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SEID-ALI MIRMIRAN-YAZDI

AFSHIN YAZDANI ELAH ABADI

NASIM SHAMS

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A rapid, efficient, and green synthesis of benzo[*a*]chromeno[2,3-*c*]phenazine derivatives via microwave assistance and DABCO catalyzed a novel domino cyclization

Seyed-Ali MIRMIRAN-YAZDI[1], **Afshin YAZDANI-ELAH-ABADI**[2,*], **Nasim SHAMS**[3], **Razieh MOHEBAT**[3]

[1]Department of Chemistry, Tabriz Branch, Islamic Azad University, Tabriz, Iran
[2]Department of Biology, Science and Art University, Yazd, Iran
[3]Young Researchers and Elite Club, Yazd Branch, Islamic Azad University, Yazd, Iran

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Abstract: An efficient, convenient, and environmentally benign procedure for the synthesis of novel benzo[*a*]chromeno[2,3-*c*]phenazine derivatives has been developed by domino four-component condensation reaction between 2-hydroxynaphthalene-1,4-dione, *o*− phenylenediamine, aromatic aldehydes, and naphthols or phenol in the presence of a catalytic amount of DABCO as an expedient, ecofriendly, and reusable base catalyst under microwave irradiation in EtOH/H_2O (1:1). This green process produces biologically and pharmacologically significant heterocycles in a single one-pot operation and offers considerable advantages such as operational simplicity, short reaction time, high yields, reusability of the catalyst, absence of any tedious workup or purification, and avoidance of hazardous reagents/solvents.

Key words: Multicomponent domino reactions, microwave irradiation, green chemistry, DABCO, benzo[*a*]chromeno[2,3-*c*]phenazine

1. Introduction

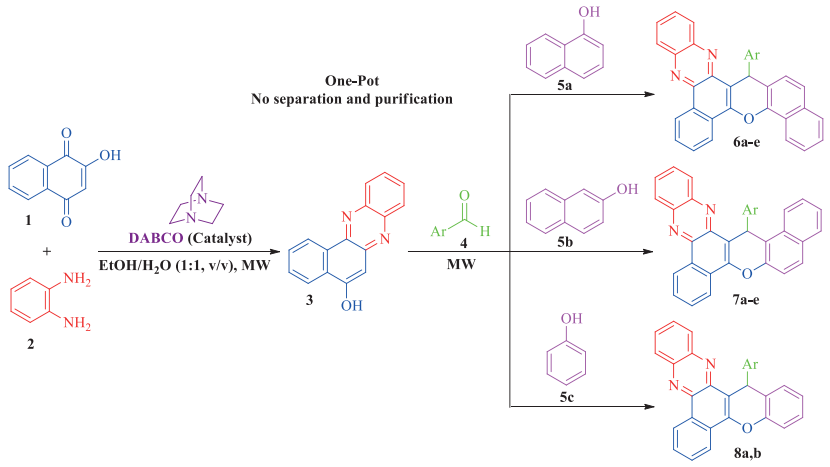
In the past few years, the development of environmentally friendly, efficient, and economical methods has received significant attention for the synthesis of biologically interesting compounds.[1,2] Considerable advances have been made on chemical processes to attain hazard-free, waste-free, and energy-effective syntheses as a final goal. In this area, multicomponent reactions involving a domino process (MDRs), in which more than two components are combined in a single synthetic operation, have been extensively used as a powerful strategy in the synthesis of chemically and biologically important organic frameworks because of their atom-, structure-, and bond-forming economy and green chemistry characteristics.[3−5] These processes can avoid time-consuming and costly processes for the purification of various precursors and tedious steps of protection and deprotection of functional groups.[6−8] Microwave-assisted organic synthesis has also become a very valuable tool, improving the outcome of multicomponent reactions,[9] because microwave heating is able to minimize side reactions, increase yields, reduce reaction times, improve reproducibility, and even enable inaccessible reactions by conventional heating. It is particularly useful for the preparation of various biologically active heterocyclic compounds.[10]

The design of novel MDRs using microwave irradiation for the synthesis of simple and complex bioactive heterocycles has remained a significant topic in the drug discovery process and the analysis of drugs[11,12]

*Correspondence: afi_yazdani@yahoo.com

Among them, heterocyclic systems, especially functionalized nitrogen and oxygen heterocycles, are of interest due to their pharmaceutical and biological activities[13,14] In this direction, heterocycles having phenazine and chromene moieties are important targets in the synthetic organic and medicinal chemistry.[15−17] Therefore, the development of the design and synthesis of new diverse polycyclic heterocycles with potential medicinal and biological activity from readily available starting materials in a cost- and time-effective manner has received significant attention for research in organic, combinatorial, and medicinal chemistry.[18−20]

Considering the considerable potential of novel phenazine and chromene derivatives as a source of valuable drug candidates and with our continued interest in multicomponent reactions and our ongoing program for the synthesis of heterocyclic systems based on green chemistry protocols,[21−25] here we report a green and efficient method for the synthesis of novel benzo[a]chromeno[2,3-c]phenazines **6**/**7**/**8** through a single-pot, domino, four-component condensation reaction between 2-hydroxy-1,4-naphthoquinone **1**, $o-$phenylenediamine **2**, aromatic aldehydes **4**, and naphthols or phenol **5** catalyzed by DABCO as an efficient, nontoxic, and reusable solid base catalyst under microwave irradiation (300 W, max. 100 °C) in EtOH/H_2O (1:1) (Scheme 1).



