Synthesis of 9-Methoxy and 9-Acetoxy-3-amino-1-(4-methoxyphenyl)-1*H*-benzo[f]chromene-2-carbonitriles *via* 2-(Imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile as Intermediate

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Z. Naturforsch. **57b,** 579–585 (2002); received September 14, 2001

Nitriles, Benzo[f]chromenes, Heterocyclic Organic Synthesis

Several new 1*H*-benzo[f]chromene derivatives (**3a–d**) were prepared by the reaction of 7-substituted-2-naphthols (**1a,b**) with substituted α-cyano-4-methoxycinnamonitriles (**2a,b**) together with 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**) as intermediate. Also, the reaction of **1a,b** with **4** without catalyst afforded 9-methoxy and 9-acetoxy-3-amino-1-(*p*-methoxyphenyl)-1*H*-benzo[f]chromene-2-carbonitrile (**3b,e**). The reaction of **3a,b** with different electrophilic and nucleophilic reagents afforded the 12*H*-7-oxa-8,10-diaza-benzo[a]anthracene derivatives **5, 9, 10** and 1*H*-benzo[f]chromene derivatives **6–8, 11**.

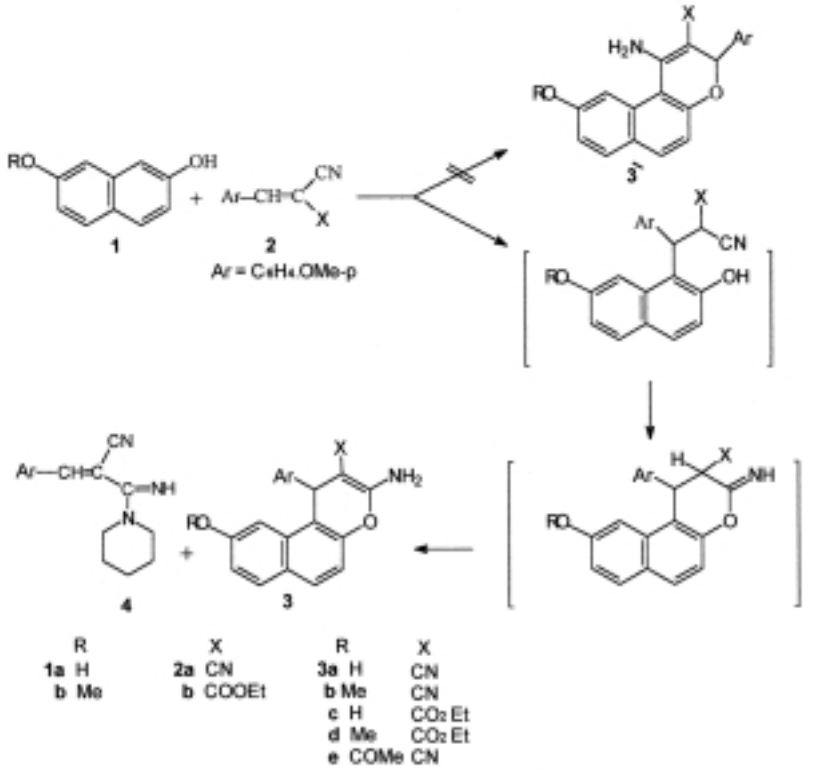
Introduction

Chromenes and fused chromenes are biologically interesting compounds with antibacterial activities [1, 2], antifungal activities [3], antitumor activity [4] and hypotensive effects [5]. Some chromene derivatives also have various biological properties like antiproliferative effects [6], molluscicidal activity [7], local anesthetic and antiarrhythmic activities [8], antiallergenic effects [9, 10], hypolipidemic activity [11], central nervous system (CNS) activity [12] and antiviral activity [13]. The present study is part of our program aimed at developing new approaches for the synthesis of fused heterocyclic systems [14–19]. We reported here the synthesis of 1*H*-benzo[f]chromene derivatives and their utility as building blocks in the synthesis of novel fused chromenes, aiming at the evaluation of their antimicrobial activity.

