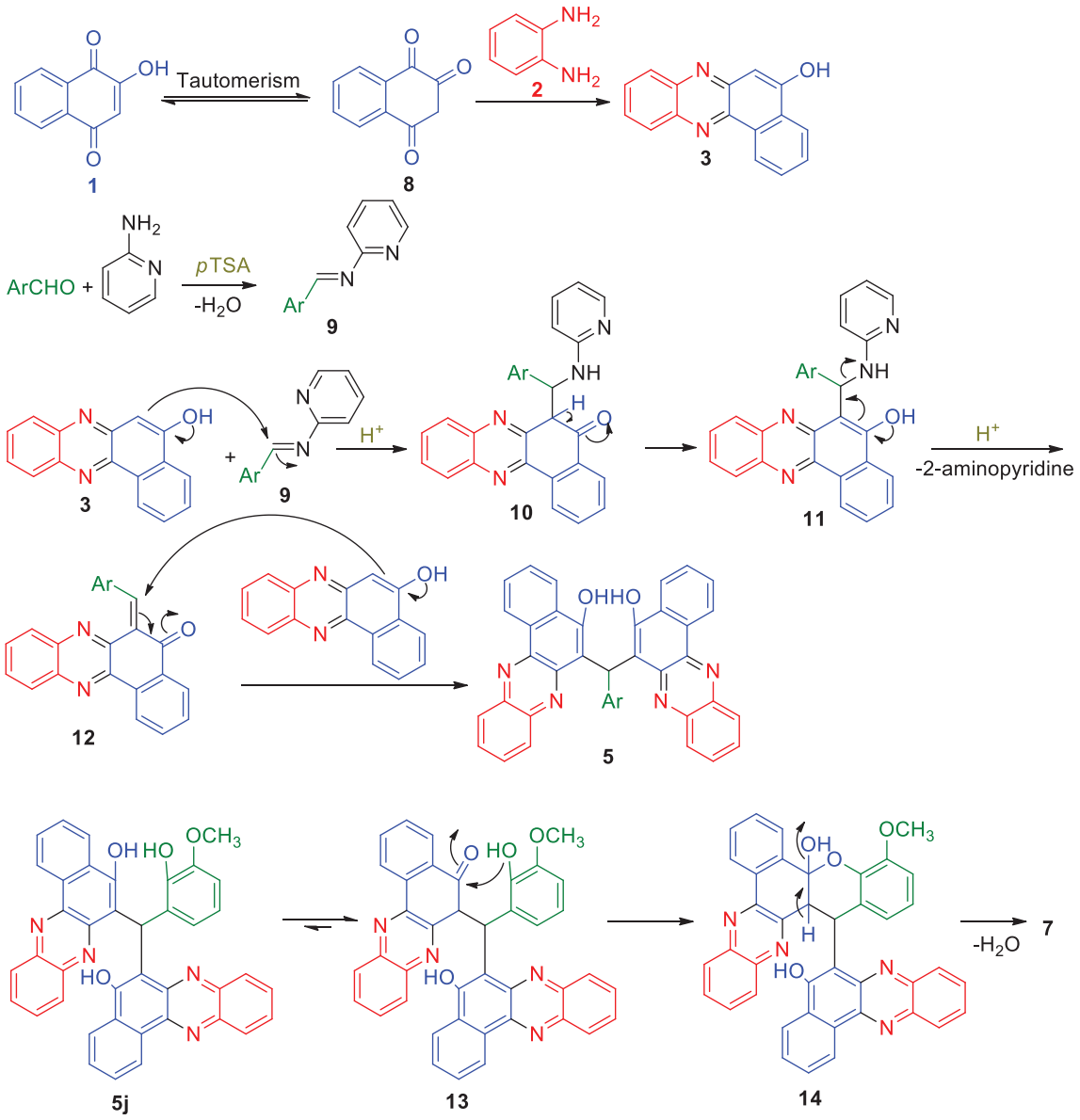
reaction, the reaction mixture was cooled to room temperature and 50 ml of $CHCl_3$ was added to this mixture. Then the mixture was stirred in boiling $CHCl_3$ and filtered. The solvent was recovered by evaporation using a rotary evaporator. The organic solid was washed with cold EtOAc and dried to give the pure product **5**.