Scheme 1. One-pot, four-component synthesis of benzo[a]chromeno[2,3-c]phenazine derivatives in the presence of DABCO as catalyst.

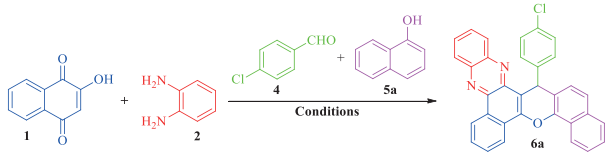
2. Results and discussion

The vast biological and pharmacological importance of phenazine and chromene derivatives inspired us to develop a novel protocol for their efficient synthesis. We desired to find a practical and general method for their synthesis in high yields and purities and, as the development of efficient and environmentally friendly synthetic procedures is always desirable, we decided to determine whether those phenazines and chromenes could be prepared by condensation of 2-hydroxy-1,4-naphthoquinone, $o-$phenylenediamine, aromatic aldehydes, and naphthols or phenol in the absence of any organic solvent.

In order to investigate the optimizing reaction conditions for the synthesis of benzo[a]chromeno[2,3-c]phenazines, we carried out the four-component domino reaction between 2-hydroxynaphthalene-1,4-dione **1** (1 mmol), $o-$phenylenediamine **2** (1 mmol), 4-chlorobenzaldehyde **4** (1 mmol), and 1-naphthol **5** (1 mmol) in EtOH as a model. Initially, to minimize the formation of byproducts, the 2-hydroxynaphthalene-1,4-dione and $o-$phenylenediamine were mixed under microwave irradiation at 180 W (max. 70 °C) until in less than 5 min an orange solid of benzo[a]phenazin-5-ol **3** was formed without using any catalyst. Next, 4-chlorobenzaldehyde and 1-naphthol were added and the mixture was irradiated under microwave irradiation at 180 W (max. 70 °C).

The desired product **6a** was not obtained when the reaction was carried out in catalyst-free conditions for 60 min (Table 1, entry 1). However, **6a** was obtained in 65% yield when the reaction was conducted in the presence of triethylamine (20 mol%) in EtOH (Table 1, entry 2). Several catalysts were evaluated in the reaction, including triethylamine, piperidine, DBU, oxalic acid, PTSA, and DABCO; these were all added in substoichiometric amounts (20 mol%) and the reactions were carried out in ethanol under microwave irradiation. DABCO showed excellent catalytic activity in terms of reaction time as well as yield of the product (Table 1, entry 5). To select the best solvent for the reaction, the synthesis of compound **6a** was also examined in different solvents (Table 1). As Table 1 indicates, the examined solvents were not efficient separately. Higher yields and shorter reaction times were obtained when the reaction was carried out in EtOH/H_2O (1:1), due to its strong hydrogen bonding ability, hydrophobic effects, and high polarity. In this experiment no other organic solvents were tested because of the green chemistry concept. We then evaluated the amount of catalyst required for this transformation. An increase in the amount of DABCO to more than 20 mol% showed no remarkable improvement in the yield, whereas the yield was reduced by decreasing the amount of DABCO to 10 mol%. Finally, the reaction was performed at different powers to determine the optimum reaction power. The reaction was conducted with 20 mol% DABCO in EtOH/H_2O (1:1) at 100, 180, and 300 W, and the desired product **6a** was formed in yields of 57%, 81%, and 86% (Table 1, entries 12, 9, and 13), respectively. Although the benzo[a]phenazin-5-ol **3** can be achieved in the absence of any catalyst, to increase the reaction rate and according to the definition of "domino reactions" coined by Tietze,[3,6,7] the catalyst was used in the first step of the reaction.

Table 1. Optimization of reaction conditions of compound **6a**[a].