Results

Thus, condensation of 7-substituted-2-naphthols (**1a,b**) with α-cyano-4-methoxycinnamonitrile (**2a**) in ethanolic piperidine afforded the 1:1 adducts **3a,b** along with 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**), while condensation of **1a,b** with ethyl α-cyano-4-methoxycinnamate (**2b**) afforded **3c,d** as the only isolable products (Scheme 1). The formation of **3a–d** indicates that the naphtholate anion attacks at the β-carbon of **2** to yield an acyclic Michael adduct which undergoes intramolecular cyclization. The formation of the 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**) can be explained on the basis that the triple bond was more susceptible than even the activated double bond to attack by piperidine to give a kinetically favored 1,2-addition product (Scheme 1). On the basis of spectral data structure **3′** was excluded [17, 19]. The structures of **3a–d** were established on the basis of the ^{1}H NMR spectra showing signals at δ = 4.93 (**3a**), δ = 5.23 (**3b**), δ = 5.26 (**3c**), and δ = 5.39 ppm (**3d**). The increased chemical shift for this signal, compared to the expected value (δ = 4.0–4.5 ppm) for such protons can be attributed to the deshielding effect by the naphthyl, aryl, and allylic π-electrons [20–22]. The UV/vis ($CHCl_3$) spectra of **3a–d** revealed a weak shoulder [19] characteristic for a 1*H*-chromene at λ_{max} (lg ε) = 275 nm (2.81–2.84) respectively, while structure **4** is supported by spectral data, IR: $\tilde{\nu}$ = 3292 (NH), 2945, 2918, 2856 (stretching CH) and 2172 cm^{-1} (CN), ^{1}H NMR δ = 1.58, 1.61, 3.32, 3.36 (m, 10H, CH_2), 3.77 (s, 3H, OMe), 6.86–7.79 ppm. (m, 5H, Ar–H and NH) and *m/z* (%) = 269 (100) [M$^+$].

0932–0776/2002/0500–0579 $06.00

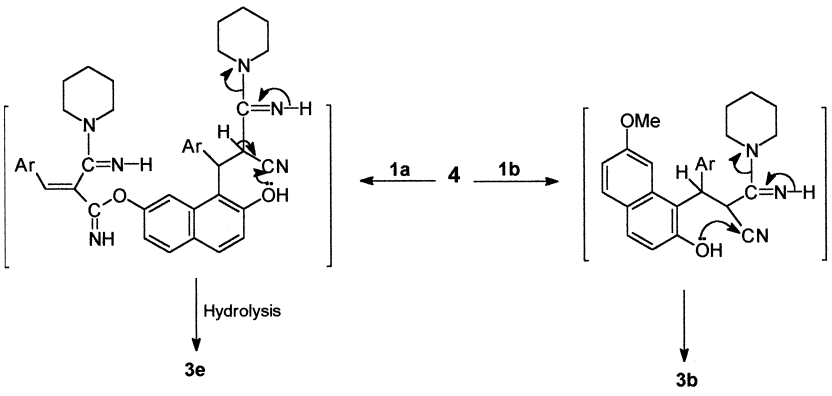


Scheme 1.

The formation of 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**) led the author to repeat the reaction between **1a,b** and **4**. Thus, condensation of **1a** with **4** in ethanolic solution without catalyst (piperidine) afforded the acetoxy derivative **3e**, while heating of **1b** with **4** gave **3b** (m.p. and mixed m.p.) as the only isolable product (Scheme 2). This is the first synthesis of the 9-acetoxy derivative **3e** by the reaction of **1a** with 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**).

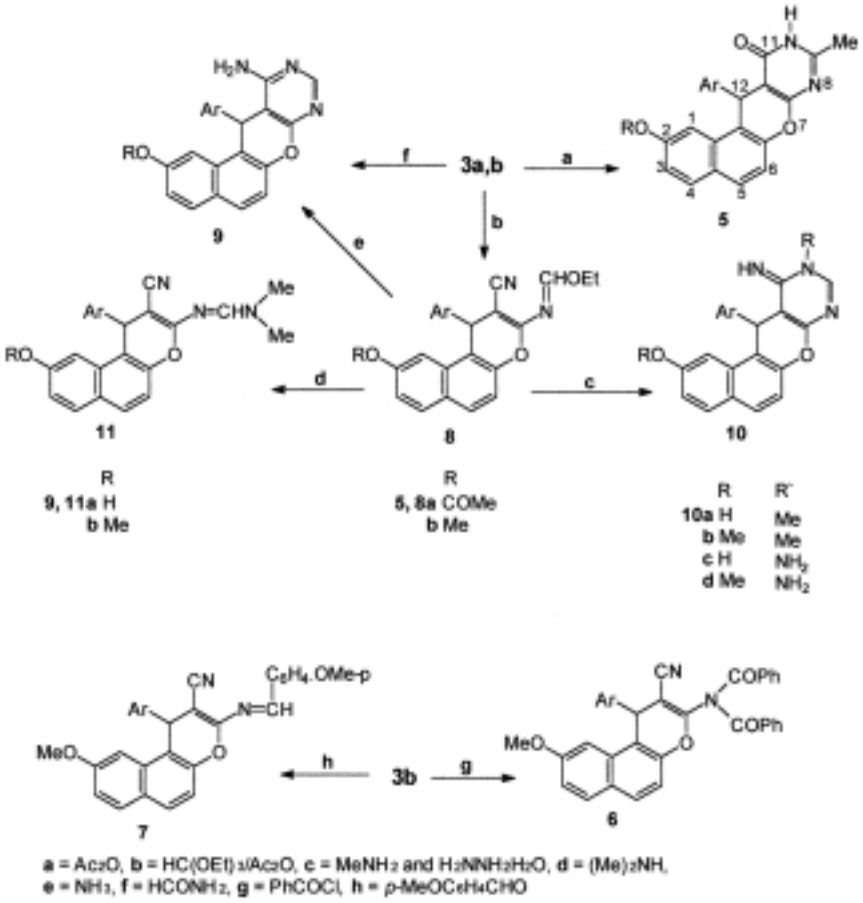
The reaction mechanism leading to **3e** involves the interaction of **1a** with two molecules of **4** *via* Michael addition to the activated double bond of 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**) and 1,2-addition to the carbonitrile group of the second molecule to form the acyclic imido ester intermediate, which then undergoes intramolecular cyclization and subsequent hydrolysis instantly to the acetoxy derivative **3e**. Compound **3b** was independently prepared by another route *via* cyclocondensation of **1b** with the intermediate 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile (**4**) (Scheme 2). Structure **3e** was established by spectral data.

