Rapid and Efficient Microwave Assisted Method for the Regioselective Synthesis of 8,8'-Methylene-bis-4-oxo-1*H* and 2*H*-chromeno[4,3-*c*]pyrazoles

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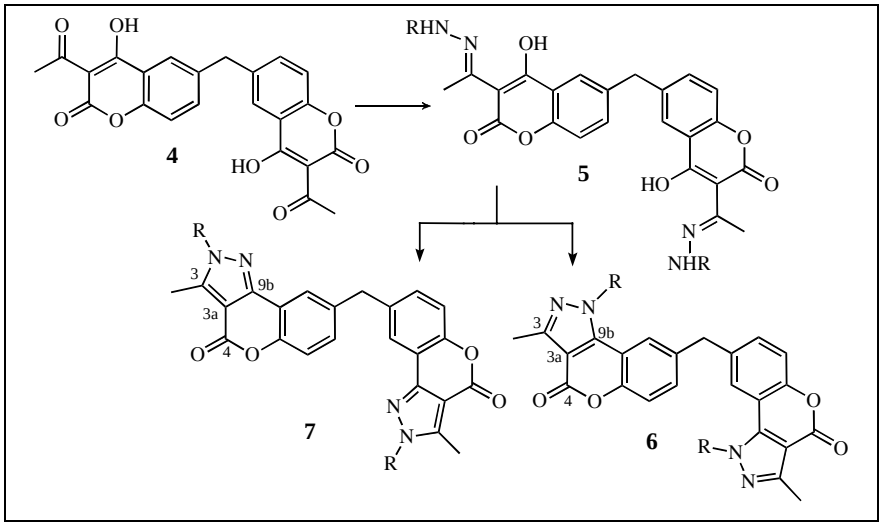

The ethyl ester of 5,5'-methylene-bis-salicyclic acid **3** was prepared by the esterification of 5,5'-methylene-bis-salicylic acid **2**. The compound **3** on reacting with ethylacetoacetate yields 6,6'-methylene-bis-(3-acetyl-4-hydroxycoumarin) **4**. The compound **4** was regioselectively converted into either 8,8'-methylene-bis-(4-oxo-1*H*-chromeno[4,3-*c*]pyrazoles) **6** or 8,8'-methylene-bis(-4-oxo-2*H*-chromeno[4,3-*c*]-pyrazoles) **7** under microwave irradiation. High yields are achieved even on a gram scale, while reaction times are considerably shortened compared to conventional heating conditions.

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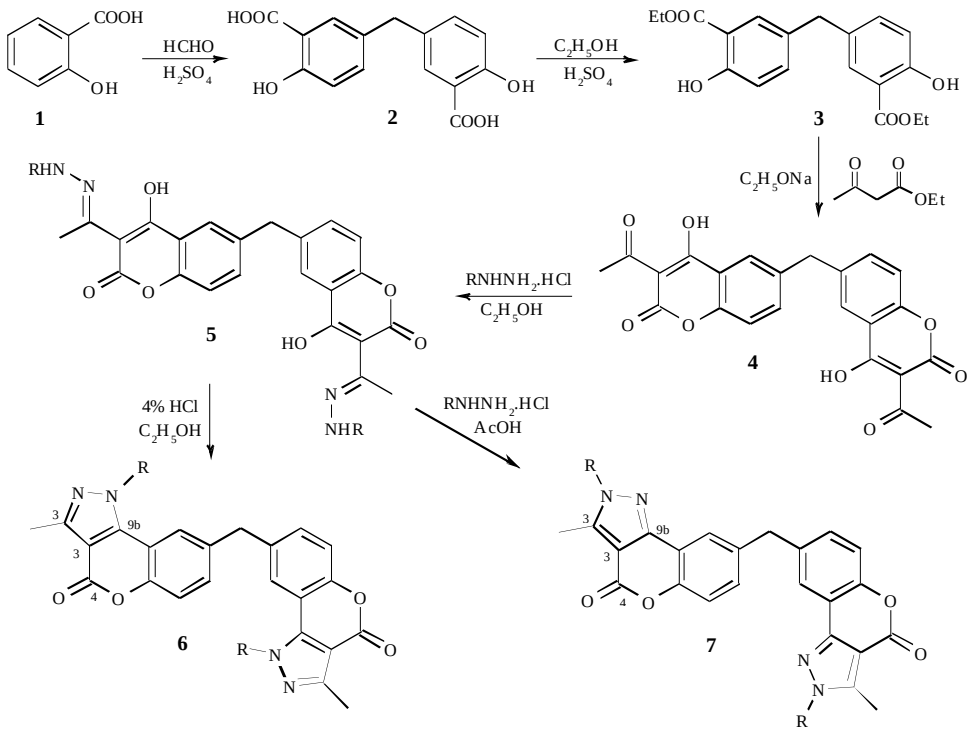
INTRODUCTION

