New Vilsmeier reaction for facile synthesis of 4-phenyl-2,4-dihydrochromeno[4,3-*c*]pyrazoles with bis(trichloromethyl) carbonate/DMF

Zhiwei Chen, Yanyan Yang and Weike Su*

Key Laboratory of Pharmaceutical Engineering of Ministry of Education, College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China

An efficient method for the synthesis of 4-phenyl-2,4- dihydrochromeno[4,3-*c*]pyrazoles via the cyclisation reaction of the easily available flavanone-4-arylhydrazones with Vilsmeier reagent (Bis(trichloromethyl) carbonate /DMF) has been developed.

Keywords: Vilsmeier reagent, pyrazoles, flavanone, cyclisation

Flavonoids are a class of plant secondary metabolites which exhibit a wide range of pharmacological activities,[1] including anti-inflammatory,[2] anti-viral[3] and anti-cancer[4] properties. The broad biological roles and versatile activities of the flavonoids have led to intensive research into their pharmacology and chemistry.[5,6] Moreover, experiments have shown that most of the flavonoids would display an enhanced biological activity after structural modification such as the introduction of heterocyclic rings.[7,8] For example, Hu and his group designed and synthesised a series of new flavonoids with a 1,2,3-thiadiazoline ring which exhibited *in vivo* inhibitory effect on tumor growth.[9]

The pyrazole ring is one of the basic fragments in medicinal chemistry.[10–13] We aimed to synthesise a mini library of novel flavonoids containing a pyrazole ring. Earlier reports from Kumar's group showed that dihydroquinolone hydrazones, after treatment with the Vilsmeier reagent (prepared from $POCl_3$ and DMF) formed 4,5-dihydropyrazolo-[4,3-*c*] quinolines in a reasonable yield. This led us to apply a similar method to the synthesis of 4-phenyl-2,4-dihydrochromeno [4,3-*c*]pyrazoles which have a structural similarity to Kumar's products.[14] However, the traditional Vilsmeier reagent employs toxic reagents such as $POCl_3$ which form phosphorus salts, that are harmful to human health and hazardous to the environment.[15] As part of our interest in developing the cyclisation potential of the Vilsmeier reagent[16] and reducing environmental pollution, we now report an efficient and green method for the preparation of 4-phenyl-2,4-dihydrochromeno[4,3-*c*] pyrazoles. In this reaction, *bis*-(trichloromethyl)carbonate (BTC) was employed as a mild, highly efficient and environmentally benign reagent for the preparation of the Vilsmeier reagent. 4-Phenyl-2,4-dihydrochromeno[4,3-*c*]pyrazoles were synthesised with the hope that they might have efficient antitumor activity and low toxicity through modification of ring C.

Most substituted flavanones **1**, which were prepared following Bu's procedure,[17] were treated with a substituted phenylhydrazine in ethanol at reflux to form a variety of flavanone-4-arylhydrazones. Unfortunately, flavanone-4-arylhydrazones with R^3 = *p*-MeO could not be prepared under these conditions. However this product could be obtained by stirring **1** and (4-methoxyphenyl)hydrazine in ethanol under the protection of N_2 at room temperature using acetic acid as catalyst. The flavanone-4-arylhydrazones **3** which were prepared were subsequently treated with the Vilsmeier reagent (BTC/DMF) under an atmosphere of N_2. A series of substituted 4-phenyl-2,4-dihydrochromeno[4,3-*c*]pyrazoles **4** were synthesised smoothly, as shown in Scheme 1.

To validate our protocol, initially, the reaction of compound **3a** with Vilsmeier reagent (BTC/DMF) was chosen as model reaction to investigate different conditions. Considerable effort was made to develop a suitable ratio of substrates and BTC/DMF using DMF as solvent. After screening a variety of ratios (Table 1), a ratio 1:2/3:2 ratio of **3a**/BTC/DMF was determined to be suitable. Solvents such as DMF, $ClCH_2CH_2Cl$, CH_2Cl_2, CH_3CN, and chlorobenzene (Table 1, entries 2, 6–9) were also tested. DMF was found to give maximum yield followed by chlorobenzene. Variations in the temperature of the reaction were also explored in DMF, and 60 °C was found to be sufficient to carry out the conversion.