Entry	Catalyst	Reaction conditions	Time (min)	Yield (%)[b]
1	No catalyst	EtOH, 180 W	60	NR
2	Et_3N (20 mol%)	EtOH, 180 W	30	65
3	Piperidine (20 mol%)	EtOH, 180 W	30	57
4	DBU (20 mol%)	EtOH, 180 W	30	53
5	DABCO (20 mol%)	EtOH, 180 W	30	74
6	PTSA (20 mol%)	EtOH, 180 W	30	NR
7	Oxalic acid (20 mol%)	EtOH, 180 W	30	Trace
8	DABCO (20 mol%)	H_2O, 180 W	30	45
9	DABCO (20 mol%)	EtOH/H_2O (1:1), 180 W	30	81
10	DABCO (30 mol%)	EtOH/H_2O (1:1), 180 W	30	80
11	DABCO (10 mol%)	EtOH/H_2O (1:1), 180 W	30	75
12	DABCO (20 mol%)	EtOH/H_2O (1:1), 100 W	60	57
13	DABCO (20 mol%)	EtOH/H_2O (1:1), 300 W	20	86
14	DABCO (20 mol%)	EtOH/H_2O (1:1), rt	180	NR

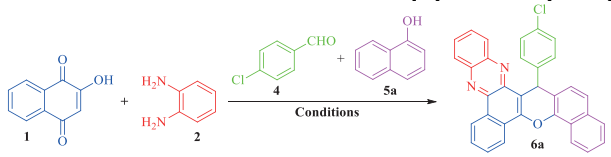
[a] Reaction conditions: 2-hydroxynaphthalene-1,4-dione (1 mmol), $o-$phenylenediamine (1 mmol), 4-chlorobenzaldehyde (1 mmol), and 1-naphthol (1 mmol) in the presence of different catalytic systems under various conditions.

[b] Isolated yields.

After extensive screening, we found that the optimized best yields and time profiles were obtained with 20 mol% of DABCO under microwave irradiation (300 W, max. 100 °C) in EtOH/H_2O (1:1), which furnished the corresponding 16-(4-chlorophenyl)-16*H*-benzo[*a*]benzo[7,8]chromeno[2,3-*c*]phenazine **6a** in 86% yield within 20 min (Table 1, entry 13).

Using these optimized conditions, we turned our attention to investigating the scope and general applicability of this methodology by carrying out the synthesis of benzo[*a*]chromeno[2,3-*c*]phenazines using different aromatic aldehydes and various naphthols. The results are summarized in Table 2.

Table 2. Domino one-pot four-component synthesis of benzo[*a*]chromeno[2,3-*c*]phenazine derivatives[a].



Entry	R	Product	Time (min)	Yield (%)[b]
1	4-Cl	**6a**	20	86
2	4-NO_2	**6b**	20	82
3	H	**6c**	30	80
4	4-Me	**6d**	40	80
5	4-OMe	**6e**	40	81
6	4-Cl	**7a**	20	89
7	4-NO_2	**7b**	20	88
8	3-NO_2	**7c**	20	85
9	H	**7d**	30	83
10	4-Me	**7e**	40	80
11	4-Cl	**8a**	40	54
12	4-NO_2	**8b**	40	67

[b] Isolated yields. [a] Reaction conditions: 2-hydroxynaphthalene-1,4-dione (1 mmol), *o*−phenylenediamine (1 mmol), aromatic aldehyde (1 mmol), naphthols or phenol (1 mmol), and DABCO (20 mol%) under microwave irradiation (300 W, max. 100 °C) in EtOH/H_2O (1:1, 10 mL).

[b] Isolated yields.

The extensive ranges of substituted and structurally various benzaldehydes afforded the corresponding products in high yields using DABCO as an environmentally friendly catalyst (20 mol%). As shown in Table 2, this domino reaction was efficiently promoted using benzaldehydes containing electron-withdrawing groups with reduced reaction times and increased yields rather than with electron-donating groups.

Additionally, the recyclability of the catalyst was investigated under reaction conditions using a model reaction of 2-hydroxynaphthalene-1,4-dione, *o*−phenylenediamine, 4-chlorobenzaldehyde, and 1-naphthol. After completion of the reaction, the reaction mixture was cooled to room temperature. Then 5 mL of water was added to the mixture and the crude solid product was filtered and washed with H_2O (2 × 5 mL). The DABCO was removed from the reaction media by washing with H_2O. Since the catalyst is soluble in water, the catalyst was recovered by evaporation of the water, washed with diethyl ether, and reused for the subsequent catalytic runs.

As shown in the Figure, the recovered catalyst works with the same performance up to the 2nd run, while in the 3rd, 4th, and 5th runs the product yield is reduced slightly, which may be due to a little weight loss of the catalyst during each recovery process.

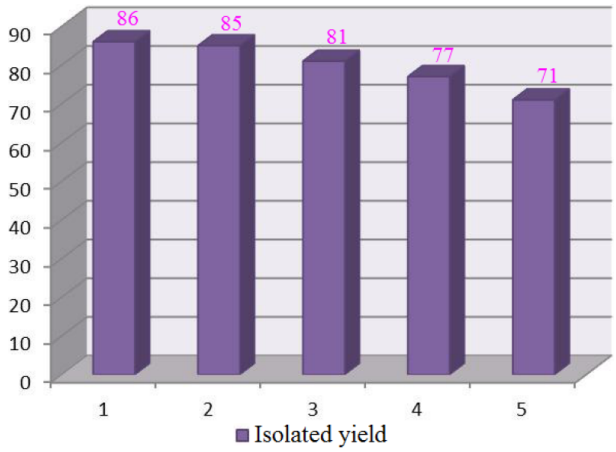


Figure. The investigation of the recycling of DABCO.