Microwave assisted reactions have attracted much interest because of the simplicity of operation and mild reaction conditions. Salient features of the microwave approach are improved yields, enhanced reaction rates, formation of pure products in high yields and ease of isolation. Heterocyclic compounds have attracted considerable attention in the design of biologically active molecules [1-2]. Coumarins are a class of compounds with biological activity [3], such as analgesics [4], anti-coagulants [5], specific inhibitors of α-chymotripsin [6], human leukocyte elastase [7] and diuretics [8]. On the other hand, the classes of pyrazoles possess a broad spectrum of biological effectiveness such as antiviral [9], antibacterial [10], antidepressants [11], inhibitors of protein kinases [12], antiagregating [13], antiarthritic [14], and cerebroprotectors [15]. Recently some aryl pyrazoles [16] were reported to have non-nucleoside HIV-1 reverse transcriptase inhibitors [17], COX-2 inhibitors [18], potent activator of the nitric oxide receptor and soluble guanylate cyclase [19]. Besides, great interest in the pyrazole molecule has been stimulated by some promising pharmacological, agrochemical and analytical applications of its derivatives [20].

A detailed literature survey indicates that, synthesis of some thiochromeno[4,3-*c*] and [3,4-*c*]pyrazoles [21], pyrazolo-pyrazoles, isoxazolo-pyrazoles, pyrazolo-pyrimidines, pyrazolo-thiazines, pyrazolo-pyridines [22], pyrazolo[4,3-*c*]diazepines, pyrazolo[3,4-*d*]triazines, benz-oxaphosphino[4,3-*c*]pyrazoles [23] and monomeric benzopyrano[4,3-*c*]pyrazoles [24] have been reported. In view of these observations it was considered of interest to synthesize some new dimeric chemical entities incorpor-ating the two active pharmacophores namely coumarin and pyrazole in a single molecular frame work.

In this article, we wish to report a novel and rapid method for the synthesis of some new 8,8'-methylene-bis-(4-oxo-1*H*-chromeno[4,3-*c*]pyrazoles) **6** and 8,8'-methylene-bis-(4-oxo-2*H*-chromeno[4,3-*c*]pyrazoles) **7**, in good yields, from 6,6'-methylene-bis-(3-acetyl-4-hydroxycoumarin) **4** and a variety of hydrazines under microwave irradiation (Scheme 1).