The subsequent study was performed under the optimised conditions as described above. Most of the corresponding products, substituted 4-phenyl-2,4-dihydrochromeno[4,3-*c*] pyrazoles **4,** were obtained in moderate yields when R^3 = H, as show in Table 2. It was observed that the process clearly tolerated different substituents R^1, and R^2.

According to the experimental results, it was found that the reaction yields were affected strongly by different substituents R^3. When R^3 = Cl, a considerable decrease in yield (only 20% yield) took place while the temperature was kept at 60 °C for 4 h. Increasing the reaction temperature changed the yield evidently to 54–60% while the temperature was elevated to 75 °C for 6 hours (Table 2, entries 9–11). Furthermore, when R^3 = 4-MeO, Treatment of **3** with BTC/DMF at 60 °C for 4 h gave no product. The detection of the considerable amount of flavanones **1** in the reaction mixture (monitored by TLC) indicated that hydrolysis of hydrazones **3** had taken place due to their thermal instability at higher temperature. However, when this reaction was proceeded in 5–10 °C for 4 h, product 4 was obtained in satisfactory yields (Table 2, entries 12–15). As noticed, strong electron-donating groups in the arylhydrazines make the formation of corresponding products easier. It might be because a higher electron density of nitrogen atom (Ar-*N*H-) led to enhanced nucleophilicity to promote the cyclisation step.

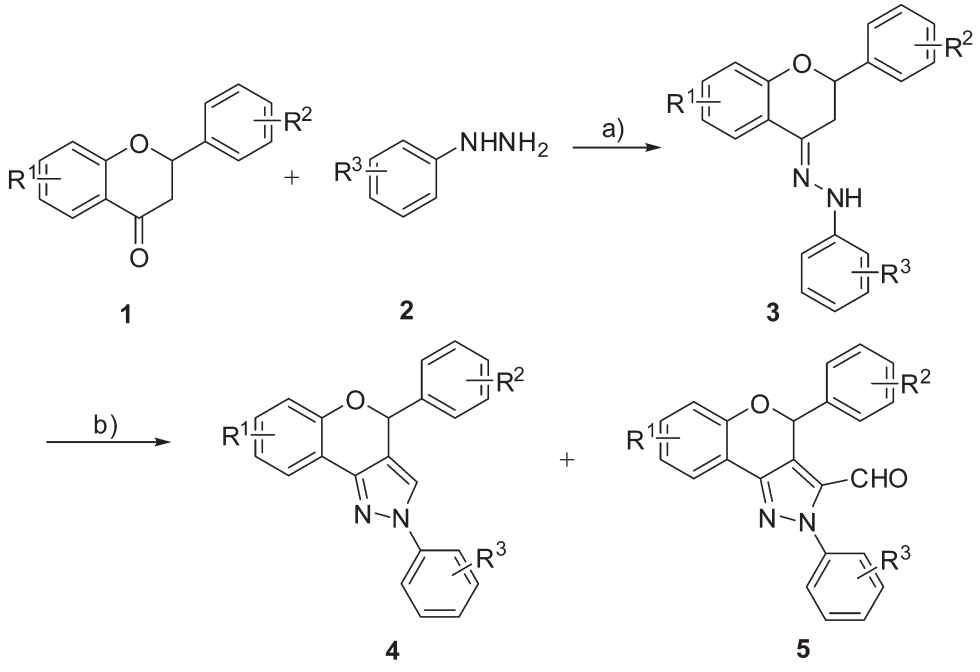
Bearing in mind the acylation activity of Vilsmeier reagents, the process might also give formylation products 5. Disappointingly, no corresponding products were observed even when a ratio 1:10/3:10 ratio of **3a**/BTC/DMF was used. This might be due to the steric hindrance of the groups on the pyrazole ring. A plausible mechanism for this cyclisation reaction is proposed in Scheme 2.

In conclusion, a mild and efficient method for the preparation of 2-substituted-4-phenyl-2,4-dihydrochromeno[4,3-*c*] pyrazoles starting from corresponding flavanones has been developed. The simplicity, easy work-up and adaptation to a wide range of substrates made it useful in the synthesis of flavonoid derivatives.