Interaction of 3-amino-9-hydroxy-1-(4-methoxyphenyl)-1*H*-benzo[f]chromene-2-carbonitrile (**3a**) with acetic anhydride for 3 h afforded 2-acetoxy-9-methyl-12-(4-methoxyphenyl)-10,11-dihydro-12*H*-7-oxa-8,10-diaza-benzo[a]-anthracene-11-one (**5a**), while heating of **3b** with acetic anhydride give the anthracene derivative (**5b**) (Scheme 3). Spectral data and analogy with our pervious work [14–19] support structure **5**. Treatment of **3b** with benzoyl chloride afforded the *N,N*-dibenzoylbenzo[f]chromene derivative (**6**), while heating of **3b** with *p*-anisaldehyde in dioxin-piperidine gave the 4-methoxyphenylmethylene-aminobenzo[f]chromene derivative (**7**) (Scheme 3). Compound **3a** failed to react with benzoyl chloride and *p*-anisaldehyde. Structure **6** was established on the basis of the spectral data, IR: $\tilde{\nu} = 2214$ (CN) and ^{1}H NMR: δ = 6.67–7.86 ppm (m, 19H, Ar–H), while **7** is supported by IR: $\tilde{\nu} = 2203$ cm^{-1} (CN) and ^{1}H NMR: δ = 6.87–8.02 (m, 13H, Ar–H) and 9.10 ppm (s, 1H, N=CH).



Scheme 2.

Interaction of **3a,b** with triethyl orthoformate in acetic anhydride at reflux gave the corresponding ethoxymethyleneaminobenzo[f]chromene derivatives (**8a,b**) with acetylation of the hydroxyl group of **3a** (Scheme 3). Ammonolysis of **8a,b** in methanol at room temperature afforded the anthracene derivatives (**9a,b**) with deacetylation of the acetoxy group of **8a**, the structure of which was supported by its independent synthesis from **3a,b** and formamide (m.p. and mixed m.p.) (Scheme 3).



Scheme 3.

Reaction of **8a,b** with methylamine yielded the anthracene derivatives (**10a,b**), while with dimethylamine the open-chain products **11a,b** were obtained (Scheme 3) with deacetylation of the acetoxy group of **8a**. Hydrazinolysis of **8a,b** in ethanol at room temperature afforded the anthracene derivatives (**10c,d**) (Scheme 3) with deacetylation of the acetoxy group of **8a**. Spectral data and analogy with our pervious work [14–19] established structures **8–11**.

Experimental Section

Mps are uncorrected. Elemental analyses were carried out in the Microanalytical Laboratories of the Faculty of Science, Cairo University. Ultraviolet spectra were recorded on Perkin Elmer Lambda-3B UV-visible spectrophotometer. IR spectra (KBr) were measured on a FT IR/5300 spectrometer, ^{1}H NMR/^{13}C NMR spectra on a Varian Mercury (300/75 MHz) spectrometer and mass spectra on a Shimadzu GC-MS-QP 1000 EX spectrometer.