Scheme 1



RESULTS AND DISCUSSION

The procedure involves esterification of 5,5'-methylene-bis-salicylic acid **2** with absolute ethyl alcohol in presence of an acid catalyst to afford ethyl ester of 5,5'-methylene-bis-salicyclic acid **3** in 82% of yield. Subsequently compound **3** reacted with ethyl acetoacetate in presence of sodium ethoxide to afford 6,6'-methylene-bis-(3-acetyl-4-hydroxycoumarin) **4**. In the first instance the compound **4** reacted with phenyl hydrazine hydrochloride to afford hydrazone **5** in excellent yields. Compound **5a**, under microwave irradiation in presence of 4% ethanolic hydrogen chloride, regioselectively was converted into the new 8,8'-methylene-bis-(3-methyl-1-phenylchromeno[4,3-*c*]pyrazol-4(1*H*)-one) **6a** in 84% yield while, in presence of phenyl hydrazinium chloride in acetic acid converted into the new 8,8'-methylene-bis-(3-methyl-2-phenyl chromeno[4,3-*c*]pyrazol-4(2*H*)-one) **7a** in 78% yield (Table 1). The molar ratio of the isomeric products **6** and **7** depends on the amount of nucleophilic reagent used. Thus in presence of one equivalent of hydrazine, compound **6** and two equivalents of hydrazines, compound **7** were formed [24g]. Further when compound **5** alone was irradiated in acetic acid, the methylene-bis-(hydroxybenzoylpyrazoles) [25] was formed instead of compound **7**. Under conventional heating the same reaction required 3-5 h and afforded low yields of desired products. The reaction rates and yields were dramatically enhanced by microwave irradiation. The rate enhancement under microwave irradiation can be attributed to the absorption of more microwave energy by the polar reactants, which generated sufficient heat energy to promote the reaction.

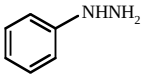
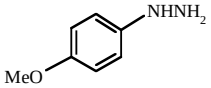
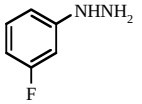
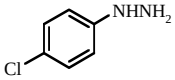
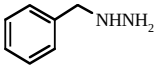
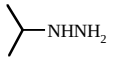
The scope and generality of the present method was then further demonstrated by converting compound **4** with different hydrazines followed by cyclization under different experimental conditions. The versatility of the reaction is well demonstrated by the fact that both aromatic (entries **a-d**, Table 1) and aliphatic (entries **e**-**g**, Table 1) hydrazines afforded their corresponding pyrazoles **6** and **7** in good yields.

The structures of all the new compounds were confirmed by IR, NMR and Mass spectral studies. The ^{13}C NMR spectra of (**6a, d**) and (**7a, d**) clearly demonstrated their structures, by comparison of the C-3, C-3a, C-9b, and CH_3 signals (Table 2). It is known that a carbon adjacent to a substituted nitrogen resonate up field of the signal of the same carbon in the other isomer (unsubstituted nitrogen). Additional support for the assignments was provided by the ^{1}H NMR spectra of each isomer.

In conclusion, we have described a rapid and efficient protocol for the regioselective synthesis of 8,8'-methylene-bis-4-oxo-1*H* and 2*H*-chromeno[4,3-*c*]-pyrazoles **6** and **7** by the reaction of 6,6'-methylene-bis-(3-acetyl-4-hydroxycoumarin) **4** and a variety of hydrazines using microwave irradiation. The present

Table 1

Synthesis of 8,8'-methylene-bis-4-oxo-1*H* and 2*H*-chromeno[4,3-c]pyrazoles **6**, **7** respectively

Entry	Hydrazine	Product[a], R=	Reaction time (min)		Yield (%)[b]	
			(6)	(7)	(6)	(7)
a		C_6H_5-	5 (5.5h)[c]	4 (3.5h)[c]	84	78
b		4-(MeO)-C_6H_4-	6 (5.5h)	4 (4.0h)	78	72
c		3-F-C_6H_4-	5 (6.0h)	3 (4.0h)	80	76
d		4-Cl-C_6H_4-	7 (5.5h)	5 (4.5h)	79	72
e		C_6H_5-CH_2-	6 (5.0h)	4 (4.0h)	78	71
f		Isopropyl	5 (5.5h)	4 (3.5h)	76	73
g	CH_3-$NHNH_2$	CH_3-	5 (5.0h)	3 (3.5h)	70	69

[a]Products were characterized by IR, NMR and Mass spectroscopy. [b]Yields refer to pure products after chromatography. [c]Time reported in parenthesis were under conventional heating.

method is a very useful process for the preparation of fused pyrazole derivatives. The reduced reaction times together with the minimization of thermal decomposition of the products are the main advantages of microwave heating.