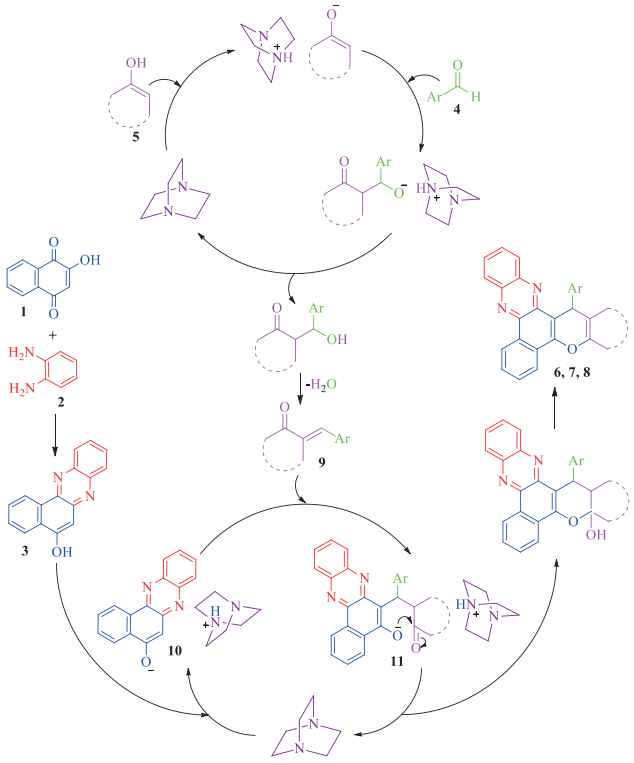
The probable mechanism for the domino cyclocondensation of benzo[*a*]chromeno[2,3-*c*]phenazines **6/7/8** using DABCO is outlined in Scheme 2 according to the literature.[19] On the basis of this mechanism, the primary condensation of 2-hydroxynaphthalene-1,4-dione **1** with benzene-1,2-diamine **2** in the presence of DABCO gives benzo[*a*]phenazin-5-ol **3**. Based on this mechanism, DABCO is an efficient catalyst to form the olefin **9**, which is readily prepared in situ from the Knoevenagel condensation of aromatic aldehyde **4** with naphthol **5**. In the presence of DABCO, benzo[*a*]phenazin-5-ol **3** converts to its corresponding enolate form **10**, to be able to react (Michael addition) easily with olefin **9** and to eventually give rise to the formation of intermediate **11**, which then makes the inner molecular ring be formed after a tautomeric proton shift to produce benzo[*a*]chromeno[2,3-*c*]phenazine derivatives **6**–**8**.

In summary, we have developed a green procedure for the facile synthesis of various potentially biologically active polyfunctionalized benzo[*a*]chromeno[2,3-*c*]phenazines in high yields, using novel four-component domino reactions under microwave irradiation in EtOH/H_2O (1:1). This single-pot condensation reaction was carried out in the presence of DABCO as an efficient and reusable solid base catalyst. This new environmentally friendly protocol with excellent green chemistry credentials, such as use of a low-loading and reusable nontoxic catalyst that is easy to handle, very short reaction time without any byproduct, avoidance of hazardous organic solvents, and easy workup, may find a wide range of applications.

3. Experimental

3.1. General

All melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-470 spectrometer. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer at the Iranian Central Petroleum Company Research Institute. Mass spectra were recorded on an Agilent Technology (HP) spectrometer operating at an ionization potential of 70 eV. The ^{1}H nuclear magnetic resonance (NMR) and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-300 spectrometer operating at 300 MHz for ^{1}H analysis and 75 MHz for ^{13}C analysis. All reactions were carried out using a laboratory microwave oven (MicroSYNTH, Milestone Company, Italy). Thin-layer chromatography (TLC) was performed on silica-gel Polygram SILG/UV 254 plates. All reagents and solvent were purchased from Merck and Aldrich and were used without further purification.



Scheme 2. Proposed mechanism for the synthesis of benzo[*a*]chromeno[2,3-*c*]phenazine derivatives.

