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Heteroaromatization with 4-phenyldiazenyl-1-naphthol. Part I: Synthesis of some new naphthopyrans and naphthopyranopyrimidines

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ABSTRACT

Reaction of 4-phenyldiazenyl /or 4-(*p*-tolyldiazenyl)-1-naphthol (1) with various substituted α-cyanocinnamonitriles (2a-h) and ethyl α-cyanocinnamates (2i-p) afforded 2-amino-4-(aryl)-6-(phenyldiazenyl /or *p*-tolyldiazenyl)-4*H*-naphtho[1,2-*b*]pyrano-3-carbonitrile (3a-h) and ethyl 2-amino-4-(aryl)-6-(phenyldiazenyl /or *p*-tolyldiazenyl)-4*H*-naphtho[1,2-*b*]pyrano-3-carboxylate (3i-p). Reaction of compound 3a with Ac_2O or PhCOCl and formic acid afforded *N*-acetylamino or *N,N*-dibenzoylamino and naphthopyranopyrimidine derivatives (4-8), respectively. The structures of these compounds were established on the basis of IR, UV, ^{1}H NMR, ^{13}C NMR, and MS data.

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1. Introduction

Nowadays, synthetic azo compounds are widely used in different application and in many fields, such as medicines, cosmetics, food, paints, plastics, shipbuilding, automobile industry, cable manufacture [1-12]. Moreover, azo compounds are known for their antineoplastics [13], antidiabetics [14], antiseptics [15], antibacterial [16] and antitumor activities [17]. Naphthopyrans are biologically interesting compounds with antimicrobial activities [18-21], inhibitors of influenza virus sialidases [22,23], DNA stand-breaking activity and mutagenicity [24], antiviral agent [25], antiproliferation agent [26], sex pheromone [27], antitumor [28,29] and central nervous system (CNS) activity [30].

As a continuation of our previous work for synthesis of naphthopyrans with arylidine skeleton [20,21,31-35], we efficiently synthesized a series of new 4-phenyldiazenyl or (*p*-tolyldiazenyl)-4*H*-naphthopyrans and 4-phenyldiazenyl or (*p*-tolyldiazenyl)-4*H*-naphthopyranopyraimidin-8-ones which are expected to possess considerable chemical and pharmacological activities.

2. Experimental

2.1. Instrumentation

Melting points were determined with a Stuart Scientific Co., Ltd. apparatus. UV spectra were measured on a Shimadzu UV-1601PC UV-Vis spectrophotometer. FT-IR spectra were determined as KBr pellets on a Jasco FT/IR 460 plus spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker AV 400 MHz spectrometer. Mass spectra were measured on a Shimadzu GC/MS-QP5050A spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 microanalyzer in the Faculty of Science, Cairo University, Cairo, Egypt

2.2. Synthesis

2.2.1. Synthesis of 4H-naphthopyran derivatives (3a-p)

A solution of 4-phenyldiazenyl/or 4-(*p*-tolyldiazenyl)-1-naphthol (10 mmol) in ethanol (30 mL) was treated with α-cyanocinnamonitriles (**2a-h**) or ethyl α-cyanocinnamates (**2i-p**) (10 mmol) and piperidine (0.5 mL). The reaction mixture was heated until complete precipitation occurred (reaction times: 2 h for compounds **2a-h**; 3 h for compounds **2i-p**).

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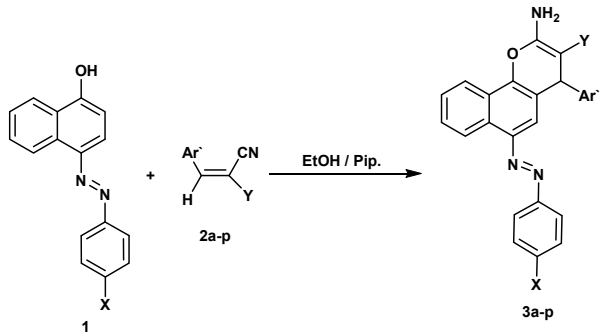


a; Ar`= *p*-Cl-C_6H_4	X = H	Y = CN	i; Ar`= *p*-Cl-C_6H_4	X = H	Y = COOEt
b; Ar`= *p*-Cl-C_6H_4	X = CH_3	Y = CN	j; Ar`= *p*-Cl-C_6H_4	X = CH_3	Y = COOEt
c; Ar`= *p*-OMe-C_6H_4	X = H	Y = CN	k; Ar`= *p*-OMe-C_6H_4	X = H	Y = COOEt
d; Ar`= *p*-OMe-C_6H_4	X = CH_3	Y = CN	l; Ar`= *p*-OMe-C_6H_4	X = CH_3	Y = COOEt
e; Ar`= *p*-OH-C_6H_4	X = H	Y = CN	m; Ar`= *p*-OH-C_6H_4	X = H	Y = COOEt
f; Ar`= *p*-OH-C_6H_4	X = CH_3	Y = CN	n; Ar`= *p*-OH-C_6H_4	X = CH_3	Y = COOEt
g; Ar`= C_6H_5	X = H	Y = CN	o; Ar`= C_6H_5	X = H	Y = COOEt
h; Ar`= C_6H_5	X = CH_3	Y = CN	p; Ar`= C_6H_5	X = CH_3	Y = COOEt

Scheme 1

The solid product which formed was collected by filtration and recrystallized from dioxane and ethanol:benzene (1:1, *v*:*v*), respectively (Scheme 1).

(E) 2-Amino-4-(p-chlorophenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3a**): Color: Yellow crystals. Yield: 90 %. M.p.: 245-246 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 268.80. FT-IR (KBr, ν, cm^{-1}): 3417, 3327, 3207 (NH_2), 3001, 2960, 2812 (CH stretching), 2196 (CN), 1666 (C=C), 1510 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.93-7.24 (m, 14H, Ar-H), 4.95 (s, 1H, CH-pyran), 4.84 (bs, 2H, NH_2, exchangeable by D_2O). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.59 (C-2), 152.94 (C-6), 116.98 (CN), 61.33(C-3), 40.74 (C-4), 144.70, 142.63, 133.44, 131.41, 133.29, 129.45, 129.20, 129.14, 127.82, 127.43, 123.75, 123.71, 123.28, 123.17, 120.90, 112.25 (aromatic). MS (EI, *m/z* (%)): 438 (M^++2, 0.0), 436 (M+, 20.4), 325 (75.8), 220 (59.9), 77 (100), 51 (18.2). Anal. calcd. for $C_{26}H_{17}ClN_4O$: C, 71.48; H, 3.92; N, 12.82. Found: C, 71.01; H, 3.40; N, 12.39%.