Experimental

Melting points were measured on a Büchi B-540 capillary melting point apparatus. The NMR spectra were measured with a Varian 400 (400 MHz) instrument using $CDCl_3$ as the solvent with TMS as

* Correspondent. E-mail: pharmlab@zjut.edu.cn



a) EtOH/HOAc; b) R^3=H, BTC/DMF, 4-5 h, 60°C, N_2;

R^3=OCH_3, BTC/DMF, 4-5 h, 5°C, N_2; R^3=Cl, BTC/DMF, 4-5 h, 75°C, N_2

Scheme 1

internal standard. IR spectra were recorded using KBr pellets on a Nicolet Aviatar-370 instrument. Mass spectra were measured with Thermo Finnigan LCQ-Advantage. High resolution mass spectral (HRMS) analysis was measured on an Agilent 6210 TOF LC/MS using APCI (electrospray ionisation) techniques.

*Preparation of 4-phenyl-2,4-dihydro -chromeno[4,3-c]pyrazoles (***4a***); general procedure*

DMF (2 mL) was placed in a 25 mL three-necked flask, and BTC (0.18 g, 0.6 mmol) was added in batch at 0 °C, then the mixture was stirred at room temperature for 30 min to form the Vilsmeier salt. The 1-phenyl-2-(2-phenylchroman-4-ylidene)hydrazine **3a** (0.9 mmol) was added. The mixture was stirred at room temperature for 30 minutes, and then on an oil bath kept at 60 °C for 4 h. After completion of the reaction, monitored by TLC (petroleum ether : ethyl acetate = 5:1), the mixture was diluted with ice water, neutralised with saturated $NaHCO_3$ solution and extracted with dichloromethane (10 mL× 3). The combined organic phases were washed with water, brine, dried over Na_2SO_4. The solvent was evaporated and the crude product was purified by on silica gel (petroleum ether: EtOAc = 20:1) to give **4a**.

2,4-diphenyl-2,4-dihydrochromeno[4,3-c]pyrazole (**4a**): White solid; m.p. 202–203 °C; IR (KBr): ν_{max} = 2915, 1600, 1505, 1228 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (dd, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.53–7.51 (m, 2H), 7.45–7.38 (m, 6H), 7.27–7.22 (m , 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.2, 144.9, 140.2, 140.1, 129.7, 129.4, 129.1 (CH×2), 128.7 (CH×2), 127.4 (CH×2), 126.4, 123.1, 122.7, 122.0, 119.0 (CH×2), 118.5, 117.8, 117.5, 76.2; MS (ESI): *m/z* = 325.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{22}H_{17}N_2O$: 325.1341. Found: 325.1355.

Table 1 Reaction of flavanone-4-arylhydrazones **3a** with DMF/BTC

Entry	**3a**:BTC:DMF	Solvent	Conditions	Yield /%[a]
1	1:1/3:1	DMF	60 °C, 4h	45
2	1:2/3:2	DMF	60 °C, 4h	62
3	1:1:3	DMF	60 °C, 4h	61
4	1:2/3:2	DMF	r.t., 4h	42
5	1:2/3:2	DMF	75 °C, 4h	60
6	1:2/3:2	$ClCH_2CH_2Cl$	60 °C, 6h	52
7	1:2/3:2	CH_2Cl_2	Reflux, 5h	51
8	1:2/3:2	Chlorobenzene	60 °C, 7h	54
9	1:2/3:2	CH_3CN	60 °C, 4h	48

[a] Isolated yields based on **3a**.

4-(3,4-dimethylphenyl)-2-phenyl-2,4-dihydrochromeno[4,3-c] pyrazole (**4b**): White solid; m.p. 204–206°C; IR (KBr): ν_{max}= 2921, 1600, 1503, 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.44–7.38 (m, 3H), 7.27–7.16 (m, 5H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.28 (s, 1H), 2.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 144.9, 139.9, 137.4, 137.3, 136.9, 129.8, 129.6, 129.2 (CH×2), 128.7, 126.2, 124.9, 123.1, 122.5, 121.7, 118.9 (CH×2), 118.6, 117.7, 117.4, 76.2, 20.0, 19.7; MS (EI): *m/z* (%) = 352 (M^+, 100). HRMS-EI: *m/z* (M^+) Calcd for $C_{24}H_{20}N_2O$: 352.1576. Found: 352.1588.