Reaction of the 7-substituted-2-naphthols (**1a,b**) *with* **2a,b**

A solution of the 7-hydroxy-2-naphthol (**1a**) or the 7-methoxy-2-naphthol (**1b**) (0.01 mol) in ethanol (30 ml) was treated with **2a,b** (0.01 mol) and piperidine (0.5 ml). The reaction mixture was heated until complete precipitation (reaction time: 30 min. for **2a**; 120 min. for **2b**). The solid product which formed was collected by filtration and recrystallized from a suitable solvent to give **3a–d** (40–80% yield) and the intermediate **4** (40% yield) (Table 1). – **3a**: IR (film): $\tilde{\nu}$ = 3464, 3348 (NH_2), 3310 (OH), 3202, 3028 (stretching CH), 2191 cm^{-1} (CN). – ^{1}H NMR (300.069 MHz, DMSO-d_6): δ = 3.67 (s, 3H, OMe), 4.93 (s, 1H, 1-H), 6.91 (br, 2H, NH_2 exchanged by D_2O), 6.74–7.72 (m, 9H, Ar–H), 9.78 ppm (s, 1H, 9-OH exchanged by D_2O). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 37.79 (C-1), 54.98 (OMe), 58.38 (C-2), 105.86 (C-10), 113.24 (C-10b), 114.04 (C-8 and aromatic), 117.12 (C-5), 120.74 (CN), 125.31 (C-6a), 128.04 (C-6), 129.14 (aromatic), 130.15 (C-7), 132.17 (C-10a), 137.71 (aromatic), 147.25 (C-9), 156.35 (C-4a), 157.91 (aromatic), 159.60 (C-3). – MS (EI, 70 eV): *m/z* (%) = 344 (100) [M$^+$], 237 (7) [M$^+$–C_6H_4·OMe], 184 (10) [M$^+$–HCN and CN]. – **3b**: IR (film): $\tilde{\nu}$ = 3427, 3323 (NH_2), 3199, 3026, 2997, 2956, 2858 (stretching CH), 2199 cm^{-1} (CN). – ^{1}H NMR (300.069 MHz, DMSO-d_6): δ = 3.67 (s, 3H, OMe), 3.76 (s, 3H, 9-OMe), 5.23 (s, 1H, 1-H), 6.93 (br, 2H, NH_2 exchanged by D_2O), 6.81–7.83 ppm (m, 9H, Ar–H). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 37.36 (C-1), 54.92 (OMe), 55.08 (OMe), 58.24 (C-2), 103.28 (C-10), 113.96 (C10b), 115.16 (C-8 and aromatic), 116.72 (C-5), 120.67 (CN), 125.98 (C-6a), 128.26 (C-6), 128.90 (aromatic), 129.90 (aromatic), 131.69 (C-7), 137.90 (C-10a), 147.13 (aromatic), 149.49 (C-4a), 157.82 (C-9), 157.89 (aromatic), 159.51 (C-3). – **3c**: IR (film): $\tilde{\nu}$ = 3410, 3310 (NH_2), 3240 (OH), 3057, 2987, 2957, 2905, 2849, 2883 (stretching CH), 1666 cm^{-1} (C=O). – ^{1}H NMR (300.069 MHz, DMSO-d_6): δ = 1.27 (t, *J* = 7.0 Hz, 3H, Me), 3.65 (s, 3H, OMe), 4.12 (q, 2H, *J* = 7.0 Hz CH_2), 5.26 (s, 1H, 1-H), 7.57 (br, 2H, NH_2 exchanged by D_2O), 6.75–7.75 (m, 9H, Ar–H), 9.84 ppm (s, 1H, 9-OH exchanged by D_2O). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 14.89 (Me), 35.54 (C-1), 54.87 (OMe), 66.33 (CH_2), 78.03 (C-2), 105.10 (C-10), 113.06 (C-10b), 113.53 (aromatic), 116.95 (C-8), 117.42 (C-5), 125.18 (C-6a), 128.33 (C-6), 130.18 (C-7 and aromatic), 132.04 (C-10a), 138.86 (aromatic), 147.43 (C-9), 156.32 (C-4a), 157.33 (aromatic), 160.57 (CO), 168.43 (C-2). – MS (EI, 70 eV): *m/z* (%) = 391 (100) [M$^+$], 284 (12) [M$^+$–C_6H_4·OMe], 212 (16) [M$^+$–C_2H_4 and CO_2], 184 (10) [M$^+$–H and HCN]. – **3d**: IR (film): $\tilde{\nu}$ = 3495, 3341 (NH_2), 1690 cm^{-1} (C=O). – ^{1}H NMR (300.069 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.2 Hz, 3H, Me), 3.70 (s, 3H, OMe), 3.85 (s, 3H, 9-OMe), 4.21 (q, *J* = 7.2 Hz, 2H, CH_2), 5.39 (s, 1H, 1-H), 6.26 (br, 2H, NH_2),6.70–7.67 ppm (m, 9H, Ar–H). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 14.42 (Me), 36.02 (C-1), 54.85 (OMe), 55.11 (OMe), 58.79 (CH_2), 77.82 (C-2), 102.83 (C-10), 113.34 (C-10b), 113.99 (aromatic), 116.42 (C-8), 117.87 (C-5), 125.63 (C-6a), 128.48 (C-6), 128.88 (aromatic), 130.14 (C-7), 131.72 (C-10a), 138.95 (aromatic), 147.02 (C-4a), 157.26 (C-9), 157.87 (aromatic), 160.11 (CO), 168.22 (C-2). – **4**: IR (film): $\tilde{\nu}$ = 2292 (NH), 2945, 2918, 2856 (stretching CH), 2172 cm^{-1} (CN). – ^{1}H NMR (300.069 MHz, $CDCl_3$): δ = 1.58, 1.61, 3.32, 3.36 (m, 10H, CH_2), 3.77 (s, 3H, OMe), 6.86–7.79 ppm (m, 5H, Ar–H and NH). – MS (EI, 70 eV): *m/z* (%) = 269 (100) [M$^+$], 184 (78) [M$^+$–piperidine].