When the reaction of benzo[*a*]phenazine (**3**) starting from 2-hydroxynaphthalene-1,4-dione (1.0 mmol) and *o*-phenylenediamine (1.0 mmol) with 2-hydroxy-3-methoxybenzaldehyde (0.5 mmol) was examined under the same reaction conditions, after 150 min, 6-(4-methoxy-16*H*-benzo[*a*]chromeno[2,3-*c*]phenazin-16-yl)benzo[*a*]phenazin-5-ol (**7**) was obtained in good yield (80%) (Scheme 4). Structural assignments of the compounds have been made on the basis of FT-IR, ^{1}H-NMR, ^{13}C-NMR, and Mass analysis. For example, the ^{1}H-NMR spectrum of compound **5a** shows two singlet signals for the hydroxyl groups localized at about δ = 14.60 and 15.11 ppm in agreement with an asymmetric structure in which they have hydrogen bonding. In addition, the ^{13}C-NMR spectrum of compound **5a** shows 37 types of carbon, which confirms the asymmetry of its structure.

A reaction mechanism consistent with the above results is shown in Scheme 5. Initially, 2-hydroxy-1,-4-naphthoquinone tautomerizes to intermediate **8**. The primary condensation of intermediate **8** with benzene-1,-2-diamine (**2**) obtain benzo[*a*]phenazin-5-ol (**3**). On the other hand, condensation of aromatic aldehyde with 2-aminopyridine in the presence of *p*-TsOH afforded Schiff base as intermediate **9**. Subsequently, nucleophilic addition of **3** to intermediate **8** led to the formation of intermediate **10**. Intermediate **9** tautomerizes to intermediate **11**. By leaving of 2-aminopyridine from intermediate **11**, *ortho*-qinonemethide **12** was produced. It should be noted that, 2-aminopyridine might act as a good leaving group in the acidic environment. Finally, Michael



SCHEME 4 Synthesis of compound **7**



SCHEME 5 Proposed mechanism for the synthesis of 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives **5a-i** and compound **7**

addition of benzo[*a*]phenazin-5-ol (**3**) to *o*-QM **12** affords the corresponding products **5**. For the formation of compound **7**, initially, intermediate **5j** was formed according to the proposed mechanism for **5a-i**. Then, intermediate **5j** tautomerizes to the keto form **13**, which undergoes intramolecular cyclization via an oxygen atom attacking

to the carbonyl group and elimination of water to afford the desired product **7**.

3 | EXPERIMENTAL

3.1 | General information

All commercially available chemicals and reagents were used without further purification. Melting points were determined with an Electrothermal model 9100 apparatus and are uncorrected. FT-IR spectra were recorded on a Shimadzu 4300 spectrophotometer. The ^{1}H-and ^{13}C-NMR spectra were recorded in $CDCl_3$ on Bruker DRX-300 Avance spectrometers. Chemical shifts (δ) are reported in parts per million and are referenced to the NMR solvent. Mass spectra of the products were obtained with a HP (Agilent technologies) 5973 Mass Selective Detector.

3.2 | General procedure for the synthesis of 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives 5

Initially, a mixture of 2-hydroxynaphthalene-1,4-dione (**1**) (1.0 mmol), *o*-phenylenediamine (**2**) (1.0 mmol), and *p*-TsOH (20 mol%) was placed in a 25 ml round-bottomed flask mounted over a magnetic stirrer. The contents were stirred magnetically in an oil-bath maintained at 90°C until after 15 min benzo[*a*]phenazin-5-ol (**3**) was formed. Then, aromatic aldehyde (**4**) (0.5 mmol), 2-aminopyridine (0.5 mmol) were added to the above reaction mixture, which was heated further at the same temperature for an appropriate time as shown in Figure 1. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion, the reaction mixture was cooled to room temperature. The crude product was dissolved in boiling chloroform (50 ml) and filtered. The solution was recovered via evaporation using a rotary evaporator and cold EtOAc (5 ml) was added. The precipitate was filtered, washed with cold EtOAc, and dried to give the pure products **5** and **7**.