(E) 2-Amino-4-(p-chlorophenyl)-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3b**): Color: Yellow crystals. Yield: 86 %. M.p.: 232-233 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 269.75. FT-IR (KBr, ν, cm^{-1}): 3410, 3330 (NH_2), 3015, 3000, 2981 (CH stretching), 2200 (CN), 1680 (C=C), 1500 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.94-7.21 (m, 13H, Ar-H), 5.01 (s, 1H, CH-pyran), 4.88 (bs, 2H, NH_2, exchangeable by D_2O), 1.42 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.63 (C-2), 152.82 (C-6), 116.97 (CN), 61.45 (C-3), 40.70 (C-4), 21.33 (CH_3), 144.71, 142.66, 133.42, 131.40, 131.27, 129.46, 129.21, 129.15, 127.80, 127.41, 123.73, 123.71, 123.26, 123.18, 120.87, 112.23 (aromatic). MS (EI, *m/z* (%)): 452 (M^++2, 40.40), 450 (M+, 100), 339 (57.6), 220 (42.3), 91(47.0), 77 (1.6), 51 (0.7), 75 (100), 50 (46). Anal. calcd. for $C_{27}H_{19}ClN_4O$: C, 71.92; H, 4.25; N, 12.43. Found: C, 71.35; H, 3.81; N, 12.11 %.

(E) 2-Amino-4-(p-methoxyphenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3c**): Color: Pale red crystals. Yield: 85 %. M.p.: 248-249 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 269.81. FT-IR (KBr, ν, cm^{-1}): 3420, 3327, 3210 (NH_2), 3076, 2938 (CH stretching), 2198 (CN), 1664 (C=C), 1515 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.90-7.11 (m, 14H, Ar-H), 5.12 (s, 1H, CH-pyran), 4.90 (bs, 2H, NH_2, exchangeable by D_2O), 3.79 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.01 (C-2), 116.90 (CN), 61.77 (C-3), 56.40 (OCH_3), 41.15 (C-4), 153.01, 144.67, 142.60, 133.45, 131.43, 131.26, 129.49, 129.23, 129.16, 127.76, 127.39, 123.77, 123.70, 123.29, 123.20, 120.87, 112.23 (aromatic). MS (EI, *m/z* (%)): 434 (M^++2, 3.6), 433 (M++1, 21.5), 432 (M+, 69.6), 325 (100), 220 (30.5), 76 (47.3), 51 (6.0). Anal. calcd. for $C_{27}H_{20}N_4O_2$: C, 74.98; H, 4.66; N, 12.95. Found: C, 74.40; H, 4.25; N, 12.45 %.

(E) 2-Amino-4-(p-methoxyphenyl)-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3d**): Color: Pale red crystals. Yield: 84 %. M.p.: 230-231 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 269.84. FT-IR (KBr, ν, cm^{-1}): 3419, 3325, 3207 (NH_2), 3030, 3009, 2981, 2940 (CH stretching), 2196 (CN), 1664 (C=C), 1510 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.84-6.96 (m, 13H, Ar-H), 5.09 (s, 1H, CH-pyran), 4.89 (bs, 2H, NH_2, exchangeable by D_2O), 3.78 (s, 3H, OCH_3), 1.37 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.31 (C-2), 127.51 (C-8), 127.51 (C-9), 121.16 (C-10), 121.16 (C-4a), 117.01 (CN), 61.89 (C-3), 56.87 (OCH_3), 41.15 (C-4), 21.40 (CH_3), 144.80, 142.66, 133.45, 131.40, 131.27, 129.46, 129.22, 129.16, 127.88, 127.40, 123.72, 123.70, 123.28, 123.18, 120.91, 112.28 (aromatic). MS (EI, *m/z* (%)): 448 (M^++2, 1.9), 447 (M^++1, 10.5), 446 (M^+, 34.4), 220 (32.4), 91 (86.0), 77 (6.3). Anal. calcd. for $C_{28}H_{22}N_4O_2$: C, 75.32; H, 4.97; N, 12.55. Found: C, 74.81; H, 4.41; N, 12.16 %.

(E) 2-Amino-4-(p-hydroxyphenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3e**): Color: Red crystals. Yield: 80 %. M.p.: 198-199 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 271.20. FT-IR (KBr, ν, cm^{-1}): 3423 (OH), 3319, 3246 (NH_2), 3055, 3010 (CH stretching), 2193 (CN), 1624 (C=C), 1541 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 9.72 (bs, 1H, OH, exchangeable by D_2O), 8.45-7.01 (m, 14H, Ar-H), 4.93 (s, 1H, CH-pyran), 4.80 (bs, 2H, NH_2, exchangeable by D_2O). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.12 (C-2), 153.40 (C-6), 117.23 (CN), 62.01 (C-3), 41.11 (C-4), 144.75, 142.60, 133.40, 131.37, 131.26, 129.40, 129.25, 129.16, 127.86, 127.45, 123.73, 123.70, 123.26, 123.19, 120.93, 112.30 (aromatic). MS (EI, *m/z* (%)): 419 (M^++1, 3.5), 418 (M^+, 16.2), 325 (100), 221 (15.1), 180 (25.3), 77 (62.1), 52 (10.5). Anal. calcd. for $C_{26}H_{18}N_4O_2$: C, 74.63; H, 4.34; N, 13.39. Found: C, 74.12; H, 4.04; N, 12.89 %.