4-(4-methoxyphenyl)-2-phenyl-2,4-dihydrochromeno[4,3-c] pyrazole (**4c**): White solid; m.p. 197–198 °C; IR (KBr): ν_{max}= 2923, 1599, 1506, 1249 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.47–7.42 (m, 5H), 7.29–7.22 (m, 2H), 7.07–6.93 (m, 4H), 6.33 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 154.5, 145.5, 140.4, 132.6, 130.1, 129.7 (CH×2), 129.4 (CH×2), 126.7, 123.5, 123.0, 122.2, 119.3 (CH×2), 119.0, 118.1, 117.8, 114.4 (CH×2), 76.2, 55.7; MS (ESI): *m/z* = 355.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{23}H_{19}N_2O_2$: 355.1447. Found: 355.1459.

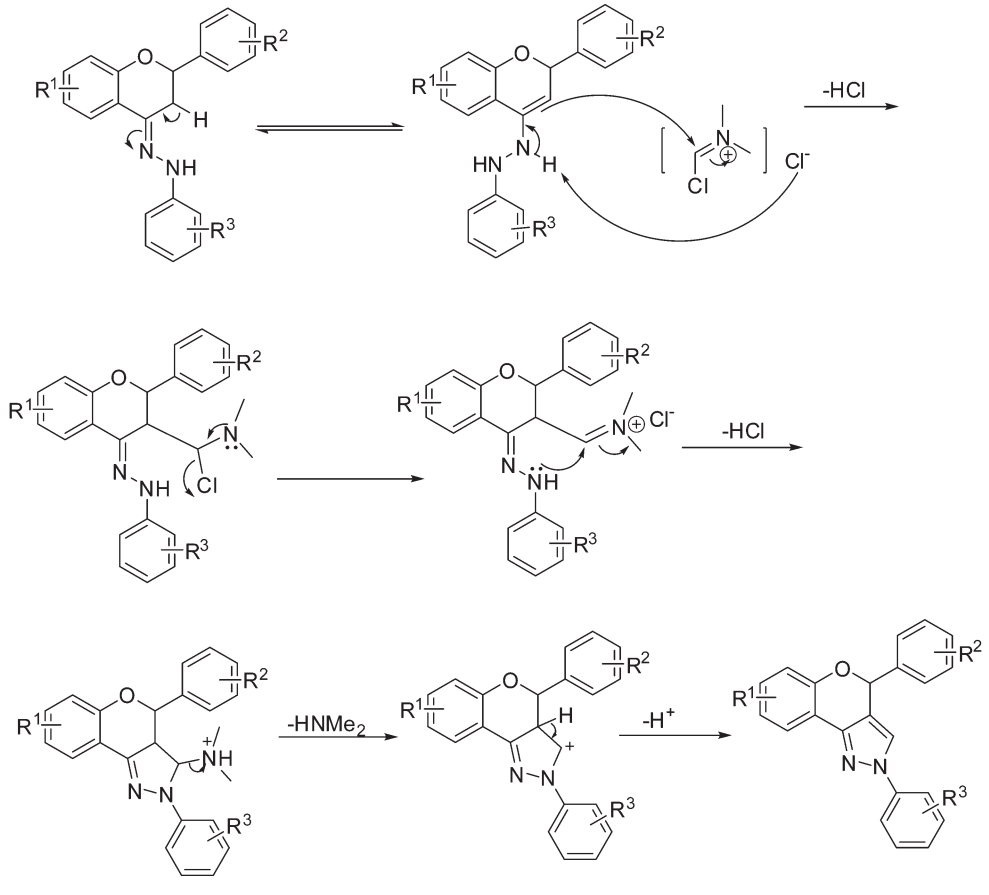
4-(4-chlorophenyl)-2-phenyl-2,4-dihydrochromeno[4,3-c]pyrazole (**4d**): white solid; m.p. 191–192 °C; IR (KBr): ν_{max} = 2919, 1600, 1505, 1228 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.46–7.37 (m, 7H), 7.30–7.23 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9, 144.9, 139.9, 138.7, 134.6, 129.9, 129.5 (CH×2), 128.9 (CH×2), 128.8 (CH×2), 126.6, 123.1, 122.7, 122.2, 119.1, 118.0 (CH×2), 117.7, 117.5, 75.4; MS (ESI): *m/z* (%) = 359.2 (M^++1, 100), 361.2 (M^++3, 30). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{22}H_{16}ClN_2O$: 359.0951. Found: 359.0935.