3.3 | 6,6′-((4-Nitrophenyl)methylene)bis(benzo[*a*]phenazin-5-ol) (5a)

Crimson powder; M.P. >350°C; IR (KBr, cm^{-1}): 3,434, 3,064, 2,902, 1,643, 1,620, 1,590, 1,516, 1,454, 1,413, 1,377, 1,346, 1,231, 1,067; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.24 (d, 2H, J = 8.7 Hz, Ar-H), 7.43 (s, 1H, methine-H), 7.64–7.88 (m, 10H, Ar-H), 7.92 (d, 2H, J = 8.7 Hz, Ar-H), 8.22 (t, 1H, J = 8.4 Hz, Ar-H), 8.31 (d, 1H, J = 8.7 Hz, Ar-H), 8.47–8.62 (m, 2H, Ar-H), 9.21–9.23 (m, 2H, Ar-H), 14.60 (s, 1H, OH), 15.11 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 38.73, 111.79, 112.38, 123.30, 124.24, 124.44, 124.60, 124.66, 125.01, 125.03, 128.16, 128.37, 128.55, 129.38, 129.44, 129.67, 129.77, 130.41, 130.52, 130.63, 130.90, 130.95, 131.21, 131.23, 136.95, 137.91, 139.38, 139.48, 140.87, 142.31, 142.57, 143.66, 146.02, 147.50, 161.46, 162.93; MS m/z (%): 625 (M^+) (<1%), 379 (0.6), 378 (0.8), 332 (2), 303 (1), 247 (7.5), 246 (40), 245 (3), 219 (3.3), 218 (19), 217 (9), 190 (6.5), 151 (1.6), 121 (0.6), 114 (3.5), 89 (6.8), 87 (11), 85 (65), 83 (100), 77 (9), 50 (10).

3.4 | 6,6′-((3-Nitrophenyl)methylene)bis(benzo[*a*]phenazin-5-ol) (5b)

Orange powder; M.P. = 303–304°C; IR (KBr, cm^{-1}): 3,444, 3,063, 2,905, 1,620, 1,590, 1,520, 1,455, 1,410, 1,376, 1,347, 1,231, 1,065; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.22 (t, 1H, J = 7.8 Hz, Ar-H), 7.39 (d, 1H, J = 7.5 Hz, Ar-H), 7.46 (s, 1H, methine-H), 7.63–7.95 (m, 11H, Ar-H), 8.19–8.26 (m, 2H, Ar-H), 8.32 (d, 1H, J = 8.4 Hz, Ar-H), 8.47–8.50 (m, 1H, Ar-H), 8.60–8.63 (m, 1H, Ar-H), 9.20–9.24 (m, 2H, Ar-H), 14.60 (s, 1H, OH), 15.10 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 38.44, 111.86, 112.50, 121.12, 122.99, 124.43, 124.63, 124.81, 124.84, 125.19, 125.24, 128.32, 128.49, 128.95, 129.52, 129.59, 129.87, 129.95, 130.61, 130.69, 130.78, 131.11, 131.17, 131.32, 134.14, 137.18, 138.13, 139.57, 139.70, 141.05, 141.82, 142.55, 142.78, 143.94, 143.65, 161.55, 163.10; MS m/z (%): 625 (M^+) (<1%), 381 (4), 380 (20), 379 (76), 378 (63), 363 (8.5), 362 (31), 334 (12), 333 (51), 332 (86.5), 305 (16.5), 304 (32), 303 (44.3), 247 (40), 246 (100), 245 (14), 219 (14), 218 (75), 217 (39), 190 (22.7), 166 (15), 152 (8.3), 123 (8.7), 116 (8.3), 115 (7), 114 (9.9), 109 (8.3), 102 (10), 90 (9.3), 89 (15.5), 77 (19), 76 (10), 50 (4.5).