3.2. General procedure for the synthesis of novel benzo[*a*]chromeno[2,3-*c*]phenazine derivatives (6–8)

DABCO (20 mol%) was added to a mixture of 2-hydroxynaphthalene-1,4-dione **1** (1 mmol) and *o*-phenylenediamine **2** (1 mmol) in EtOH/H_2O (1:1, v/v) (10 mL) and this mixture was irradiated in a microwave oven at 300 W until in less than 3 min an orange solid of benzo[*a*]phenazin-5-ol **3** was formed. The microwave was programmed to give a maximum internal temperature of 100 °C. Aryl aldehydes **4** (1 mmol) and naphthols or phenol (1 mmol) **5** were then added to the above reaction mixture, which was irradiated further at the same temperature (300 W, max. 100 °C) for an appropriate time as shown in Table 2. Upon completion of the reaction, monitored by TLC, the reaction mixture was allowed to cool to room temperature. Then 5 mL of water was added to the mixture and filtered for separation of the crude product. The separated product was washed twice with water (2 × 5 mL). The solid crude product subsequently recrystallized from hot ethanol to give the pure product **6**/**7**/**8**. The spectral and analytical data are presented below.

3.2.1. 16-(4-Chlorophenyl)-16*H*-benzo[*a*]benzo[7,8]chromeno[2,3-*c*]phenazine (6a)

Yellow powder; yield 0.425 g (86%), mp 286–288 °C; IR (KBr): ν_{max} = 3032, 1654, 1630, 1595, 1482, 1357, 1226, 1152, 1075, 759 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.95 (s, 1H, CH), 7.17 (d, 2H, J = 8.1 Hz, Ar-H), 7.51 (d, 2H, J = 8.1 Hz, Ar-H), 7.69 (dd, 1H, J_1 = 2.1 Hz, J_2 = 7.8 Hz, Ar-H), 7.91–8.02 (m, 6H, Ar-H), 8.08 (t, 2H, J = 6.9 Hz, Ar-H), 8.20–8.24 (m, 2H, Ar-H), 8.41 (d, 1H, J = 7.8 Hz, Ar-H), 8.66 (d, 1H, J = 7.8 Hz, Ar-H), 9.27 (d, 1H, J = 7.8 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.7 (CH), 114.5, 116.3, 120.5, 121.8, 122.0, 122.5, 124.5, 125.4, 125.8, 126.7, 128.5, 128.7, 129.2, 129.6, 129.9 (2x), 130.0, 130.5 (2x), 130.7

(2x), 131.1 (2x), 131.4, 132.1, 140.5, 141.6, 142.7, 144.8, 145.7, 149.9, and 156.4 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 494 (M^+, 7); Anal. Calcd. for $C_{33}H_{19}ClN_2O$: C, 80.08; H, 3.87; N, 5.66 %. Found: C, 80.51; H, 4.21; N, 5.92 %.

3.2.2. 16-(4-Nitrophenyl)-16*H*-benzo[*a*]benzo[7,8]chromeno[2,3-*c*]phenazine (6b)

Yellow powder; yield 0.414 g (82%), mp 272–275 °C; IR (KBr): ν_{max} = 3010, 1665, 1633, 1580, 1523, 1345, 1296, 1152, 1074, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.91 (s, 1H, CH), 7.22 (d, 2H, J = 8.1 Hz, Ar-H), 7.71 (d, 2H, J = 8.1 Hz, Ar-H), 7.85–7.97 (m, 7H, Ar-H), 8.00 (d, 2H, J = 8.4 Hz, Ar-H), 8.12 (t, 2H, J = 8.4 Hz, Ar-H), 8.33 (d, 1H, J = 7.8 Hz, Ar-H), 8.53 (d, 1H, J = 7.8 Hz, Ar-H), 9.27 (d, 1H, J = 8.1 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.4 (CH), 115.7, 116.1, 121.0, 121.5, 122.2, 122.5, 123.9, 125.1 (2x), 125.9, 127.2, 128.5 (2x), 128.8, 129.1, 129.7 (2x), 130.0, 130.2, 130.5 (2x), 131.3, 131.9, 132.4 (2x), 141.1, 141.8, 142.5, 145.2, 145.7, 150.5, and 155.9 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 505 (M^+, 4); Anal. Calcd. for $C_{33}H_{19}N_3O_3$: C, 78.40; H, 3.79; N, 8.31 %. Found: C, 78.69; H, 4.11; N, 8.64 %.

3.2.3. 16-Phenyl-16*H*-benzo[*a*]benzo[7,8]chromeno[2,3-*c*]phenazine (6c)

Yellow powder; yield 0.368 g (80%), mp 280–282 °C; IR (KBr): ν_{max} = 3125, 1658, 1625, 1595, 1544, 1381, 1267, 1162, 1053, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.78 (s, 1H, CH), 7.06-7.10 (m, 1H, Ar-H), 7.32–7.44 (m, 6H, Ar-H), 7.74–7.83 (m, 5H, Ar-H), 8.09–8.14 (m, 3H, Ar-H), 8.20–8.25 (m, 2H, Ar-H), 8.41 (d 1H, J = 7.8 Hz, Ar-H), 9.18 (d, 1H, J = 7.8 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.1 (CH), 115.5, 117.3, 120.2, 121.3, 122.3, 123.4, 125.4 (2x), 126.2 (2x), 127.3 (2x), 128.6 (2x), 129.1, 129.8, 130.1 (2x), 130.2 (2x), 130.7, 131.2, 131.4, 132.3 (2x), 140.5, 142.1, 142.5, 145.5, 146.9, 150.2, and 156.2 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 460 (M^+, 11); Anal. Calcd. for $C_{33}H_{20}N_2O$: C, 86.07; H, 4.38; N, 6.08 %. Found: C, 86.25; H, 4.70; N, 6.34 %.