(E) 2-Amino-4-(p-hydroxyphenyl)-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3f**): Color: Red crystals. Yield: 87 %. M.p.: 207-208 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 271.01. FT-IR (KBr, ν, cm^{-1}): 3430 (OH), 3321, 3249 (NH_2), 3041, 3012 (CH stretching), 2197 (CN), 1628 (C=C), 1539 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 9.70 (bs, 1H, OH, exchangeable by D_2O), 8.51-6.83 (m, 13H, Ar-H), 5.10 (s, 1H, CH-pyran), 4.91 (bs, 2H, NH_2, exchangeable by D_2O), 2.41 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.01 (C-2), 153.41 (C-6), 116.92 (CN), 61.80 (C-3), 41.11 (C-4), 21.65

(CH_3), 144.71, 142.62, 133.42, 131.40, 133.27, 129.43, 129.22, 129.16, 127.84, 127.46, 123.76, 123.74, 123.27, 123.19, 120.88, 112.30 (aromatic). MS (EI, *m/z* (%)): 432 (M^+, 14.40), 339 (12.07), 314 (20.10), 221 (1.1), 172 (35.26), 106 (100), 77 (6.4), 53 (14.4). Anal. calcd. for $C_{27}H_{20}N_4O_2$: C, 74.98; H, 4.66; N, 12.95. Found: C, 74.34; H, 4.20; N, 12.23 %.

(E) 2-Amino-4-phenyl-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3g**): Color: Red crystals. Yield: 86 %. M.p.: 265-266 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 270.80. FT-IR (KBr, ν, cm^{-1}): 3466, 3327, 3198 (NH_2), 3050, 3020, 2985 (CH stretching), 2196 (CN), 1664 (C=C), 1510 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.80-7.20 (m, 15H, Ar-H), 5.21 (s, 1H, CH-pyran), 4.99 (bs, 2H, NH_2, exchangeable by D_2O). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.76 (C-2), 152.78 (C-6), 116.97 (CN), 62.03 (C-3), 41.19 (C-4), 144.74, 142.60, 133.42, 131.42, 131.27, 129.43, 129.22, 129.16, 127.81, 127.42, 127.81, 127.40, 123.72, 123.70, 123.26, 123.14, 120.78, 112.22 (aromatic). MS (EI, *m/z* (%)): 404 (M^++2, 5.0), 403 (M^++1, 27.0), 402 (M+, 100), 325 (66.5), 220 (36.8), 76 (18.0), 51 (1.75). Anal. calcd. for $C_{26}H_{18}N_4O$: C, 77.59; H, 4.51; N, 13.92. Found: C, 77.08; H, 4.07; N, 13.46 %.

(E) 2-Amino-4-phenyl-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (**3h**): Color: Yellow crystals. Yield: 83 %. M.p.: 260-261 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 270.64. FT-IR (KBr, ν, cm^{-1}): 3468, 3300, 3188 (NH_2), 3048, 3027, 2988 (CH stretching), 2191 (CN), 1664 (C=C), 1512 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.99-7.10 (m, 14H, Ar-H), 5.17 (s, 1H, CH-pyran), 4.91 (bs, 2H, NH_2, exchangeable by D_2O), 2.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.07 (C-2), 153.05 (C-6), 117.01 (CN), 61.53 (C-3), 41.27 (C-4), 144.66, 142.56, 133.41, 131.40, 131.27, 129.42, 129.21, 129.17, 127.81, 127.40, 123.73, 123.70, 123.26, 123.15, 120.91, 112.26 (aromatic). MS (EI, *m/z* (%)): 418 (M^++2, 4.5), 417 (M^++1, 13.7), 416 (M^+, 45.1), 339 (100), 297 (33.9), 220 (81.8), 91 (84.2), 77 (10.3). Anal. calcd. for $C_{27}H_{20}N_4O$: C, 77.87; H, 4.84; N, 13.45 %. Found: C, 77.48; H, 4.34; N, 13.02 %.

(E) Ethyl 2-amino-4-(p-chlorophenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3i**): Color: Yellow crystals. Yield: 75 %. M.p.: 208-209 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 267.58. FT-IR (KBr, ν, cm^{-1}): 3417, 3380, 3126 (NH_2), 3060, 3010, 2960, (CH stretching), 1675 (CO), 1629 (C=C), 1539 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.92-7.20 (m, 14H, Ar-H), 6.54 (bs, 2H, NH_2, exchangeable by D_2O), 5.14 (s, 1H, CH-pyran), 4.11 (q, 2H, CH_2, *J* = 7.0 Hz), 1.21 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 169.15 (CO), 159.62 (C-2), 153.08 (C-6), 79.01 (C-3), 59.73 (CH_2), 40.37 (C-4), 14.37 (CH_3), 145.81, 145.79, 145.68, 144.26, 132.05, 131.24, 131.02, 129.61, 129.37,129.13, 128.45, 128.36, 127.32, 127.00, 126.40, 123.79, 123.61, 123.11, 120.54, 112.76 (aromatic). MS (EI, *m/z* (%)): 485 (M^++2, 5.41), 483 (M^+, 9.22), 372 (35.2), 268 (18.5), 181 (6.7), 91 (100), 75 (60.1), 51 (9.3). Anal. calcd. for $C_{28}H_{22}ClN_3O_3$: C, 69.49; H, 4.58; N, 8.68. Found: C, 69.05; H, 4.12; N, 8.25 %.