3.5 | 6,6′-(Phenylmethylene)bis(benzo[*a*]phenazin-5-ol) (5c)

Crimson powder; M.P. = 302°C dec.; IR (KBr, cm^{-1}): 3,440, 3,065, 2,926, 1,638, 1,590, 1,528, 1,498, 1,448, 1,411, 1,373, 1,348, 1,322, 1,231, 1,063; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.05 (s, 5H, ph-H), 7.49 (s, 1H, methine-H), 7.63–7.87 (m, 8H, Ar-H), 7.99–8.02 (m, 1H, Ar-H), 8.19–8.27 (m, 2H, Ar-H), 8.34 (d, 1H, J = 8.7 Hz, Ar-H), 8.51–8.62 (m, 2H, Ar-H), 9.23–9.25 (m, 2H, Ar-H), 14.51 (s, 1H, OH), 15.11 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 38.54, 113.08, 114.07, 124.59, 124.69, 125.06, 125.11, 125.26, 125.71, 127.34, 127.79, 128.16,

128.33, 129.12, 129.15, 129.70, 129.85, 130.47, 130.57, 130.68, 130.95, 131.08, 131.25, 137.71, 138.70, 138.96, 139.65, 139.72, 139.75, 141.77, 142.42, 142.65, 144.59, 146.71, 152.62, 160.68, 161.78; MS m/z (%): 580 (M^+) (<1%), 335 (11.8), 334 (55.5), 333 (100), 305 (18), 304 (7.5), 303 (12.7), 247 (13), 246 (73), 218 (40), 217 (20), 190 (15), 116 (7), 114 (7.5), 102 (7), 90 (7), 89 (13), 83 (7.5), 77 (18.5), 76 (8.2).

3.6 | 6,6′-((4-Chlorophenyl)methylene) bis(benzo[*a*]phenazin-5-ol) (5d)

Orange powder; M.P. = 304–306°C; IR (KBr, cm^{-1}): 3,433, 3,061, 2,910, 1,620, 1,589, 1,531, 1,488, 1,455, 1,411, 1,370, 1,348, 1,283, 1,231, 1,068; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.98 (d, 2H, J = 8.7 Hz, Ar-H), 7.03 (d, 2H, J = 8.7 Hz, Ar-H), 7.40 (s, 1H, methine-H), 7.65–7.88 (m, 8H, Ar-H), 8.01–8.04 (m, 1H, Ar-H), 8.20–8.28 (m, 2H, Ar-H), 8.34 (d, 1H, J = 8.7 Hz, Ar-H), 8.50–8.62 (m, 2H, Ar-H), 9.24 (d, 2H, J = 5.7 Hz, Ar-H), 14.56 (s, 1H, OH), 15.13 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 38.13, 112.68, 113.51, 114.45, 114.83, 115.74, 115.87, 124.57, 124.74, 124.89, 125.10, 125.14, 128.26, 128.44, 129.27, 129.32, 129.74, 129.88, 130.56, 130.65, 131.06, 131.09, 131.15, 131.20, 131.43, 137.50, 137.63, 138.49, 139.71, 141.45, 142.43, 142.97, 144.47, 152.32, 155.78, 160.94, 162.19; MS m/z (%): 616 $(M + 2)^+$ (<1%), 614 (M^+) (<1%), 370 (11.5), 368 (25), 367 (46), 339 (8), 334 (5), 333 (22), 303 (14.6), 299 (15.7), 247 (14), 246 (78), 245 (6), 218 (39), 217 (22), 216 (9.6), 190 (14.5), 166 (18.5), 125 (4.5), 123 (8.2), 116 (8.7), 115 (9), 114 (9), 85 (65), 83 (100), 79 (73), 47 (36).

3.7 | 6,6′-((4-Bromophenyl)methylene) bis(benzo[*a*]phenazin-5-ol) (5e)