3.2.4. 16-(*p*-Tolyl)-16*H*-benzo[*a*]benzo[7,8]chromeno[2,3-*c*]phenazine (6d)

Yellow powder; yield 0.379 g (80%), mp 235–237 °C; IR (KBr): ν_{max} = 2985, 1651, 1627, 1592, 1530, 1356, 1285, 1132, 1051, 761 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H, CH_3), 5.63 (s, 1H, CH), 6.95 (t, 1H, J = 7.8 Hz, Ar-H), 7.09 (d, 2H, J = 8.1 Hz, Ar-H), 7.29 (d, 2H, J = 8.1 Hz, Ar-H), 7.37–7.42 (m, 2H, Ar-H), 7.85–8.11 (m, 7H, Ar-H), 8.31 (t, 1H, J = 8.1 Hz, Ar-H), 8.52–8.56 (m, 2H, Ar-H), 9.24–9.26 (m, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.4 (CH_3), 40.1 (CH), 116.2, 118.2, 120.3 (2x), 121.5, 122.4, 122.5, 122.9, 125.4, 126.4 (2x), 128.2, 128.8 (2x), 129.1, 129.5 (2x), 129.8, 130.1, 130.2, 130.4, 130.6, 131.5, 132.3 (2x), 136.6, 140.2, 141.4, 141.9, 145.7, 151.4, and 157.2 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 474 (M^+, 7); Anal. Calcd. for $C_{34}H_{22}N_2O$: C, 86.05; H, 4.67; N, 5.90 %. Found: C, 86.42; H, 4.36; N, 6.07 %.

3.2.5. 16-(4-Methoxyphenyl)-16*H*-benzo[*a*]benzo[7,8]chromeno[2,3-*c*]phenazine (6e)

Brown powder; yield 0.397 g (81%), mp 296–297 °C; IR (KBr): ν_{max} = 3025, 1654, 1632, 1590, 1514, 1351, 1291, 1154, 1075, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.52 (s, 3H, CH_3), 5.58 (s, 1H, CH), 6.78–6.82 (m, 1H, Ar-H), 6.92 (d, 1H, J = 7.8 Hz, Ar-H), 7.30 (d, 1H, J = 7.8 Hz, Ar-H), 7.36 (d, 1H, J = 7.8 Hz, Ar-H), 7.67–7.75 (m, 5H, Ar-H), 7.99–8.10 (m, 5H, Ar-H), 8.32 (d, 1H, J = 7.8 Hz, Ar-H), 8.50 (t, 1H, J =

8.1 Hz, Ar-H), 8.73 (d, 1H, J = 7.8 Hz, Ar-H), 9.29–9.32 (m, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.5 (CH), 55.4 (OCH_3), 117.1, 117.8, 120.6, 121.3, 121.4, 122.4, 122.5, 124.7, 125.8, 126.4, 128.6, 128.8, 129.3, 129.6 (2x), 129.8, 130.4, 130.5 (2x), 130.6, 130.9, 132.2 (2x), 132.4, 138.3, 140.5, 141.7, 141.8, 146.4, 150.3, 155.7, and 157.2 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 490 (M^+, 2); Anal. Calcd. for $C_{34}H_{22}N_2O_2$: C, 83.25; H, 4.52; N, 5.71 %. Found: C, 83.63; H, 5.01; N, 6.98 %.

3.2.6. 18-(4-Chlorophenyl)-18*H*-benzo[*a*]benzo[5,6]chromeno[2,3-*c*]phenazine (7a)

Yellow powder; yield 0.440 g (89%), mp 292–294 °C; IR (KBr): ν_{max} = 2920, 1651, 1625, 1593, 1528, 1345, 1286, 1177, 1043, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.02 (s, 1H, CH), 7.21 (d, 2H, J = 7.8 Hz, Ar-H), 7.46 (d, 2H, J = 7.8 Hz, Ar-H), 7.62–8.65 (m, 1H, Ar-H), 7.96–8.07 (m, 6H, Ar-H), 8.12–8.17 (m, 2H, Ar-H), 8.27–8.31 (m, 2H, Ar-H), 8.48 (d, 1H, J = 7.8 Hz, Ar-H), 8.62 (d, 1H, J = 7.8 Hz, Ar-H), 9.31 (d, 1H, J = 7.8 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.2 (CH), 115.4, 116.1, 121.5, 121.8, 122.2, 123.1, 124.5, 125.6 (2x), 125.9, 127.2, 128.3, 128.7, 129.2, 129.4, 129.5, 129.7 (2x), 130.4, 130.9, 131.2 (2x), 131.5, 133.2 (2x), 141.5, 141.6, 142.5, 144.3, 144.9, 150.7, and 155.2 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 494 (M^+, 12); Anal. Calcd. for $C_{33}H_{19}ClN_2O$: C, 80.08; H, 3.87; N, 5.66 %. Found: C, 80.38; H, 3.98; N, 5.98 %.