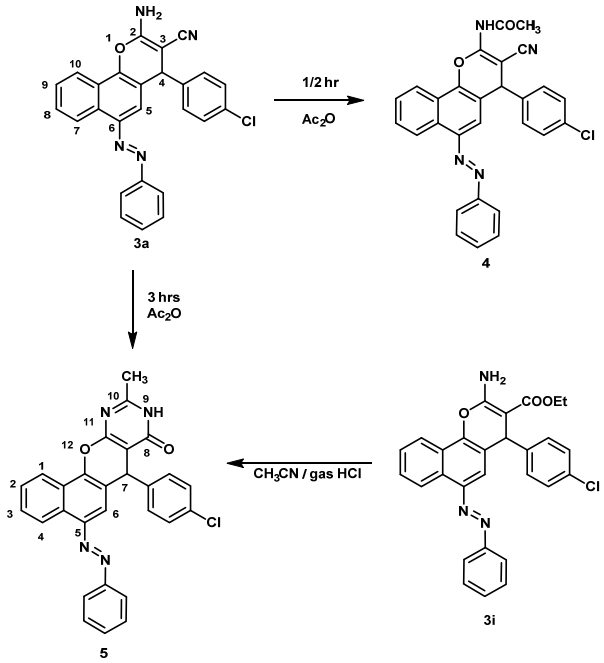
(E) Ethyl 2-amino-4-(p-chlorophenyl)-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3j**): Color: Yellow crystals. Yield: 71 %. M.p.: 222-223 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 267.82. FT-IR (KBr, ν, cm^{-1}): 3454, 3321, 3290 (NH_2), 3020, 3001, 2980, (CH stretching), 1680 (CO), 1670 (C=C), 1521 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.90-7.11 (m, 13H, Ar-H), 6.41 (bs, 2H, NH_2, exchangeable by D_2O), 5.12 (s, 1H, CH-pyran), 4.19 (q, 2H, CH_2, *J* = 7.0 Hz), 2.40 (s, 3H, CH_3), 1.23 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 170.00 (CO), 160.10 (C-2), 153.60 (C-6), 80.00 (C-3), 60.21 (CH_2), 41.13 (C-4), 21.58, (CH_3), 14.37 (CH_3), 145.80, 145.78, 145.70, 144.28, 132.10, 131.22, 131.08, 129.60, 129.36, 129.15, 128.43, 128.34, 127.30, 127.02, 126.42, 123.78, 123.60, 123.16, 120.56, 112.78 (aromatic). MS (EI, *m/z* (%)): 499 (M^++2, 2.17), 497 (M^+, 4.61), 386 (43.5), 221 (19.51), 220 (1.87), 91 (100), 75 (3.7), 51 (2.2). Anal. calcd. for $C_{29}H_{24}ClN_3O_3$: C, 69.95; H, 4.86; N, 8.44. Found: C, 69.51; H, 4.40; N, 8.02 %.

(E) Ethyl 2-amino-4-(p-methoxyphenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3k**): Color: Yellow crystals. Yield: 72 %. M.p.: 290-291 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 268.30. FT-IR (KBr, ν, cm^{-1}): 3383, 3259 (NH2), 3066, 3012, 2955, (CH stretching), 1672 (CO), 1618 (C=C), 1529 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 9.21-7.42 (m, 14H, Ar-H), 6.39 (bs, 2H, NH_2, exchangeable by D_2O), 5.06 (s, 1H, CH-pyran), 4.25 (q, 2H, CH_2, *J* = 7.0 Hz), 2.67 (s, 3H, CH_3), 1.41 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 170.20 (CO), 160.30 (C-2), 154.77 (C-6), 81.02 (C-3), 60.25 (CH_2), 58.10 (OCH_3), 41.17 (C-4), 14.39 (CH_3), 145.84, 145.77, 145.69, 144.28, 132.08, 131.27, 131.09, 129.70, 129.36, 129.17, 128.46, 128.34, 127.30, 127.10, 126.38, 123.81, 123.62, 123.15, 120.55, 112.73 (aromatic). MS (EI, *m/z* (%)): 479 (M^+, 0.7), 406 (0.8), 220 (1.63), 155 (27.6), 77 (100), 51 (45.1). Anal. calcd. for $C_{29}H_{25}N_3O_4$: C, 72.64; H, 5.26; N, 8.76. Found: C, 72.21; H, 4.83; N, 8.42 %.

(E) Ethyl 2-Amino-4-(p-methoxyphenyl)-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3l**): Color: Yellow crystals. Yield: 87 %. M.p.: 268-269 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 268.27. FT-IR (KBr, ν, cm^{-1}): 3439, 3270 (NH_2), 3060, 3017, 2986 (CH stretching), 1670 (CO), 1620 (C=C), 1531 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.39-6.80 (m, 13H, Ar-H), 6.15 (bs, 2H, NH_2, exchangeable by D_2O), 5.14 (s, 1H, CH-pyran), 4.10 (q, 2H, CH_2, *J* = 7.0 Hz), 3.59 (s, 3H,OCH_3), 2.40 (s, 3H, CH_3), 1.27 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 170.08 (CO), 160.02 (C-2), 153.06 (C-6), 80.15 (C-3), 61.79 (CH_2), 56.15 (OCH_3), 40.81 (C-4), 21.15 (CH_3), 14.20 (CH_3), 145.80, 145.79, 145.68, 144.24, 132.10, 131.26, 131.02, 129.60, 129.37, 129.11, 128.52, 128.44, 127.25, 127.05, 126.42, 123.76, 123.63, 123.14, 120.80, 120.60, 112.69 (aromatic). MS (EI, *m/z* (%)): 493 (M^+, 11.4), 386 (32.4), 221 (18.6), 155 (27.1), 77 (100), 51 (60.7). Anal. calcd. for $C_{30}H_{27}N_3O_4$: C, 73.01; H, 5.51; N, 8.51. Found: C, 72.64; H, 5.10; N, 8.14 %.

(E) Ethyl 2-amino-4-(p-hydroxyphenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3m**): Color: Red crystals. Yield: 69 %. M.p.: 190-191 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 267.75. FT-IR (KBr, ν, cm^{-1}): 3439 (OH), 3259, 3132 (NH_2), 3033, 3012, 2950, (CH stretching), 1672 (CO), 1620 (C=C), 1510 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 9.70 (bs, 1H, OH), 8.76-6.80 (m, 14H, Ar-H), 6.25 (bs, 2H, NH_2, exchangeable by D_2O), 5.07 (s, 1H, CH-pyran), 4.36 (q, 2H, CH_2, *J* = 7.0 Hz), 1.29 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 170.02 (CO), 160.61 (C-2), 153.02 (C-6), 80.20 (C-3), 62.21 (CH_2), 40.34 (C-4), 14.15 (CH_3), 145.90, 145.80, 145.78, 144.29, 132.15, 131.30, 131.10, 129.80, 129.40, 129.21, 128.56, 128.48, 127.29, 127.10, 126.44, 123.80, 123.65, 123.18, 120.85, 120.70, 112.70 (aromatic). MS (EI, *m/z* (%)): 465 (M^+, 21.2), 372 (3.8), 262 (20.3), 220 (29.1), 142 (52.6), 115 (48.4), 65 (100), 50 (30.1). Anal. calcd. for $C_{28}H_{23}N_3O_4$: C, 72.25; H, 4.98; N, 9.03. Found: C, 71.80; H, 4.52; N, 8.66 %.