7-methyl-2,4-diphenyl-2,4-dihydrochromeno[4,3-c]pyrazole(**4e**): White solid; m.p. 188–189 °C; IR (KBr): ν_{max} = 2919, 1597, 1504,

Table 2 preparation of 4-phenyl-2,4-dihydrochromeno[4,3-*c*]pyrazoles

Entry	R^1	R^2	R^3	Product	Conditions[a]	Yield /%[b]
1	H	H	H	**4a**	60 °C,4 h	62
2	H	3,4-$(CH_3)_2$	H	**4b**	60 °C,4 h	65
3	H	4-OCH_3	H	**4c**	60 °C,4 h	63
4	H	4-Cl	H	**4d**	60 °C,4 h	60
5	5-CH_3	H	H	**4e**	60 °C,4 h	64
6	5-CH_3	4-Cl	H	**4f**	60 °C,4 h	61
7	5-CH_3	3,4-$(OCH_3)_2$	H	**4g**	60 °C,4 h	62
8	5-CH_3	4-OCH_3	H	**4h**	60 °C,4 h	65
9	H	3,4-$(CH_3)_2$	4-Cl	**4i**	75 °C,6 h	60
10	5-CH_3	4-OCH_3	4-Cl	**4j**	75 °C,6 h	56
11	H	4-Cl	4-Cl	**4k**	75 °C,6 h	54
12	H	3,4-$(CH_3)_2$	4-OCH_3	**4l**	5 °C,2 h	64
13	H	4-OCH_3	4-OCH_3	**4m**	5 °C,2 h	62
14	5-CH_3	4-OCH_3	4-OCH_3	**4n**	5 °C,2 h	62
15	5-CH_3	3,4-$(CH_3)_2$	4-OCH_3	**4o**	5 °C,2 h	58

[a] Monitored by TLC, reaction ceased when **3** was fully consumed.
[b] Isolated yield by column chromatography.



Scheme 2

1245 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.0 Hz , 2H), 7.52 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2H), 7.46–7.40 (m, 6H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.84 (s, 1H), 6.36 (s, 1H), 2.34 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 145.1, 140.2, 140.1, 129.4 (CH×2), 128.7 (CH×2), 127.4 (CH×2), 126.4, 123.1, 122.9, 122.5, 119.0, 118.2 (CH×2), 117.9, 114.9, 76.2, 21.60. MS (ESI): *m/z* = 339.4 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{23}H_{19}N_2O$: 339.1497. Found: 339.1507.

4-(4-chlorophenyl)-7-methyl-2-phenyl-2,4-dihydrochromeno[4,3-c] pyrazole(**4f**): White solid; m.p. 180–181 °C; IR (KBr): ν_{max} = 2905, 1598, 1504 , 1243 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.46–7.37 (m, 7H), 7.28 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 6.33 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 145.1, 140.3, 140.0, 138.9, 134.6, 129.4 (CH×2), 128.9 (CH×2), 128.8 (CH×2), 126.5, 123.1, 123.0, 122.5, 119.0 (CH×2), 117.9, 117.7, 114.9, 75.4, 21.6; MS (ESI): *m/z* (%) = 373.3 (M^++1, 100), 375.2 (M^++3, 33). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{23}H_{18}ClN_2O$: 373.1108. Found: 373.1093.