3.2.7. 18-(4-Nitrophenyl)-18*H*-benzo[*a*]benzo[5,6]chromeno[2,3-*c*]phenazine (7b)

Yellow powder; yield 0.444 g (88%), mp 267–269 °C; IR (KBr): ν_{max} = 3012, 1657, 1635, 1592, 1536, 1342, 1265, 1187, 1071, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.94 (s, 1H, CH), 7.47–7.51 (m, 1H, Ar-H), 7.71–7.75 (m, 2H, Ar-H), 7.87–7.98 (m, 7H, Ar-H), 8.13 (d, 2H, J = 8.1 Hz, Ar-H), 8.20–8.23 (m, 1H, Ar-H), 8.30–8.37 (m, 3H, Ar-H), 8.61 (d, 1H, J = 8.1 Hz, Ar-H), 9.23–9.26 (m, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 40.7 (CH), 114.2, 117.5, 119.5, 121.2 (2x), 121.4, 122.7 (2x), 124.2, 125.8, 126.4, 128.3, 128.5, 128.7, 129.0 (2x), 129.5, 129.6, 130.7 (2x), 130.8, 130.9, 131.5, 132.0, 133.1, 140.4, 142.3, 142.5, 146.1, 146.4, 152.6, and 156.1 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 505 (M^+, 2); Anal. Calcd. for $C_{33}H_{19}N_3O_3$: C, 78.40; H, 3.79; N, 8.31 %. Found: C, 78.18; H, 3.96; N, 8.02 %.

3.2.8. 18-(3-Nitrophenyl)-18*H*-benzo[*a*]benzo[5,6]chromeno[2,3-*c*]phenazine (7c)

Yellow powder; yield 0.429 g (85%), mp 248–250 °C; IR (KBr): ν_{max} = 3012, 1657, 1635, 1592, 1536, 1342, 1265, 1187, 1071, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.14 (s, 1H, CH), 7.35 (t, 1H, J = 7.8 Hz, Ar-H), 7.61 (t, 1H, J = 7.8 Hz, Ar-H), 7.86–8.14 (m, 10H, Ar-H), 8.31–8.35 (m, 2H, Ar-H), 8.47 (s, 1H, Ar-H), 8.62 (d, 1H, J = 8.1 Hz, Ar-H), 8.83 (d, 1H, J = 8.1 Hz, Ar-H), 9.17 (d, 1H, J = 8.1 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.9 (CH), 116.4, 118.3, 119.7, 120.3, 121.6 (2x), 122.8, 123.9, 125.5, 125.7 (2x), 128.2, 128.7, 129.0 (2x), 129.2, 129.5, 129.7 (2x), 129.9, 130.4, 130.8, 130.9, 131.7, 132.2, 140.6, 141.2, 143.5, 145.4, 146.4, 150.8, and 157.3 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 505 (M^+, 9); Anal. Calcd. for $C_{33}H_{19}N_3O_3$: C, 78.40; H, 3.79; N, 8.31 %. Found: C, 78.81; H, 4.05; N, 8.62 %.

3.2.9. 18-Phenyl-18*H*-benzo[*a*]benzo[5,6]chromeno[2,3-*c*]phenazine (7d)

Yellow powder; yield 0.382 g (83%), mp 277–278 °C; IR (KBr): ν_{max} = 3043, 1655, 1631, 1592, 1536, 1392, 1271, 1185, 1035, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.81 (s, 1H, CH), 7.09 (d, 1H, J = 7.8 Hz,

Ar-H), 7.21 (dd, 1H, J_1 = 2.1 Hz, J_2 = 7.8 Hz, Ar-H), 7.41–7.48 (m, 4H, Ar-H), 7.81–7.95 (m, 6H, Ar-H), 8.02–8.08 (m, 2H, Ar-H), 8.28–8.34 (m, 3H, Ar-H), 8.53 (d, 1H, J = 8.1 Hz, Ar-H), 9.27–9.30 (m, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.7 (CH), 118.2, 120.4, 120.6, 122.1 (2x), 122.3, 123.5 (2x), 124.1, 126.8, 128.3, 128.8, 129.0, 129.2 (2x), 129.5, 129.6 (2x), 130.1 (2x), 130.6, 131.4, 132.4 (2x), 133.7, 140.4, 141.3, 142.7, 144.2, 146.8, 152.6, and 155.6 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 460 (M^+, 5); Anal. Calcd. for $C_{33}H_{20}N_2O$: C, 86.07; H, 4.38; N, 6.08 %. Found: C, 86.51; H, 4.53; N, 6.37 %.