(E) Ethyl 2-amino-4-(p-hydroxyphenyl)-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3n**): Color: Pale red crystals. Yield: 68 %. M.p.: 252-253 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 267.64. FT-IR (KBr, ν, cm^{-1}): 3423 (OH), 3256, 3136 (NH_2), 3082, 3010, 2941 (CH stretching), 1670 (CO), 1614 (C=C), 1508 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 9.76 (bs, 1H, OH, exchangeable by D_2O), 8.26-6.98 (m, 13H, Ar-H), 6.28 (bs, 2H, NH_2, exchangeable by D_2O), 4.96 (s, 1H, CH-pyran), 4.31 (q, 2H, CH_2, *J* = 7.0 Hz), 2.30 (s, 3H, CH_3), 1.27 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 169.99 (CO), 159.50 (C-2), 153.40 (C-6), 80.77 (C-3), 62.53 (CH_2), 40.42 (C-4), 21.17 (CH_3), 14.18 (CH_3), 145.92, 145.83, 145.76, 144.27, 132.16, 131.32, 131.15, 129.86, 129.42, 129.22, 128.58, 128.47, 127.28, 127.12, 126.43, 123.81, 123.66, 123.20, 120.83, 120.71, 112.65 (aromatic). MS (EI, *m/z* (%)): 479 (M^+, 1.20), 386 (0.7), 262 (20.3), 219 (23.0), 143 (56.4), 115 (78.8), 65 (100), 50 (42.7). Anal. calcd. for $C_{29}H_{25}N_3O_4$: C, 72.64; H, 5.26; N, 8.76. Found: C, 72.20; H, 4.78; N, 8.32 %.



Scheme 2

(E) Ethyl 2-amino-4-phenyl-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3o**): Color: Pale red crystals. Yield: 65 %. M.p.: 206-207 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 268.15. FT-IR (KBr, ν, cm^{-1}): 3300, 3184, 3165, 3124 (NH_2), 3026, 2999, 2982 (CH stretching), 1650 (CO), 1610 (C=C), 1533 (N=N). ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.88-7.10 (m, 15H, Ar-H), 6.40 (bs, 2H, NH_2, exchangeable by D_2O), 5.10 (s, 1H, CH-pyran), 4.10 (q, 2H, CH_2, *J* = 7.0 Hz), 1.28 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 169.89 (CO), 159.30 (C-2), 153.10 (C-6), 80.30 (C-3), 62.40 (CH_2), 40.60 (C-4), 14.75 (CH_3), 145.87, 145.81, 145.79, 144.28, 132.17, 131.31, 131.17, 129.81, 129.42, 129.26, 128.58, 128.46, 127.27, 127.13, 126.45, 123.82, 123.60, 123.20, 120.82, 120.68, 112.63 (aromatic). MS (EI, *m/z* (%)): 449 (M^+, 2.95), 374 (8.4), 271 (100), 104 (94.6), 48 (47.2). Anal. calcd. for $C_{28}H_{23}N_3O_3$: C, 74.82; H, 5.16; N, 9.35. Found: C, 74.43; H, 4.65; N, 8.84 %.

(E) Ethyl 2-amino-4-phenyl-6-(p-tolyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carboxylate (**3p**): Color: Pale red crystals. Yield: 63 %. M.p.: 240-241 °C. UV/Vis (CH_3COCH_3, λ_{max}, nm): 268.06. FT-IR (KBr, ν, cm^{-1}): 3454, 3381, 3321 (NH_2), 3027, 3010, 2933 (CH stretching), 1680 (CO), 1666 (C=C), 1520 (N=N). ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.73-7.21 (m, 14H, Ar-H), 6.45 (bs, 2H, NH_2, exchangeable by D_2O), 5.13 (s, 1H, CH-pyran), 4.30 (q, 2H, CH_2, *J* = 7.0 Hz), 2.39 (s, 3H, CH_3), 1.24 (t, 3H, CH_3, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 169.50 (CO), 159.10 (C-2), 153.30 (C-6), 80.60 (C-3), 62.30 (CH_2), 40.39 (C-4), 21.28 (CH_3), 14.19 (CH_3), 145.86, 145.78, 145.80, 144.27, 132.15, 131.30, 131.16, 129.80, 129.40, 129.25, 128.56, 128.43, 127.25, 127.16, 126.46, 123.80, 123.64, 123.22, 120.81, 120.69, 112.60 (aromatic). MS (EI, *m/z* (%)): 463 (M^+, 7.50), 387 (100), 244 (45.18), 143 (20.1), 99 (8.5), 57 (0.1), 55 (0.2).

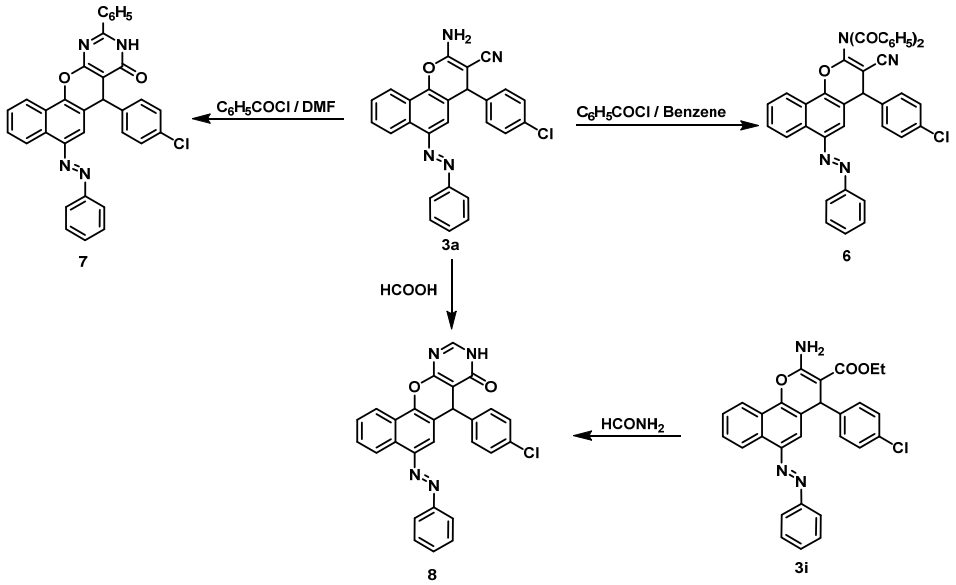
2.2.2. Synthesis of 2-acetylamino-4-(p-chlorophenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile **(4)**