9-Acetoxy-3-amino-1-(4-methoxyphenyl)-1H-benzo[f]chromene-2-carbonitrile (**3e**)

A solution of **1a** (0.01 mol) in ethanol (30 ml) was treated with **4** (0.01 mol) to give **3e** (45% yield) (Table 1). – **3e**: UV/vis ($CHCl_3$): λ_{max} (lg ε) = 275 nm (2.85). – IR (film): $\tilde{\nu}$ = 3456, 3348

Table 1. Physical and analytical data of the newly prepared compounds.

Comp.	M.p. (Solvent)	Colour (Yield%)	M. formula (M. Wt.)	Calcd (Found) C	H	N
3a	240 (benzene)	colourless (60)	$C_{21}H_{16}N_2O_3$ (344)	73.26 (73.2)	4.65 (4.3)	8.14 (8.0)
3b	219 (benzene)	colourless (55)	$C_{22}H_{18}N_2O_3$ (358)	73.74 (73.6)	5.03 (4.9)	7.82 (7.6)
3c	228 (dioxan)	colourless (80)	$C_{23}H_{21}NO_5$ (391)	70.59 (70.3)	5.37 (5.2)	3.58 (3.5)
3d	150 (benzene)	colourless (75)	$C_{24}H_{23}NO_5$ (405)	71.11 (71.0)	5.68 (5.6)	3.46 (3.3)
3e	240 (EtOH)	colourless (60)	$C_{23}H_{18}N_2O_4$ (386)	71.50 (71.3)	4.66 (4.5)	7.25 (7.0)
4	180 (EtOH)	colourless (40)	$C_{16}H_{19}N_3O$ (269)	71.38 (71.2)	7.06 (7.0)	15.61 (15.3)
5a	314 (dioxan)	colourless (75)	$C_{25}H_{20}N_2O_5$ (428)	70.09 (70.0)	4.67 (4.3)	6.54 (6.4)
5b	310 (dioxan)	colourless (80)	$C_{24}H_{20}N_2O_4$ (400)	72.00 (71.8)	5.00 (4.8)	7.00 (6.8)
6	180 (EtOH)	colourless (81)	$C_{36}H_{26}N_2O_5$ (566)	76.33 (76.1)	4.59 (4.4)	4.95 (4.8)
7	242 (benzene)	colourless (87)	$C_{30}H_{24}N_2O_4$ (476)	75.63 (75.3)	5.04 (4.8)	5.88 (5.6)
8a	188 (EtOH)	colourless (78)	$C_{26}H_{22}N_2O_5$ (442)	70.59 (70.4)	4.98 (4.8)	6.33 (6.1)
8b	195 (EtOH)	colourless (81)	$C_{25}H_{22}N_2O_4$ (414)	72.46 (72.2)	5.31 (5.1)	6.76 (6.4)
9a	198 (EtOH)	colourless (85)	$C_{22}H_{17}N_3O_3$ (371)	71.16 (71.0)	4.58 (4.4)	11.32 (11.1)
9b	256 (benzene)	colourless (90)	$C_{23}H_{19}N_3O_3$ (385)	71.69 (71.5)	4.94 (4.7)	10.91 (10.8)
10a	310 (dioxan)	colourless (70)	$C_{23}H_{19}N_3O_3$ (385)	71.69 (71.6)	4.94 (4.8)	10.91 (10.7)
10b	170 (EtOH)	colourless (85)	$C_{24}H_{21}N_3O_3$ (399)	72.18 (72.0)	5.26 (5.1)	10.53 (10.3)
10c	264 (benzene)	colourless (80)	$C_{22}H_{18}N_4O_3$ (368)	68.39 (68.1)	4.66 (4.4)	14.51 (14.2)
10d	229 (benzene)	colourless (82)	$C_{22}H_{20}N_4O_3$ (400)	69.00 (68.8)	5.00 (4.8)	14.00 (13.8)
11a	286 (benzene)	colourless (84)	$C_{24}H_{21}N_3O_3$ (399)	72.18 (72.0)	5.26 (5.1)	10.53 (10.4)
11b	208 (benzene)	colourless (82)	$C_{25}H_{23}N_3O_3$ (413)	72.64 (72.4)	5.57 (5.4)	10.17 (10.0)