Table 2

Selected ^{13}C NMR spectral data (δ ppm).

Comp	C-3	C-3a	C-4	C-9b	CH_3
6a	149.1	107.6	156.4	137.6	14.1
6d	149.3	107.4	156.6	137.9	14.1
7a	144.4	106.7	157.1	152.0	13.3
7d	144.7	105.9	158.2	151.2	13.2

EXPERIMENTAL

The melting points were determined using a Fischer-Johns apparatus and were uncorrected. ^1H NMR and ^{13}C NMR spectra were obtained on a Varian Gemini spectrometer at 300 MHz and 100 MHz respectively. Chemical shifts ware reported as δ ppm with respect to internal TMS, and J values are quoted in Hz. IR spectra were recorded on a Perkin-Elmer BX series spectro meter in KBr and only the most significant absorptions in cm^{-1} are indicated. Mass spectra were recorded on a VG-Micromass 7070H spectrometer. Satisfactory elemental analyses were obtained using a Perkin-Elmer CHN analyzer. For the microwave irradiation, a conventional house hold microwave oven was used. The compound **2** was prepared according to reported procedure [26]. All other reagents were purchased from Aldrich chemicals and were used without further purification. Crude products were purified by column chromatography on silica gel of 60-120 mesh.

Ethyl ester of 5,5'-methylene-bis-salicyclic acid (3). To the solution of **2** (1 mmol) in absolute ethyl alcohol (20 mL), concentrate sulfuric acid (1.5 mL) was added. The mixture was refluxed for 3 h. After completion of the reaction, the mixture was poured into the ice water. Crude product was collected by filtration, washed with 10% $NaHCO_3$ solution, dried and recrystallized from ethyl alcohol to give pure **3** (82%), mp 220-222 °C; ^1H NMR (DMSO-d_6): δ 10.2 (2H, s), 7.7-7.1 (6H, m), 4.3 (4H, q, J = 7.2 Hz), 4.00 (2H, s), 1.41 (6H, t, J = 7.2 Hz); ^{13}C NMR: δ 170.2, 141.1, 132.3, 121.1, 113.4, 62.7, 43.9, 16.0; IR (KBr): υ 3367, 1718, 1220 cm^{-1}; MS: m/z 344 (M^+). *Anal*. calcd. for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.26; H, 5.80.

6,6'-Methylene-bis-(3-acetyl-4-hydroxycoumarin) (4). To a stirred solution of **3** (1 mmol) in absolute ethyl alcohol (10 mL) and ethyl acetoacetate (2.5 mmol) was added sodium ethoxide (1.5 mmol). The mixture was refluxed at 110 °C with stirring for 3 h. After completion of the reaction, monitored by TLC (EtOAc: hexane, 1:3), the mixture was acidified with dilute HCl (10 mL). Crude product was filtered off, washed with water, dried and recrystallized from ethanol to give pure **4** (86%), mp 118-120 °C; ^1H NMR (DMSO-d_6): δ 12.3 (2H, s), 7.22-7.70 (6H, m), 4.00 (2H, s), 2.32 (6H, s); ^{13}C NMR: δ 184.2, 159.7, 149.8, 137.3, 121.9, 117.2, 101.2, 45.7, 22.0; IR (KBr): υ 3440, 1728, 1680, 1560, 1180 cm^{-1}; MS: m/z 420 (M^+). *Anal*. calcd. for $C_{23}H_{16}O_8$: C, 65.72; H, 3.84. Found: C, 65.70; H, 3.75.