A solution of compound **3a** (0.43 g, 10 mmol) in Ac_2O (20 mL) was heated under reflux for 30 min. The solid product formed was filtered off and washed with cold ethanol; the solid obtained was filtered off and recrystallized from ethanol (Scheme 2). Color: Yellow crystals. Yield: 83 %. M.p.: 181-182 °C. FT-IR (KBr, ν, cm^{-1}): 3450 (NH), 3120, 2943 (CH-stretching), 2231 (CN), 1715 (CO), 1650 (C=C), 1541 (N=N). ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 10.29 (bs, 1H, NH, exchangeable by D_2O), 8.83-6.93 (m, 14H, Ar-H), 5.18 (s, 1H, pyran CH), 2.19 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 170.50 (CO), 160.41 (C-2), 152.88 (C-6), 116.43 (CN), 60.13 (C-3), 41.12 (C-4), 22.65 (CH_3), 145.79, 145.71, 145.68, 144.24, 132.11, 131.26, 131.02, 129.50, 129.37, 129.13, 128.40, 128.31, 127.24, 127.01, 126.40, 123.79, 123.61, 120.82, 120.68, 112.62 (aromatic). MS (EI, *m/z* (%)): 480 (M^++2, 2.31), 478 (M^+, 7.20), 367 (45.2), 308 (56.1), 179 (33.1), 77 (100), 50 (37.4). Anal. calcd. for $C_{28}H_{19}ClN_4O_2$: C, 70.22; H, 4.00; N, 11.70. Found: C, 69.85; H, 3.61; N, 11.42%.

2.2.3. Synthesis of 7-(4-chlorophenyl)-10-methyl-5-(phenyl diazenyl)-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d] pyrimidin-8-one **(5)**

Method A: A solution of compound **3a** (0.43 g, 10 mmol) in Ac_2O (20 mL) was heated under reflux for 3 h. The precipitate was filtered off, washed with cold ethanol. The solid obtained was filtered off and recrystallized from DMF.

Method B: Gaseous dry HCl was bubbled through the mixture of compound **3i** (0.48 g, 10 mmol) and CH_3CN (30 mL) for 6 h. The reaction mixture was poured into ice water and alkalized with 10% aqueous ammonium hydroxide to give compound **5** (Scheme 2). Color: Yellow crystals. Yield: 85 %. M.p.: > 360 °C. FT-IR (KBr, ν, cm^{-1}): 3456 (NH), 3020, 3005, 2920 (CH- stretching), 1680 (CO), 1643 (C=C), 1540 (N=N). ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.81-7.71 (m, 15H, Ar-H + NH), 5.37 (s, 1H, pyran CH), 2.40 (s, 3H, CH_3). MS (EI, *m/z* (%)): 480 (M^++2, 11.58), 478 (M+, 11.47), 433 (73.1), 328 (64.8), 293 (84.7), 77 (100), 51 (29.7). Anal. calcd. for $C_{28}H_{19}ClN_4O_2$: C, 70.22; H, 4.00; N, 11.70. Found: C, 69.80; H, 3.75; N, 11.53 %.



Scheme 3

2.2.4. Synthesis of 2-N,N-dibenzoylamino-4-(p-chloro phenyl)-6-(phenyldiazenyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile (6)

A solution of compound **3a** (0.43 g, 10 mmol) in benzoyl chloride (10 mL) in dry benzene (20 mL) was heated under reflux for 6 h. The excess of benzoyl chloride was removed under reduced pressure and the residue was poured into cold water. The precipitate was collected by filtration, washed with carbon tetrachloride (10 mL) to remove the formed benzoic acid and the residue was dried. The solid obtained was filtered off and recrystallized from DMF (Scheme 3). Color: Pale yellow crystals. Yield: 70 %. M.p.: >360 °C. FT-IR (KBr, ν, cm^{-1}): 3076, 3015 (CH- stretching), 2231 (CN), 1735 (CO), 1641 (C=C), 1541 (N=N). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 8.99-6.90 (m, 24H, Ar-H), 5.20 (s, 1H, pyran CH). MS (EI, *m/z* (%)): 646 (M^++2, 0.0), 644 (M^+, 0.1), 435 (37.6), 330 (41.0), 302 (100), 238 (21.3), 77 (47.7). Anal. calcd. for $C_{40}H_{25}ClN_4O_3$: C, 74.47; H, 3.91; N, 8.68. Found: C, 74.02; H, 3.50; N, 8.24 %.

2.2.5. Synthesis of 7-(4-chlorophenyl)-10-phenyl-5-(phenyl diazenyl)-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d] pyrimidin-8-one (7)

A solution of compound **3a** (0.43 g, 10 mmol) in benzoyl chloride (10 mL) in DMF (20 mL) was heated under reflux for 6 h. The excess of benzoyl chloride was removed under reduced pressure and the residue was poured into cold water. The precipitate was collected by filtration, washed with carbon tetrachloride (10 mL) to remove the formed benzoic acid and the residue was dried. The solid obtained was filtered off and recrystallized from DMF (Scheme 3). Color: Pale yellow crystals. Yield: 78 %. M.p.: >360 °C. FT-IR (KBr, ν, cm^{-1}): 3452 (NH), 3041, 3023 (CH stretching), 1695 (CO), 1633 (C=C), 1542 (N=N). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.92 (br, 1H, NH, exchangeable by D_2O), 8.78-6.96 (m, 19 H, Ar-H), 5.14 (s, 1H, pyran CH). MS (EI, *m/z* (%)): 542 (M++2, 4.21), 542 (M+, 9.31), 429 (46.3), 353 (100), 248 (37.5), 77 (16.4), 50 (7.3). Anal. calcd. for $C_{33}H_{21}ClN_4O_2$: C, 73.26; H, 3.91; N, 10.36. Found: C, 72.80; H, 3.56; N, 9.78 %.