Orange powder; M.P. = 295°C dec.; IR (KBr, cm^{-1}): 3,431, 3,060, 2,910, 1,620, 1,589, 1,531, 1,484, 1,455, 1,410, 1,376, 1,348, 1,284, 1,231, 1,067; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.93 (d, 2H, J = 8.1 Hz, Ar-H), 7.16 (d, 2H, J = 8.1 Hz, Ar-H), 7.38 (s, 1H, methine-H), 7.67–7.88 (m, 8H, Ar-H), 8.01–8.04 (m, 1H, Ar-H), 8.20–8.28 (m, 2H, Ar-H), 8.34 (d, 1H, J = 8.7 Hz, Ar-H), 8.50–8.53 (m, 1H, Ar-H), 8.59–8.62 (m, 1H, Ar-H), 9.23–9.25 (m, 2H, Ar-H), 14.56 (s, 1H, OH), 15.13 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 38.21, 119.56, 124.06, 124.25, 124.58, 124.74, 124.89, 125.09, 125.14, 128.24, 128.45, 129.28, 129.34, 129.68, 129.88, 130.55, 131.19, 138.16, 138.21, 138.48, 139.62, 143.23, 144.12, 145.14, 147.50, 151.93, 153.06, 153.50, 153.95, 154.46, 155.56, 156.16, 157.33, 157.69, 158.16, 160.11, 160.20; MS m/z (%): 660 $(M + 2)^+$ (<1%), 658 (M^+) (<1%), 414 (2.3), 413 (2), 379 (2.1), 333 (5.4), 332 (3.8), 331 (3), 305 (2.1), 304 (2.5), 303 (4.6), 299 (4.2), 272 (5.1), 262 (3.2), 261 (3.6), 260 (2.5), 259 (3.5), 246 (16), 218 (8.3), 193 (3.8), 192 (3.5), 155 (2.2), 154 (2.8), 152 (3), 123 (3.5), 116 (3.4), 115 (5.4), 94 (36), 85 (54), 83 (83), 79 (100), 78 (16.5), 77 (9), 67 (33), 52 (17).

3.8 | 6,6′-((4-(Dimethylamino)phenyl) methylene)bis(benzo[*a*]phenazin-5-ol) (5f)

Brown powder; M.P. = 233°C dec.; IR (KBr, cm^{-1}): 3,402, 3,062, 2,877, 2,797, 1,609, 1,590, 1,518, 1,455, 1,410, 1,373, 1,347, 1,230, 1,159, 1,066; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.74 (s, 6H, 2 x CH_3), 6.44 (d, 2H, J = 9.0 Hz, Ar-H), 6.87 (d, 2H, J = 9.0 Hz, Ar-H), 7.42 (s, 1H, methine-H), 7.65–7.86 (m, 8H, Ar-H), 8.06–8.09 (m, 1H, Ar-H), 8.19–8.26 (m, 2H, Ar-H), 8.34 (d, 1H, J = 8.1 Hz, Ar-H), 8.53–8.62 (m, 2H, Ar-H), 9.22–9.25 (m, 2H, Ar-H), 14.48 (s, 1H, OH), 15.12 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 37.67, 40.86, 112.79, 113.63, 114.65, 124.52, 124.63, 125.07, 125.35, 126.22, 126.71, 128.04, 128.21, 128.47, 128.94, 128.98, 129.11, 129.64, 129.79, 130.38, 130.48, 130.75, 130.96, 130.99, 131.04, 131.33, 137.86, 138.80, 139.10, 139.62, 139.67, 141.94, 142.37, 142.60, 144.71, 148.77, 160.45, 161.39; MS m/z (%): 623 (M^+) (<1%), 379 (6.3), 378 (4.5), 377 (16.7), 376 (19.8), 362 (4.4), 360 (4.2), 334 (3.5), 333 (9.6), 332 (3.4), 258 (5), 247 (10.4), 246 (54), 237 (30.4), 236 (14), 218 (28), 217 (14), 190 (10.5), 134 (12.5), 122 (9.5), 121 (100), 120 (37.8), 107 (21), 102 (4.2), 83 (4), 77 (12.5).

3.9 | 6,6′-((4-Methoxyphenyl)methylene) bis(benzo[*a*]phenazin-5-ol) (5g)