Phenylhydrazone of 6,6'-methylene-bis-(3-acetyl-4-hydroxycoumarin) (5a). To a stirred solution of compound **4** (5 mmol) in ethyl alcohol (25 mL) was added the phenyl hydrazine hydrochloride (11 mmol) and the reaction mixture was refluxed for 1.5 h. After completion of the reaction (TLC), the mixture was cooled. The precipitated hydrazones was collected by filtration, washed with water, dried and recrystalized from ethyl alcohol to give pure **5a** (82%), mp 141-143 °C; ^{1}H NMR (DMSO-d_6): δ 11.28 (2H, s), 9.1 (2H, bs), 7.22-7.61 (6H, m), 7.00-7.16 (10H, m), 4.00 (2H, s), 2.16 (6H, s); IR (KBr): υ 3450-3354, 1719, 1590, 1470, 1171 cm^{-1}; MS: m/z 601 (M^+). *Anal*. calcd. for $C_{35}H_{28}N_4O_6$: C, 69.99; H, 4.70; N, 9.33. Found: C, 70.00; H, 4.61; N, 9.19. The other compounds **5b-g** were also prepared by the similar procedure.

General procedure for the preparation of 8,8'-methylene-bis-(4-oxo-1*H*-chromeno[4,3-*c*]pyrazoles) (6). To a solution of compound **5** (1 mmol) in ethyl alcohol (5 mL) was added 4% ethanolic hydrogen chloride (3 mL) and the reaction mixture, in a closed vessel was subjected to microwave irradiation using a conventional house hold microwave oven operated at 360 W for an appropriate time (Table 1). The reaction temperature was controlled using a pulsed irradiation technique (1 min with 20 sec intervals) and the temperature was measured after each pulse. The lowest observed temperature was ~70 °C after irradiation for 1 min at 320 W and the highest temperature was ~120 °C after irradiation for 3 min at the same power. After complete conversion of the reaction as indicated by TLC (EtOAc: hexane, 3:1), the mixture was quenched with water and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, evaporated and the crude product purified by column chromatography on silica gel to give the corresponding **6** in excellent yields (Table 1).

8,8'-Methylene-bis-(3-methyl-1-phenylchromeno[4,3-*c*]-pyrazol-4(1*H*)-one) (6a). This compound was obtained as brown solid, mp 202-203 °C; ^{1}H NMR (DMSO-d_6): δ 7.72-7.16 (16H, m), 4.0 (2H, s), 2.47 (6H, s); ^{13}C NMR: δ 156.4, 149.1, 137.6, 131.4, 128.9, 124.4, 118.9, 112.4, 107.6, 47.1, 14.1; IR (KBr): ν 3028, 1724, 1567, 1562 cm^{-1}; MS: m/z 564 (M^+). Anal. calcd. for $C_{35}H_{24}N_4O_4$: C, 74.46; H, 4.26; N, 9.92. Found: C, 74.35; H, 4. 20; N, 9.91.

8,8'-Methylene-bis-(1-(4-methoxyphenyl)-3-methylchromeno[4,3-*c*]pyrazol-4(1*H*)-one) (6b). This compound was obtained as gray solid, mp 216-218 °C; ^{1}H NMR (DMSO-d_6): δ 7.72-7.36 (6H, m), 7.42 (4H, d, J = 8.7 Hz), 7.10 (4H, d, J = 8.7 Hz), 4.0 (2H, s), 3.90 (6H, s), 2.47 (6H, s); ^{13}C NMR: δ 158.5, 149.9, 138.4, 131.4, 129.9, 124.3, 119.1, 113.9, 107.2, 54.3, 43.9, 14.2; IR (KBr): ν 3090, 1710, 1585, 1569, 1245 cm^{-1}; MS: m/z 624 (M^+). *Anal*. calcd. for $C_{37}H_{28}N_4O_6$: C, 71.14; H, 4.52; N, 8.97. Found: C, 71.13; H, 4.49; N, 8.94.