2.2.6. Synthesis 7-(4-chlorophenyl)-5-(phenyldiazenyl)-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d]pyrimidin-8-one (8)

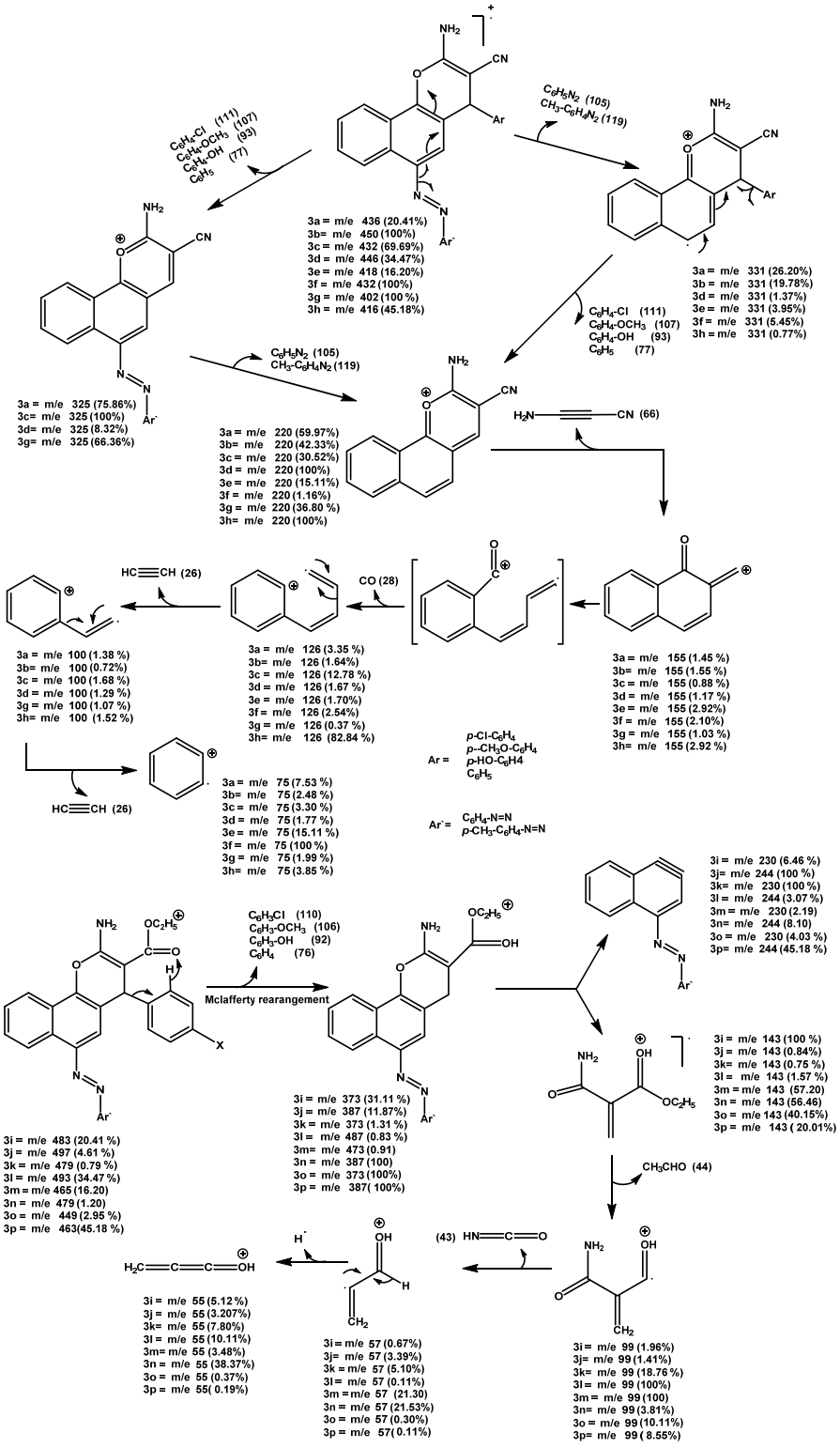
Method A: A solution of compound **3a** (0.43 g, 10 mmol) in formic acid (20 mL) was heated under reflux for 10 h. The solid obtained was filtered off and recrystallized from dioxane.

Method B: A solution of compound **3i** (0.48 g, 10 mmol) in formamide (20 mL) was heated under reflux for 6 h to give compound **8** (Scheme 3). Color: Pale yellow crystals. Yield: 84 %. M.p.: >190-191 °C. FT-IR (KBr, ν, cm^{-1}): 3433 (NH), 3064, 2911 (CH- stretching), 1718 (CO), 1662 (C=C), 1540 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 11.21 (br, 1H, NH, exchangeable by D_2O), 8.42-6.70 (m, 15H, Ar-H + CH-pyrimidine), 5.15 (s, 1H, pyran CH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 165.70 (CO), 161.41 (C11a), 155.10 (C-10), 41.65 (C-7), 61.26 (C-7a), 145.78 145.70, 145.67, 144.23, 132.10, 131.24, 131.01, 129.51, 129.36, 129.16, 128.41, 128.30, 127.33, 127.05, 126.41, 123.77, 123.60, 123.17, 120.40, 112.60 (aromatic). MS (EI, *m/z* (%)): 466 (M^++2, 0.0), 464 (M^+, 0.1), 265 (51.6), 202 (47.5), 133 (72.9), 108 (100), 76 (37.5), 51 (16.0). Anal. calcd. for $C_{27}H_{17}ClN_4O_2$: C, 69.75; H, 3.69; N, 12.05. Found: C, 69.35; H, 3.21; N, 11.74 %.

3. Results and discussion

Condensation of various substituted α-cyanocinnamonitriles (**2a**-**h**) and ethyl α-cyanocinnamates (**2i**-**p**) with 4-phenyldiazenyl /or 4-(*p*-tolyldiazenyl)-1-naphthol (**1**) in ethanolic piperidine afforded the corresponding 2-amino-4-(aryl)-6-(phenyldiazenyl/or *p*-tolyldiazenyl)-4*H*-naphtho[1,2-*b*]pyran-3-carbonitrile (**3a**-**h**) and ethyl-2-amino-4-(aryl)-6-(phenyldiazenyl /or *p*-tolyldiazenyl)-4*H*-naphtho[1,2-*b*]pyran-3-carboxylate (**3i**-**p**), respectively (Scheme 1).