(NH_2), 3179, 3090, 3050, 2939, 2839 (stretching CH), 2183 (CN), 1744 cm^{-1} (C=O acetoxy). – ^1H NMR (300.069 MHz, $CDCl_3$): δ = 2.28 (s, 3H, 9-COMe), 3.74 (s, 3H, OMe), 4.56 (br, 2H, NH_2), 5.10 (s, 1H, 1-H), 6.78–7.81 ppm (m, 9H, Ar–H). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 21.61 (Me), 37.82 (C-1), 55.68 (OMe), 58.99 (C-2), 114.81 (aromatic), 115.57 (C-10), 116.74 (C-10b), 117.30 (C-5), 121.11 (CN), 121.29 (C-8), 128.63 (C-6a), 129.46 (aromatic), 129.86 (C-6), 130.61 (C-7), 131.68 (C-10a), 138.23 (aromatic), 148.04 (C-9), 149.98 (C-4a), 158.61 (aromatic), 160.33 (C-3), 169.86 (CO). – MS (EI, 70 eV): *m/z* (%) = 386 (29) [M^+], 279 (66) [$M^+ - C_6H_4 \cdot OMe$], 237 (100) [$M^+ - CH_2CO$], 184 (16) [$M^+ - HCN$ and CN].

2-Acetoxy/methoxy-9-methyl-12-(4-methoxyphenyl)-10,11-dihydro-12H-7-oxa-8,10-diazabenzo[a]anthracene-11-one (**5a,b**)

A solution of **3a,b** (0.01 ml) in acetic anhydride (20 ml) was heated under reflux for 3 h to give **5a,b** (75–82% yield) (Table 1). – **5a**: IR (film): $\tilde{\nu}$ = 3200 (NH), 3009, 2847, 2785 (stretching CH), 1767 (C=O acetoxy), 1659 cm^{-1} (C=O). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 2.25 (s, 3H, 9- Me),

2.32 (s, 3H, 2-COMe), 3.90 (s, 3H, OMe), 5.59 (s, 1H, 1-H), 6.76–8.00 (m, 9H, Ar–H), 10.60 ppm (br, 1H, NH). – **5b**: IR (film): $\tilde{\nu}$ = 3195 (NH), 3000, 2950, 2810 (stretching CH), 1659 cm^{-1} (C=O). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 2.27 (s, 3H, 9- Me), 3.62 (s, 3H, OMe), 3.79 (s, 3H, 2-OMe), 5.59 (s, 1H, 1-H), 6.73–7.84 (m, 9H, Ar–H), 12.45 ppm (br, 1H, NH).

3-(N,N-Dibenzoyl)-9-methoxy-1-(4-methoxyphenyl)-1H-benzo[f]chromene-2-carbonitrile (**6**)

A solution of **3b** (0.01 mol) in benzoyl chloride (20 ml) was heated under reflux for 3 h to give **6** (81% yield) (Table 1). – IR (film): $\tilde{\nu}$ = 3000, 2952, 2932, 2839 (stretching CH), 2214 (CN), 1713 cm^{-1} (C=O). – ^1H NMR (300.069 MHz, $CDCl_3$): δ = 3.70 (s, 3H, OMe), 3.74 (s, 3H, 9-OMe), 5.22 (s, 1H, 1-H), 6.69–7.86 ppm (m, 19H, Ar–H).

9-Methoxy-3-(4-methoxyphenylmethyleneamino)-1-(4-methoxyphenyl)-1H-benzo[f]chromene-2-carbonitrile (**7**)

A solution of **3b** (0.01 mol) in dioxan (20 ml) and piperidine (0.5 ml) was treated with *p*-anisaldehyde (0.01 mol) under reflux for 2h to give **7** (87% yield) (Table 1). – IR (film): $\tilde{\nu}$ = 2932, 2833 (stretching CH), 2203 cm^{-1} (CN). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.69 (s, 3H, OMe), 3.77 (s, 3H, OMe), 3.88 (s, 3H, 9-OMe), 5.64 (s, 1H,1-H), 6.87–8.02 (m, 13H, Ar–H), 9.10 ppm (s, 1H, N=CH).