8,8'-Methylene-bis-(1-(3-fluorophenyl)-3-methylchromeno-[4,3-*c*]pyrazol-4(1*H*)-one) (6c). This compound was obtained as pink solid, mp 233-234 °C; ^{1}H NMR (DMSO-d_6): δ 7.8-6.63 (10H, m), 7.68 (2H, d, J = 6.2 Hz), 7.27 (2H, d, J = 6.2 Hz), 4.0 (2H, s), 2.47 (6H, s); ^{13}C NMR: δ 166.2, 154.5, 147.2, 138.9, 130.4, 120.3, 119.2, 111.9, 106.2, 44.54, 14.32; IR (KBr): ν 3080, 1715, 1569, 1584 cm^{-1}; MS: m/z 600 (M^+). *Anal*. calcd. for $C_{35}H_{22}F_2N_2O_4$: C, 70.00; H, 3.69; N, 9.33. Found: C, 69.99; H, 3.59; N, 9.32.

8,8'-Methylene-bis-(1-(4-chlorophenyl)-3-methylchromeno-[4,3-*c*]pyrazol-4(1*H*)-one) (6d). This compound was obtained as yellow solid, mp 209-211 °C; ^{1}H NMR (DMSO-d_6): δ 7.70-7.10 (6H, m), 7.62 (4H, d, J = 8.3 Hz), 7.54 (4H, d, J = 8.3 Hz), 4.0 (2H, s), 2.47 (6H, s); ^{13}C NMR: δ 156.6, 149.3, 137.9, 135.6, 131.4, 125.7, 117.9, 112.3, 107.4, 44.1, 14.1; IR (KBr): ν 3080, 1721, 1570, 1557, 1187 cm^{-1}; MS: m/z 632 (M^+). *Anal*. calcd. for $C_{35}H_{22}Cl_2N_4O_4$: C, 66.36; H, 3.50; Cl, 11.19. Found: C, 66.27; H, 3.34; Cl, 11.20.

8,8'-Methylene-bis-(1-benzyl-3-methylchromeno[4,3-*c*]pyrazol-4(1*H*)-one) (6e). This compound was obtained as pink solid, mp 217-218 °C; ^{1}H NMR (DMSO-d_6): δ 7.75-7.10 (6H, m), 7.52-7.15 (10H, m), 5.13 (4H, s), 4.0 (2H, s), 2.39 (6H, s); ^{13}C NMR: δ 158.7, 150.2, 139.7, 135.0, 131.2, 127.9, 120.4, 112.6, 102.1, 56.1, 43.1, 15.2; IR (KBr): υ 3080, 1714, 1585, 1560, 1180 cm^{-1}; MS: m/z 592 (M^+). *Anal*. calcd. for $C_{37}H_{28}N_4O_4$: C, 77.99; H, 4.76; N, 9.45. Found: C, 74.98; H, 4.73; N, 9.44.

8,8'-Methylene-bis-(1-isopropyl-3-methylchromeno[4,3-*c*]-pyrazol-4(1*H*)-one) (6f). This compound was obtained as yellow solid, mp 221-223 °C; ^{1}H NMR (DMSO-d_6): δ 7.42 (2H, m), 7.39 (2H, d, J = 6.8 Hz), 7.12 (2H, d, J = 6.8 Hz) 5.77 (2H, m), 4.0 (2H, s), 2.37 (6H, s), 1.52 (12H, d, J = 6.7 Hz); ^{13}C NMR: δ 159.1, 149.3, 138.3, 131.4, 118.1, 112.4, 101.9, 59.1, 44.4, 23.2, 15.7; IR (KBr): υ 3080, 2985, 1720, 1600, 1585, 1567, 1183 cm^{-1}; MS: m/z 496 (M^+). Anal. calcd. for $C_{29}H_{28}N_4O_4$: C, 70.15; H, 5.68; N, 11.28. Found: C, 70.14; H, 5.63; N, 11.26.