4-(3,4-dimethoxyphenyl)-8-methyl-2-phenyl-2,4-dihydrochromeno [4,3-c]pyrazole(**4g**): White solid; m.p. 193–194 °C; IR (KBr): ν_{max} = 2941, 1639, 1598, 1511, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.45–7.41 (m, 3H), 7.28–7.25 (m, 1H), 7.08–7.03 (m, 3H), 6.90 (dd, J_1 = 8.0 Hz, J_2 = 11.6 Hz, 2H), 6.25 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.1, 149.5, 149.2, 145.4, 140.0, 132.5, 131.4, 130.4, 129.4 (CH×2), 126.4, 123.2, 122.9, 122.4, 120.2, 118.9 (CH×2), 117.5, 117.2, 110.8, 110.6, 76.2, 55.9 (CH×2), 20.7; MS (ESI): *m/z* = 399.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{25}H_{23}N_2O_3$: 399.1709. Found: 399.1720.

4-(4-methoxyphenyl)-7-methyl-2-phenyl-2,4-dihydrochromeno[4,3-c]pyrazole(**4h**): White solid; m.p. 176–177 °C; IR (KBr): ν_{max} = 2915, 1623, 1598, 1502, 1256 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.47 (s, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.28–7.24 (m, 1H), 7.10–7.07 (m, 2H), 6.93–6.85 (m, 3H), 6.32 (s, 1H), 3.81 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 154.1, 145.1, 141.9, 140.2, 140.1, 129.7, 129.4 (CH×2), 126.3, 123.1, 122.9, 122.5, 119.6, 119.0, 118.2 (CH×2), 118.0, 115.0, 114.3, 112.8, 76.1, 55.3, 21.6; MS (ESI): *m/z* = 369.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{24}H_{21}N_2O_2$: 369.1603. Found: 369.1611.

2-(4-chlorophenyl)-4-(3,4-dimethylphenyl)-2,4-dihydrochromeno[4,3-c]pyrazole(**4i**)**:** White solid; m.p. 205–207 °C; IR (KBr): ν_{max} = 2919, 1614, 1595, 1498, 1261 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ = 7.99 (d, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.50–7.46 (m, 3H), 7.37–7.27 (m, 4H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.36 (s, 1H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 145.4, 138.6, 137.5, 137.4, 137.1, 131.7, 130.0 (CH×2), 129.5 (CH×2), 128.8, 125.0, 123.1, 122.7, 121.9, 120.0 (CH×2), 119.1, 117.6, 117.5, 76.2, 19.9, 19.6; MS (ESI): *m/z* (%) = 387.4 (M^++1, 60), 385.4 (M^+-1, 100). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{24}H_{20}ClN_2O$: 387.1264. Found: 387.1249.

2-(4-chlorophenyl)-4-(4-methoxyphenyl)-8-methyl-2,4-dihydrochromeno[4,3-c]pyrazole(**4j**): White solid; m.p. 202–203 °C; IR (KBr): ν_{max} = 2905, 1612, 1597, 1498, 1249 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ = 7.73 (s, 1H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.45–7.38 (m, 5H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.25 (s, 1H), 3.83 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 152.1, 145.7, 138.6, 132.1, 131.7, 131.3, 130.6, 129.4 (CH×2), 129.0 (CH×2), 123.0, 122.9, 119.9 (CH×2), 119.3, 117.3, 117.2, 114.1 (CH×2), 75.7, 55.3, 20.7; MS (ESI): *m/z* (%) = 403.3 (M^++1, 100), 405.3 (M^++3, 33), 401.3 (M^+-1, 70). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{24}H_{20}ClN_2O_2$: 403.1213. Found: 403.1193.

2,4-bis(4-chlorophenyl)-2,4-dihydrochromeno[4,3-c]pyrazole(**4k**)**:** White solid; m.p. 201–203 °C; IR (KBr): ν_{max} = 2912, 1617, 1596, 1498, 1253 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.46–7.38 (m, 7H), 7.28–7.24 (m, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9, 145.1, 138.5, 138.4, 134.7, 131.9, 130.1, 129.5 (CH×2), 129.0 (CH×2), 128.8 (CH×2), 122.9, 122.7, 122.2, 120.0 (CH×2), 118.4, 117.5, 117.4, 75.3; MS (ESI): *m/z* (%) = 393.4 (M^++1, 48), 359.1 (M^++2-Cl, 100). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{22}H_{15}Cl_2N_2O$: 393.0561. Found: 393.0571.