Crimson powder; M.P. = 307–308°C; IR (KBr, cm^{-1}): 3,443, 3,061, 2,948, 2,830, 1,619, 1,589, 1,530, 1,508, 1,454, 1,407, 1,371, 1,348, 1,245, 1,178, 1,067; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.63 (s, 3H, OCH_3), 6.60 (d, 2H, J = 8.7 Hz, Ar-H), 6.94 (d, 2H, J = 8.7 Hz, Ar-H), 7.42 (s, 1H, methine-H), 7.63–7.87 (m, 8H, Ar-H), 8.02–8.05 (m, 1H, Ar-H), 8.19–8.26 (m, 2H, Ar-H), 8.34 (d, 1H, J = 8.1 Hz, Ar-H), 8.51–8.62 (m, 2H, Ar-H), 9.21–9.24 (m, 2H, Ar-H), 14.52 (s, 1H, OH), 15.12 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 37.82, 55.28, 113.56, 114.28, 124.55, 124.68, 125.10, 125.25, 127.53, 128.15, 128.33, 128.82, 129.10, 129.14, 129.68, 129.83, 130.47, 130.58, 130.71, 130.76, 130.93, 131.01, 131.06, 131.09, 131.28, 137.69, 138.66, 139.37, 139.61, 139.68, 140.20, 141.74, 142.65, 152.93, 157.56, 160.67, 161.72, 165.11; MS m/z (%): 610 (M^+) (<1%), 379 (5.7), 364 (25),

363 (44.9), 349 (11), 333 (21.7), 329 (9), 321 (9.6), 320 (15.8), 313 (7), 299 (34.6), 292 (19.8), 247 (20), 246 (100), 236 (18.3), 218 (50), 217 (26.5), 190 (22), 152 (11), 123 (16), 109 (16), 98 (33), 97 (25.5), 95 (21), 89 (22), 85 (28), 84 (38), 83 (44), 79 (26), 77 (29), 51 (9.3).

3.10 | 6,6′-(*p*-Tolylmethylene)bis(benzo[*a*]phenazin-5-ol) (5h)

Crimson powder; M.P. = 280°C dec.; IR (KBr, cm^{-1}): 3,431, 3,058, 2,918, 1,620, 1,590, 1,531, 1,505, 1,454, 1,410, 1,372, 1,348, 1,286, 1,233, 1,067; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.16 (s, 3H, CH_3), 6.85 (d, 2H, J = 8.1 Hz, Ar-H), 6.92 (d, 2H, J = 8.1 Hz, Ar-H), 7.43 (s, 1H, methine-H), 7.63–7.87 (m, 8H, Ar-H), 8.02–8.05 (m, 1H, Ar-H), 8.19–8.27 (m, 2H, Ar-H), 8.33 (d, 1H, J = 7.5 Hz, Ar-H), 8.52–8.62 (m, 2H, Ar-H), 9.24 (d, 2H, J = 5.4 Hz, Ar-H), 14.50 (s, 1H, OH), 15.12 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.06, 38.18, 113.32, 114.13, 124.59, 124.69, 125.06, 125.09, 125.19, 127.65, 128.11, 128.27, 128.90, 129.09, 129.14, 129.69, 129.83, 130.46, 130.57, 130. 74, 130.91, 131.02, 131.07, 131.32, 135.08, 135.76, 137.63, 138.61, 139.58, 139.66, 141.74, 142.43, 142.66, 144.53, 160.79, 161.87; MS m/z (%): 594 (M^+) (<1), 349 (6), 348 (25.6), 347 (56.7), 334 (17.7), 333 (68), 319 (9), 299 (11.3), 247 (18), 246 (100), 245 (7), 218 (48.3), 217 (25), 190 (20.4), 174 (13.7), 166 (11.9), 123 (11), 115 (11), 114 (10.6), 102 (10), 90 (10.6), 89 (22), 79 (11.4), 77 (27.2), 76 (14), 51 (7).

3.11 | 6,6′-(Furan-2-ylmethylene)bis(benzo[*a*]phenazin-5-ol) (5i)