8,8'-Methylene-bis-(1,3-dimethylchromeno[4,3-*c*]pyrazol-4(1*H*)-one) (6g). This compound was obtained as yellow solid, mp 198-199 °C; ^{1}H NMR (DMSO-d_6): δ 7.33 (2H, m), 7.67 (2H, d, J = 6.8 Hz), 7.12 (2H, d, J = 6.8 Hz) 4.00 (2H, s), 3.90 (6H,s), 2.39 (6H, s); ^{13}C NMR: δ 158.3, 149.2, 138.7, 131.7, 118.6, 112.2, 102.6, 43.7, 37.1, 14.1; IR (KBr): υ 3078, 2985, 1710, 1595, 1180 cm^{-1}; MS: m/z 441 (M^+). *Anal*. calcd. for $C_{25}H_{20}N_4O_4$: C, 68.17; H, 4.58; N, 12.72. Found: C, 67.93; H, 4.43; N, 12.58.

General procedure for the synthesis of 8,8'-methylene-bis-(4-oxo-2*H*-chromeno[4,3-*c*]pyrazoles) (7). To a solution of compound **5** (1 mmol) in acetic acid (5 mL) was added the corresponding hydrazine hydrochloride (2 mmol) in acetic acid (5 mL) and the reaction mixture, in a closed vessel was subjected to microwave irradiation using a conventional house hold microwave oven operated at 360 W for an appropriate time (Table 1). The reaction temperature was controlled using a pulsed irradiation technique (1 min with 20 sec intervals) and the temperature was measured after each pulse. The lowest observed temperature was ~70 °C after irradiation for 1 min at 320 W and the highest temperature was ~120 °C after irradiation for 3 min at the same power. After completion of the reaction as indicated by TLC (EtOAc: benzene, 3:1), the mixture was quenched with water and extracted with dichloromethane, washed with 10% K_2CO_3 solution, brine, dried over Na_2SO_4, evaporated and the crude product chromatographed on silica gel resulted **7** in excellent yields (Table 1) and **6** (7-10% yields) as the minor products.

8,8'-Methylene-bis-(3-methyl-2-phenylchromeno[4,3-*c*]-pyrazol-4(2*H*)-one) (7a). This compound was obtained as brown solid, mp 211-212 °C; ^{1}H NMR (DMSO-d_6): δ 7.8-6.9 (6H, m), 7.26-7.52 (10H, s), 4.0 (2H, s), 2.69 (6H, s); ^{13}C NMR: δ 157.1, 152.0, 149.3, 144.4, 136.2, 131.2, 127.2, 120.1, 106.2, 40.8, 13.3; IR (KBr): ν 1732, 1590, 1600 cm^{-1}; MS: m/z 564 (M^+). *Anal*. calcd. for $C_{35}H_{24}N_4O_4$: C, 74.46; H, 4.28; N, 9.92. Found: C, 74.4; H, 4.22; N, 9.9.

8,8'-Methylene-bis-(2-(4-methoxyphenyl)-3-methylchromeno[4,3-*c*]pyrazol-4(2*H*)-one) (7b). This compound was obtained as brown solid, mp 221-223 °C; ^{1}H NMR (DMSO-d_6):

δ 7.72-7.36 (6H, m), 7.42 (4H, d, J = 8.3 Hz), 7.10 (4H, d, J = 8.3 Hz), 4.0 (2H, s), 3.9 (6H, s), 2.67 (6H, s); ^{13}C NMR: δ 158.5, 150.3, 144.3, 134.7, 131.4, 127.1, 120.9, 106.2, 55.3, 40.7, 13.1; IR (KBr): ν 1730, 1587, 1610 cm^{-1}; MS: m/z 624 (M$^+$). *Anal.* calcd. for. $C_{37}H_{28}N_4O_6$: C, 71.14; H, 4.52; N, 8.97. Found: C, 71.12; H, 4.40; N, 8.95.

8,8'-Methylene-bis-(2-(3-fluorophenyl)-3-methylchromeno-[4,3-*c*]pyrazol-4(2*H*)-one) (7c). This compound was obtained as brown solid, mp 202-204 °C; ^{1}H NMR (DMSO-d_6): δ 7.7-6.20 (10H, m), 7.67 (2H, d, J = 6.2 Hz), 7.12 (2H, d, J = 6.2 Hz), 4.0 (2H, s), 2.68 (6H, s); ^{13}C NMR: δ 168.1, 157.2, 152.0, 143.4, 132.7, 122.7, 112.1, 104.7, 40.7, 13.1; IR (KBr): ν 1728, 1591, 1602 cm^{-1}; MS: m/z 600 (M$^+$). *Anal.* calcd. for $C_{35}H_{22}F_2N_2O_4$: C, 70.00; H, 3.69; N, 9.33. Found: C, 69.9; H, 3.62; N, 9.30.