4-(3,4-dimethylphenyl)-2-(4-methoxyphenyl)-2,4-dihydrochromeno[4,3-c]pyrazole(**4l**): White solid; m.p. 203–205 °C; IR (KBr): ν_{max} = 2914, 1614, 1511, 1249 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.37–6.89 (s, 10H), 5.13 (d, *J* = 10.8 Hz, 1H), 3.81 (s, 3H), 2.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 158.4, 158.1, 155.7, 137.1, 136.9, 136.4, 133.4, 129.8 (CH×2), 127.5, 126.9, 126.2, 123.8 (CH×2), 122.4, 121.2, 118.4, 117.7, 114.5 (CH×2), 77.7, 55.6, 20.0, 19.7; MS (EI): *m/z* (%) = 382 (M^+, 40), 133 (100). HRMS-EI: *m/z* (M^+) Calcd for $C_{25}H_{22}N_2O_2$: 382.1681. Found: 382.1669.

2,4-bis(4-methoxyphenyl)-2,4-dihydrochromeno[4,3-c]pyrazole(**4m**): White solid; m.p. 206–208 °C; IR (KBr): ν_{max} = 2962, 1613, 1517, 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.37 (s, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.99–6.93 (m, 5H), 6.32 (s, 1H), 3.84 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 158.3, 154.2, 144.8, 133.9, 132.5, 129.7, 129.2 (CH×2), 123.4, 122.6, 122.0, 120.8 (CH×2), 118.3, 118.1, 117.6, 114.6 (CH×2), 114.2 (CH×2), 76.1, 55.7, 55.4; MS (ESI): *m/z* = 385.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{24}H_{21}N_2O_3$: 385.1552. Found: 385.1548.

2,4-bis(4-methoxyphenyl)-8-methyl-2,4-dihydrochromeno[4,3-c]pyrazole (**4n**)**:** White solid; m.p. 212–213 °C; IR (KBr): ν_{max} = 2950, 1612, 1515, 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (s, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.36 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.96-6.92 (m, 4H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.27 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H) , 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 158.2, 152.0, 144.9, 133.8, 132.4, 131.2, 130.2, 129.0 (CH× 2), 123.3, 122.8, 120.8 (CH×2), 118.4, 117.5, 117.2, 114.5 (CH×2), 114. 0 (CH×2), 75.8, 55.6, 55.3, 20.7; MS (ESI): *m/z* = 399.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{25}H_{23}N_2O_3$: 399.1709. Found: 399.1700.

4-(3,4-dimethylphenyl)-2-(4-methoxyphenyl)-8-methyl-2,4-dihydrochromeno[4,3-c]pyrazole(**4o**): White solid; m.p. 213–215 °C; IR (KBr): ν_{max} = 2915, 1593, 1515, 1243 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.36 (s, 1H), 7.30–7.23 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.26 (s, 1H), 3.84 (s, 3H), 2.35 (s, 3H), 2.28(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 152.0, 137.7, 137.3, 137.0, 133.9, 131.2, 130.2, 129.9, 128.8, 125.0, 123.3, 122.7, 120.7 (CH×2), 118.4, 117.5, 117.2 (CH×2), 114.4 (CH×2), 76.1, 55.6, 20.7, 19.9, 19.6; MS (ESI): *m/z* = 397.3 (M^++1). HRMS-ESI: *m/z* (M^++1) Calcd for $C_{26}H_{25}N_2O_2$: 397.1916. Found: 397.1897.

1-Phenyl-2-(2-phenylchroman-4-ylidene)hydrazine(**3a**): ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.41 (s, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.44–7.34 (m, 3H), 7.25–7.17 (m, 5H), 7.00 (t, *J* = 8.0, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 6.8 Hz, 1H), 5.19 (dd, J_1 = 2.8 Hz, J_2 = 12.0 Hz, 1H), 3.38–3.32 (m, 1H), 2.70 (dd, J_1 = 12.0 Hz, J_2 = 16.8 Hz, 1H); ^{13}C NMR(100 MHz, DMSO-d_6) δ = 155.3, 145.5, 140.2, 135.0, 134.7, 128.7 (CH×2), 128.3 (CH×2), 128.0, 126.3 (CH×2), 123.3, 121.6, 121.3, 118.8, 117.2, 112.4 (CH×2), 76.4, 32.3.

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