Crimson powder; M.P. = 283–285°C; IR (KBr, cm^{-1}): 3,442, 3,052, 2,961, 1,620, 1,590, 1,530, 1,502, 1,455, 1,411, 1,371, 1,350, 1,324, 1,287, 1,233, 1,067; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 5.87 (dd, 1H, J = 0.9, 1.8 Hz, Ar-H), 6.18–6.20 (dd, 1H, J = 1.2, 3.0 Hz, Ar-H), 7.11–7.13 (dd, 1H, J = 0.9, 1.5 Hz, Ar-H), 7.29 (s, 1H, methine-H), 7.68–7.87 (m, 8H, Ar-H), 8.14 (d, 1H, J = 8.4 Hz, Ar-H), 8.23(t, 2H, J = 7.8 Hz, Ar-H), 8.33 (d, 1H, J = 8.1 Hz, Ar-H), 8.54–8.62 (m, 2H, Ar-H), 9.19–9.23 (m, 2H, Ar-H), 14.44 (s, 1H, OH), 15.19 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 34.60, 107.46, 109.43, 110.39, 110.46, 110.73, 110.77, 111.73, 112.51, 124.62, 124.76, 125.11, 127.99, 128.16, 128.79, 129.24, 129.28, 129.77, 129.85, 130.50, 130.57, 130. 77, 131.07, 131.13, 131.28, 137.42, 138.14, 139.44, 139.46, 141.15, 141.58, 142.48, 142.60, 143.50, 152.90, 162.08, 162.18; MS m/z (%): 570 (M^+) (<1), 325 (5.7), 324 (22.4), 296 (10.5), 295 (31.8), 283 (33.8), 270 (13.3), 266 (22.8), 247 (19), 246 (100), 218 (53.5), 217 (28), 190 (21.5), 118 (10.3), 116 (10.5), 114 (12), 94 (51.3), 89 (19.6), 83 (22), 79 (12), 77 (22.6), 76 (11.4), 67 (48), 51 (13).

3.12 | 6-(4-Methoxy-16*H*-benzo[a]chromeno[2,3-*c*]phenazin-16-yl)benzo[*a*]phenazin-5-ol (7)

Brown powder; M.P. = 286–287°C; IR (KBr, cm^{-1}): 3,396, 3,057, 2,933, 1,585, 1,531, 1,497, 1,459, 1,414, 1,342, 1,270, 1,220, 1,096, 1,059; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.01 (s, 3H, OCH_3), 6.71–6.73 (m, 2H, methine-H, Ar-H), 7.49–8.01 (m, 12H, Ar-H), 8.21 (d, 1H, J = 8.4 Hz, Ar-H), 8.43 (d, 1H, J = 9.0 Hz, Ar-H), 8.64 (d, 1H, J = 8.1 Hz, Ar-H), 8.89 (d, 1H, J = 7.8 Hz, Ar-H), 9.11 (d, 1H, J = 7.8 Hz, Ar-H), 9.22 (d, 1H, J = 7.8 Hz, Ar-H), 12.94 (s, 1H, OH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 32.77, 56.68, 110.68, 111.16, 119.88, 120.68, 123.11,123.42, 124.14, 125.04, 125.37, 125.81, 126.11, 126.97, 128.08, 128.21, 128.75, 129.01, 129.10, 129.18, 129.23, 129.78, 129.94, 130.38, 130.55, 130.66, 130.95, 131.54, 139.63, 140.29, 140.49, 141.06, 141.88, 141.95, 142.12, 142.37, 143.90, 147.66, 151.64, 152.87; MS m/z (%): 608 (M^+) (<1), 364 (9.2), 299 (12), 246 (32), 218 (17.8), 171 (32), 115 (8.2), 105 (12.6), 94 (56.5), 85 (66.8), 83 (100), 79 (11.6), 77 (20), 67 (54.5), 57 (16.8), 48 (21), 47 (40).

4 | CONCLUSIONS

In summary, we have demonstrated a green, simple, efficient, and environment-friendly one-pot pseudo-five-component procedure for the synthesis of novel 6,6′-(arylmethylene)bis(benzo[*a*]phenazin-5-ol) derivatives via the reaction of 2-hydroxynaphthalene-1,-4-dione, benzene-1,2-diamine, aromatic aldehydes by using 2-aminopyridine as co-catalyst and a catalytic amount of *p*-TsOH (20 mol%) at 90°C under solvent-free conditions. In this process, addition of 2-aminopyridine as co-catalyst to the reaction mixture showed better performance in terms of reaction time as well as yield of the product. Moreover, simple experimental, clean reaction profile, avoidance of hazardous organic solvents, easy work-up as well as an isolation of the pure products without chromatography with high yields make it a useful protocol for the green synthesis of these compounds.

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