8,8'-Methylene-bis-(2-(4-chlorophenyl)-3-methylchromeno-[4,3-*c*]pyrazol-4(2*H*)-one) (7d). This compound was obtained as yellow solid, mp 227-228 °C; ^{1}H NMR (DMSO-d_6): δ 7.70-7.10 (6H, m), 7.52 (4H, d, J = 8.3 Hz), 7.60 (4H, d, J = 8.3 Hz), 4.0 (2H, s), 2.68 (6H, s); ^{13}C NMR: δ 158.1, 151.2, 144.7, 135.3, 130.2, 126.7, 120.5, 105.9, 42.3, 13.2; IR (KBr): ν 1727, 1586, 1601 cm^{-1}; MS: m/z 633 (M$^+$). *Anal.* calcd. for $C_{35}H_{22}Cl_2N_4O_4$: C, 66.36; H, 3.50; Cl, 11.19. Found: C, 66.31; H, 3.45; Cl, 11.19.

8,8'-Methylene-bis-(2-benzyl-3-methylchromeno[4,3-*c*]-pyrazol-4(2*H*)-one) (7e). This compound was obtained as brown solid, mp 197-200 °C; ^{1}H NMR (DMSO-d_6): δ 7.75-7.0 (16H, m), 5.31 (4H, s), 4.0 (2H, s), 2.57 (6H, s); ^{13}C NMR: δ 158.0, 150.9, 144.7, 133.2, 128.7, 120.3, 102.4, 55.2, 42.0, 13.1; IR (KBr): □ 1728, 1587, 1602 cm^{-1}; MS: m/z 592 (M$^+$). *Anal.* calcd. for $C_{37}H_{28}N_4O_4$: C, 74.99; H, 4.76; N, 9.45. Found: C, 74.9; H, 4.71; N, 9.43.

8,8'-Methylene-bis-(2-isopropyl-3-methylchromeno[4,3-*c*]-pyrazol-4(2*H*)-one) (7f). This compound was obtained as yellow solid, mp 212-213 °C; ^{1}H NMR (DMSO-d_6): δ 7.7-6.9 (6H, m), 5.70 (2H, m), 4.0 (2H, s), 2.52 (6H, s), 1.35 (12H, d, J = 6.7 Hz); ^{13}C NMR: δ 159.1, 150.7, 140.3, 131.7, 119.8, 101.7, 57.2, 41.9, 22.3, 13.1; IR (KBr): ν 1729, 1587, 1601 cm^{-1}; MS: m/z 496 (M$^+$). *Anal.* calcd. for $C_{29}H_{28}N_4O_4$: C, 70.15; H, 5.68; N, 11.28. Found: C, 70.12; H, 5.61; N, 11.27.

8,8'-Methylene-bis-(2,3-dimethylchromeno[4,3-*c*]pyrazol-4(2*H*)-one) (7g). This compound was obtained as yellow solid, mp 186-188 °C; ^{1}H NMR (DMSO-d_6): δ 7.76-6.92 (6H, m), 4.00 (2H, s), 3.71 (6H,s), 2.52 (6H, s); ^{13}C NMR: δ 158.2, 150.6, 142.1, 133.6, 119.4, 101.8, 41.9, 32.5, 11.2; IR (KBr): ν 3050, 2985, 1710, 1595, 1590, 1180 cm^{-1}; MS: m/z 441 (M$^+$). Anal. calcd. for $C_{25}H_{20}N_4O_4$: C, 68.17; H, 4.58; N, 12.72. Found: C, 67.99; H, 4.49; N, 12.62.

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