9-Acetoxy/methoxy-3-ethoxymethyleneamino-1H-benzo[f]chromene-2-carbonitrile (**8a,b**)

A mixture of **3a,b** (0.01 mol), triethyl orthoformate (0.01 mol) and acetic anhydride (20 ml) was refluxed for 3 h to give **8a,b** (78–81% yield) (Table 1). – **8a**: IR (film): $\tilde{\nu}$ = 3010, 2940, 2970, 2841 (stretching CH), 2216 (CN), 1761 cm^{-1} (C=O acetoxy). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 1.30 (t, J = 7.2 Hz, 3H, Me), 2.27 (s, 3H, 9-COMe), 3.66 (s, 3H, OMe), 4.32 (q, J = 7.2 Hz, 2H, CH_2), 5.40 (s, 1H, 1-H), 6.82–7.97 (m, 9H, Ar–H), 8.68 (s, 1H, N=CH). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 14.57 (Me), 21.60 (Me), 39.08 (C-1), 55.72 (OMe), 64.63 (CH_2), 82.22 (C-2), 114.98 (aromatic), 115.66 (C-10), 117.62 (C-10b), 118.57 (C-5), 121.54 (CN), 121.78 (C-8), 129.27 (aromatic), 129.79 (C-6a), 130.24 (C-6), 130.67 (C-7), 131.61 (C-10a), 136.26 (aromatic), 148.24 (C-9), 150.02 (C-4a), 157.31 (aromatic), 158.99 (C-3), 162.41 (CH), 169.82 (CO). – MS (EI, 70 eV): *m/z* (%) = 442 (20) [M^+], 336 (100) [$M^+ - C_6H_3 \cdot OMe$], 294 (38) [$M^+ - CH_2CO$], 237 (64) [$M^+ - C_2H_4$, CO and H], 184 (11) [M^+ – HCN and CN].

8b: IR (film): $\tilde{\nu}$ = 3086, 3061, 2999, 2955, 2888 (stretching CH), 2208 cm^{-1} (CN). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 1.32 (t, J = 7.2 Hz, 3H, Me), 3.69 (s, 3H, OMe), 3.75 (s, 3H, 9-OMe), 4.34 (q, J = 7.2 Hz, 2H, CH_2), 5.48 (s, 1H, 1-H), 6.85- 7.87 (m, 9H, Ar–H), 8.70 ppm (s, 1H, N=CH). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 14.12 (Me), 38.26 (C-1), 54.97 (OMe), 55.09 (OMe), 63.85 (CH_2), 81.40 (C-2), 103.40 (C-10), 113.51 (C10b), 114.12 (aromatic), 116.92 (C-5 and 8), 118.08 (CN), 126.29 (C-6a), 128.87 (C-6), 130.02 (C-7), 131.58 (C-10a), 135.92 (aromatic), 147.31 (C-4a), 156.50 (C-9), 157.94 (aromatic), 158.20 (CH), 161.50 (C-3).

2-Substituted-11-amino-12-(4-methoxyphenyl)-12H-7-oxa-8,10-diaza-benzo[a]anthracene (**9a,b**)

(a) A stream of NH_3 gas was passed through **8a,b** (0.01 mol) in methanol for 1h. The solid product formed on cooling was collected to give **9a,b** (85–90% yield). – **9a**: IR (film): $\tilde{\nu}$ = 3400, 3240 (NH_2), and 3140 cm^{-1} (OH). – **9b**: IR (film): $\tilde{\nu}$ = 3395, 3325 cm^{-1} (NH_2). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.63 (s, 3H, OMe), 3.93 (s, 3H, 2-OMe), 5.85 (s, 1H, 1-H), 7.16 (br, 2H, NH_2 exchanged by D_2O), 6.77- 8.11 (m, 9H, Ar–H), 8.12 ppm (s, 1H, 9-H).

(b) A solution of **3a,b** (0.01 mol) in formamide (20 ml) was heated under reflux for 6h to give **9a,b** (70–72% yield) (Table 1).

Reaction of **8a,b** *with hydrazine hydrate and various amines* **10a–d**, **11a,b**

A solution of **8a,b** (0.01 mol) and methylamine (0.01 mol), hydrazine hydrate (99%, 5 ml) or dimethylamine (0.01 mol) in ethanol (50 ml) was stirred for 45 min. to give 2-hydroxy/methoxy-10-methyl-11-imino-12-(4-methoxyphenyl)-10,11-dihydro-12*H*-7-oxa-8,10-diaza-benzo[a]anthracene (**10a,b**), 10-amino-2-hydroxy/methoxy-11-imino-12-(4-methoxyphenyl)-10,11-dihydro-12*H*-7-oxa-8,10-diaza-benzo[a]anthracene (**10c,d**) and 3-dimethylaminomethyleneamino-9-hydroxyl/methoxy-1-(4-methoxyphenyl)-1*H*-benzo[f]chromene-2-carbonitrile (**11a,b**) (70–85% yield) (Table 1). – **10a**: IR (film): $\tilde{\nu}$ = 3566, 3508 (NH), 3356 (OH), 3050, 2837 (stretching CH), 1645 cm^{-1} (C=N). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.33 (s, 3H, 10-N–Me), 3.63 (s, 3H, OMe), 3.64 (s, 3H, 2-OMe), 5.59 (s, 1H, 1-H), 7.36 (br, 1H, NH exchanged by D_2O), 6.75–7.75 (m, 9H, Ar–H), 8.06 (s, 1H, 9-H), 9.80 ppm (br, 1H, 2-OH exchanged