3.2.10. 18-(*p*-Tolyl)-18*H*-benzo[*a*]benzo[5,6]chromeno[2,3-*c*]phenazine (7e)

Yellow powder; yield 0.379 g (80%), mp 242–244 °C; IR (KBr): ν_{max} = 2992, 1660, 1631, 1590, 1532, 1354, 1267, 1156, 1072, 758 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.24 (s, 3H, CH_3), 5.73 (s, 1H, CH), 7.06 (d, 2H, J = 7.5 Hz, Ar-H), 7.39 (d, 2H, J = 7.5 Hz, Ar-H), 7.52 (td, 1H, J_1 = 2.1 Hz, J_2 = 7.8 Hz, Ar-H), 7.94–8.07 (m, 7H, Ar-H), 8.18–8.23 (m, 3H, Ar-H), 8.33 (d, 1H, J = 7.8 Hz, Ar-H), 8.54 (d, 1H, J = 8.1 Hz, Ar-H), 9.22 (d, 1H, J = 8.1 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.2 (CH_3), 41.3 (CH), 114.1, 116.8, 121.2, 121.7, 122.2, 122.4, 123.6, 124.1, 126.2, 126.5 (2x), 128.1, 128.8, 129.3, 129.4, 129.6 (2x), 129.9 (2x), 130.2, 130.4, 130.5, 130.8, 131.5, 132.3, 140.2, 141.6, 142.3, 144.0, 145.4, 150.4, and 156.1 ppm; MS (m/z, %): 474 (M^+, 8); Anal. Calcd. for $C_{34}H_{22}N_2O$: C, 86.05; H, 4.67; N, 5.90 %. Found: C, 86.31; H, 4.94; N, 5.71 %.

3.2.11. 16-(4-Chlorophenyl)-16*H*-benzo[*a*]chromeno[2,3-*c*]phenazine (8a)

Yellow powder; yield 0.240 g (54%), mp 258–260 °C; IR (KBr): ν_{max} = 3172, 1660, 1624, 1593, 1487, 1385, 1266, 1164, 1056, 758 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.91 (s, 1H, CH), 7.38–7.40 (m, 4H, Ar-H), 7.85–7.92 (m, 5H, Ar-H), 8.05–8.10 (m, 3H, Ar-H), 8.21–8.24 (m, 1H, Ar-H), 8.38 (d, 1H, J = 8.1 Hz, Ar-H), 8.61 (d, 1H, J = 8.1 Hz, Ar-H), 9.31–9.33 (m, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.8 (CH), 114.3, 117.7, 121.0, 121.4 (2x), 122.2, 123.6, 124.5, 124.8, 126.2 (2x), 126.7, 128.6, 129.1, 129.6 (2x), 129.7, 129.9, 130.2, 130.4, 130.7, 131.8, 140.5, 140.8, 142.5, 146.2, 150.5, and 157.2 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 444 (M^+, 4); Anal. Calcd. for $C_{29}H_{17}ClN_2O$: C, 78.29; H, 3.85; N, 6.30 %. Found: C, 78.54; H, 4.25; N, 6.12 %.

3.2.12. 16-(4-Nitrophenyl)-16*H*-benzo[*a*]chromeno[2,3-*c*]phenazine (8b)

Yellow powder; yield 0.305 g (67%), mp 229–231 °C; IR (KBr): ν_{max} = 3055, 1658, 1630, 1592, 1474, 1387, 1263, 1171, 1042, 762 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.94 (s, 1H, CH), 7.33 (d, 2H, J = 8.1 Hz, Ar-H), 7.56 (d, 2H, J = 8.1 Hz, Ar-H), 7.94–8.08 (m, 6H, Ar-H), 8.12 (d, 2H, J = 7.5 Hz, Ar-H), 8.19–8.21 (m, 1H, Ar-H), 8.28–8.30 (m, 1H, Ar-H), 8.52 (d, 1H, J = 8.1 Hz, Ar-H), 9.26–9.29 (m, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 41.2 (CH), 116.1, 117.5, 120.4, 121.3, 122.2 (2x), 122.6, 125.2, 126.4, 126.6, 128.1 (2x), 129.3, 129.6, 129.8 (2x), 130.0, 130.2, 130.3, 130.5 (2x), 130.9, 141.2, 141.8, 142.4, 144.7, 151.4 and 156.8 ($C_{olefinic}$ and C_{arom}) ppm; MS (m/z, %): 455 (M^+, 11); Anal. Calcd. for $C_{29}H_{17}N_3O_3$: C, 76.47; H, 3.76; N, 9.23 %. Found: C, 76.77; H, 3.90; N, 9.62 %.

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