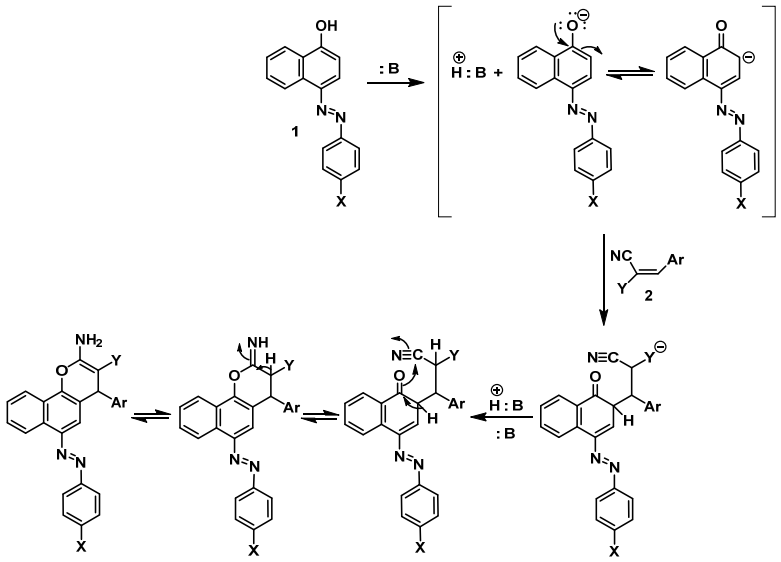
The structures of compounds **3a**-**p** were established on the basis of ^{1}H NMR and ^{13}C NMR spectra, which showed 4*H*-pyran at δ 4.85-5.15 and C-4 at δ 40.15-41.27 ppm. The IR spectra of compounds **3a**-**i** showed *ν*(NH_2) stretch at 3440-3405, 3327-3307 and 3216-3196 cm^{-1}; *ν*(CN) stretch at 2200-2191 cm^{-1}, and compounds **3g**-**p** showed *ν*(CO) stretch at 1680-1670 cm^{-1}. The UV spectrum of compound **3a**-**p** revealed a weak shoulder characteristic for 4*H*-pyran [36] at λ_{max} (CH_3COCH_3): 267.58-271.20 nm (log ε = 4.82-4.81). The mass spectra of compounds **3a**-**p** showed, the corresponding molecular ion peaks at *m/z* 436 (M^+, 20.4), 450 (M^+, 100), 432 (M^+, 69.6), 446 (M^+, 33.4), 418 (M^+, 16.2), 432 (M^+, 14.40), 402 (M^+, 100), 416 (M^+, 45.1), 483 (M^+, 9.22), 497 (M^+, 4.61), 479 (M^+, 0.79), 493 (M^+, 11.44),



Scheme 4

465 (M^+, 20.23), 479 (M^+, 1.20), 449 (M^+, 0.90), 463 (M^+, 7.50). The fragmentation patterns of compounds **3a**-**p**, respectively (Scheme 4).

The formation of compound **3a**-**p** indicates that the naphtholate anion (C-2) of compound **1** attack at the *β*-carbon of compound **2** to yield an acyclic Michael adduct [37], which underwent cyclization as shown in Scheme 5.



Scheme 5

Interaction of 2-amino-4-(*p*-chlorophenyl)-6-(phenyldiazenyl)-4*H*-naphtho[1,2-*b*]pyran-3-carbonitrile (**3a**) with acetic anhydride for 30 min afforded the *N*-acetylamino derivative **4** while heating of compound **3a** with acetic anhydride for 6 h afforded 8,9-dihydro-10-methyl-5-(phenyldiazenyl)- 7-(*p*-chlorophenyl)-7*H*-naphtho [1,2-*b*]pyrano[2,3-*d*]pyrimidin-8-one (**5**) (Scheme 2).

The structure of compound **4** was established on the basis of IR which showed the presence of CN group stretch at 2225 cm^{-1} and CO of acetyl stretch at 1715 cm^{-1}, while for compound **5** the absence of CN, the presence of NH stretch at 3450 and CO of amide stretch at 1655 cm^{-1}. ^1H NMR spectra for compound **4** revealed the presence of signal at δ 2.19 ppm (s, 3H, $COCH_3$) and δ 10.29 ppm (br, 1H, NH), while for compound **5** showed δ 2.40 (s, 3H, CH_3) and δ 8.81-7.10 ppm (m, 15H, Ar-H + NH). The structure of compound **5** was also supported by an independent synthesis of the same products from compound **3i** and acetonitrile in the presence of HCl gas [38] (M.p. and mixed m.p.) (Scheme 5). Interaction of compound **3a** with benzoyl chloride in benzene for 6 h afforded *N,N*-dibenzoylamino derivatives **6**, while heating of compound **3a** with benzoyl chloride in DMF for 6 h afforded 7-(4-chlorophenyl)-10-phenyl-5-(phenyldiazenyl)-7,9-dihydro-8*H*-benzo[7,8]chromeno[2,3-d]pyrimidin-8-one (**7**). Treatment of compound **3a** with formic acid for 10 h afforded naphthapyranopyrimidine-8-one derivative **8**, the structure of compound **8** was supported by an independent synthesis from compound **3i** and formamide (Scheme 3).

The structures of compounds **6-8** were confirmed by IR, ^1H NMR and MS. The IR spectrum of compound **6** showed *v*(CN) stretch at 2214 cm^{-1} and (CO of benzoyl) group stretch at 1735 cm^{-1}, while for compound **7**, (CO of amide) group stretch at 1659 cm^{-1} and compound **8** showed *v*(NH) stretch at 3433 cm^{-1} and *v*(CO) stretch at 1718 cm^{-1}. ^1H NMR of spectra for compound **7** revealed the presence of signal at δ 11.89 ppm (br, 1H, NH, D_2O exchangeable), while for compound **8** showed δ 8.45 ppm (s, 1H, CH-Pyimidine), 11.21 ppm (br, 1H, NH D_2O exchan-geable). The mass spectra of compounds **6-8** showed the corresponding molecular ion peaks *m/z* 540 (M^+, 10.5), *m/z* 644 (0.01) and 464 (M^+, 0.17), respectively.

4. Conclusions

Synthesis of several new heterocyclic compounds reported such as 4-phenyldiazenyl or (*p*-tolyldiazenyl)-4*H*-naphthopyrans and 4-phenyldiazenyl or (*p*-tolyldiazenyl)-4*H*-naphtho pyranopyraimidin-8-ones. The synthesized com-pounds exhibited expected biological activities and physiological properties.

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