by D_2O). – **10b**: IR (film): $\tilde{\nu}$ = 3363 (NH), 3000, 2939, 2820 (stretching CH), 1643 cm^{-1} (C=N). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.34 (s, 3H, 10-N–Me), 3.63 (s, 3H, OMe), 3.92 (s, 3H, 2-OMe), 5.79 (s, 1H, 1-H), 7.34 (br, 1H, NH exchanged by D_2O), 6.77–7.81 (m, 9H, Ar–H), 8.10 ppm (s, 1H, 9-H). – **10c**: IR (film): $\tilde{\nu}$ = 3400, 3320 (NH_2), 3317 (NH), 3275 (OH), 3067, 2984, 2910, 2833 (stretching CH), 1647 cm^{-1} (C=N). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.62 (s, 3H, OMe), 5.59 (s, 1H, 1-H), 5.66 (br, 2H, NH_2), 6.73–7.74 (m, 9H, Ar–H), 8.02 (s, 1H, 9-H), 9.82 (br, 1H, NH), 10.50 (s, 1H, 2-OH). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 36.02 (C-12), 55.66 (OMe), 100.64 (C-11a), 106.45 (C-1), 110.00 (C-1b), 114.21 (C-3), 114.48 (aromatic), 115.81 (C-6), 117.56 (C-4a), 126.04 (C-5), 128.00 (C-4), 129.47 (aromatic), 129.96 (C-1a), 130.06 (C-6a), 133.06 (aromatic), 136.63 (C-2), 148.52 (C-7a), 155.80 (aromatic), 157.00 (C-9), 158.47 (C-11). – MS (EI, 70 eV): *m/z* (%) = 386 (14) [M^+], 265 (100) [$M^+ - C_6H_3 \cdot$OMe and NH], 238 (28) [M^+–HCN], 184 (5) [$M^+ - 2$HCN]. – **10d**: IR (film): $\tilde{\nu}$ = 3364, 3283 (NH_2), 3200 (NH), 3005, 2934, 2934, 2908, 2833 (stretching CH), 1655 cm^{-1} (C=N). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.63 (s, 3H, OMe), 3.89 (s, 3H, 2-OMe), 5.70 (s, 1H, 1-H), 6.02 (br, 2H, NH_2 exchanged by D_2O), 7.44 (br, 1H, NH exchanged by D_2O), 6.76–7.81 (m, 9H, Ar–H), 8.09 ppm (s, 1H, 9-H). – ^{13}C NMR (75.461 MHz, DMSO-d_6): δ = 35.33 (C-12), 54.89 (OMe), 55.30 (OMe), 99.65 (C-11a), 103.12 (C-1), 113.55 (C-1b), 114.69 (aromatic), 115.92 (C-3), 116.64 (C-6), 118.73 (C-4a), 118.75 (C-5), 126.05 (C-4), 128.73 (aromatic), 129.40 (C-1a), 130.05 (C-6a), 131.92 (aromatic), 135.93 (C-2), 147.75 (C-7a), 155.08 (aromatic), 157.80 (C-9), 158.02 (C-11). – **11a**: IR (film): $\tilde{\nu}$ = 3348 (OH), 2950, 2918, 2887, 2841, 2808 (stretching CH), 2185 cm^{-1} (CN). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 2.99 (s, 3H, N–Me), 3.15 (s, 3H, N–Me), 3.69 (s, 3H, OMe), 5.07 (s, 1H, 1-H), 6.82–7.80 (m, 9H,Ar–H), 8.44 (s, 1H, N=CH), 9.81 ppm (s, 1H, 9-OH). – **11b**: IR (film): $\tilde{\nu}$ = 3030, 3000, 2939, 2800 (stretching CH), 2191 cm^{-1} (CN). – ^1H NMR (300.069 MHz, DMSO-d_6): δ = 3.01 (s, 3H, N–Me), 3.16 (s, 3H, N–Me), 3.68 (s, 3H, OMe), 3.76 (s, 3H, 9-OMe), 5.35 (s, 1H, 1-H), 6.82–7.85 (m, 9H, Ar–H), 8.47 ppm (s, 1H, N=CH).

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