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## AN EFFICIENT SYNTHESIS OF FUNCTIONALIZED CHROMENO[4,3-*d*]PYRAZOLO[3,4-*b*]PYRIDINE DERIVATIVES

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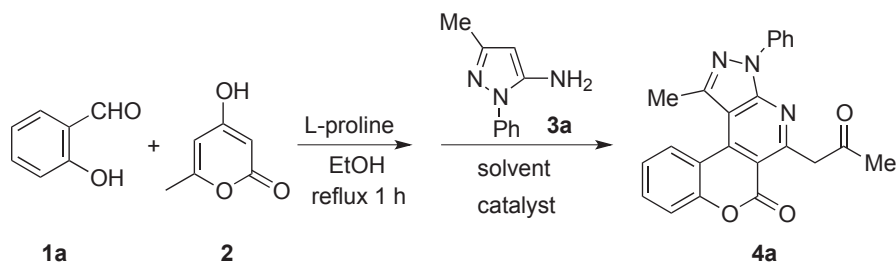
**Abstract** — A series of functionalized chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridine derivatives were synthesized via one-pot three-component reaction of salicylaldehydes, 4-hydroxy-6-methyl-2*H*-pyran-2-one and pyrazol-5-amines catalyzed by L-proline and CuSO<sub>4</sub> in ethanol. The structures of all synthesized were identified by their IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS analyses, and the structure of compound **4h** was confirmed by X-ray diffraction analysis.

Nitrogen-containing heterocyclic compounds are ubiquitous system in natural products and are considered as privileged structures in drug discovery.<sup>1</sup> Among the various heteroaromatic compounds, coumarin is one of important heterocyclic compound found in many plants. Compounds bearing the coumarin moiety exhibit antitumor,<sup>2</sup> anti-inflammatory,<sup>3</sup> anti-coagulant,<sup>4</sup> and anti-oxidant<sup>5</sup> activities. Some coumarin derivatives have a high fluorescent quantum yield<sup>6</sup> and have been widely used as laser dyes, fluorescent probes, solar energy collector, and nonlinear optical dyes.<sup>7</sup> Meanwhile, some heteroaryl-condensed coumarin derivatives have been to attract interest because of their broad spectrum of useful biological activities and fluorescent properties.<sup>8</sup> Diverse synthetic methodologies available for the construction of coumarin derivatives have been developed, including Pechmann reaction,<sup>9</sup> Knoevenagel condensation,<sup>10</sup> Wittig reaction,<sup>11</sup> C-H activating methods,<sup>12</sup> and multi-component reactions.<sup>13</sup> However, to the best of our knowledge, only a few literatures<sup>14</sup> reported the preparation of chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridine derivatives. As a part of our research on the synthesis of novel functionalized coumarin derivatives,<sup>15</sup> herein, we reported the efficient synthesis of novel functionalized chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridine derivatives.

At first the reaction conditions were examined. According to our previously reported synthetic procedure of 3-(1-hydroxy-3-oxobut-1-en-1-yl)-2*H*-chromen-2-one from the reaction of salicylaldehydes with

4-hydroxy-6-methyl-2*H*-pyran-2-one,<sup>16</sup> salicylaldehydes (**1a**) was treated with 4-hydroxy-6-methyl-2*H*-pyran-2-one (**2**) in ethanol catalyzed by L-proline (10 mol%) for 1 h to give the desired 3-(1-hydroxy-3-oxobut-1-en-1-yl)-2*H*-chromen-2-one. Then 3-methyl-1-phenyl-pyrazol-5-amine (**3a**) was added and the mixture was stirred at different conditions to optimize the reaction conditions. The results are summarized in Table 1. In the absence of catalyst, the desired product **4a** was only obtained in 12% yield (Table 1, entry 1). To improve the yield, several catalysts were evaluated, i.e. *p*-TSA, piperidine, CuSO<sub>4</sub>·5H<sub>2</sub>O, CuSO<sub>4</sub>, CuSO<sub>4</sub>·2H<sub>2</sub>O, Cu(OAc)<sub>2</sub>·H<sub>2</sub>O and CuI (Table 1, entries 2-8). The results showed that the best catalyst was CuSO<sub>4</sub>. Subsequently, we further evaluated the effect of solvents. Of all the solvents tested, i.e. ethanol, acetonitrile, DMF, toluene, acetic acid, and THF, ethanol gave the best result (Table 1, entries 5 and 9-13). To optimize the catalyst loading, 5, 10, 15, 20, and 25 mol% of

**Table 1.** Optimization of the reaction conditions for the synthesis of compound **4a**



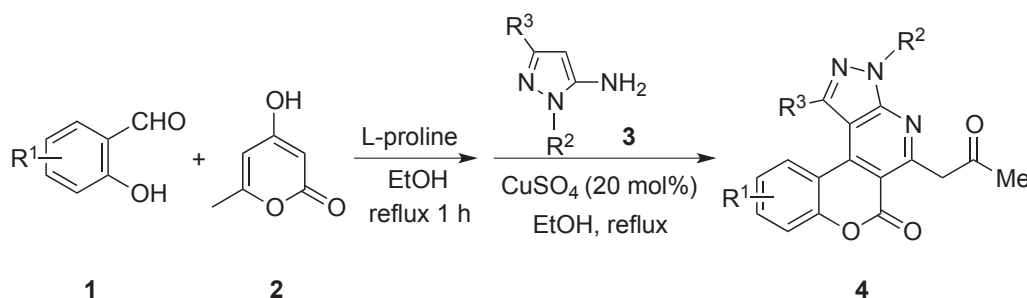
Entry	Catalyst (mol%)	Solvent	Temperature (°C)	Time (h)	Yield <sup>a</sup> (%)
1	no	EtOH	reflux	24	12
2	<i>p</i> -TSA (10)	EtOH	reflux	24	15
3	piperidine (10)	EtOH	reflux	6	trace
4	CuSO <sub>4</sub> ·5H <sub>2</sub> O (10)	EtOH	reflux	6	66
5	CuSO <sub>4</sub> (10)	EtOH	reflux	6	70
6	CuSO <sub>4</sub> ·2H <sub>2</sub> O (10)	EtOH	reflux	6	55
7	Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O (10)	EtOH	reflux	24	10
8	CuI (10)	EtOH	reflux	24	13
9	CuSO <sub>4</sub> (10)	MeCN	reflux	10	53
10	CuSO <sub>4</sub> (10)	DMF	120	4	51
11	CuSO <sub>4</sub> (10)	toluene	110	14	47
12	CuSO <sub>4</sub> (10)	AcOH	110	6	62
13	CuSO <sub>4</sub> (10)	THF	reflux	16	36
14	CuSO <sub>4</sub> (5)	EtOH	reflux	9	65
15	CuSO <sub>4</sub> (15)	EtOH	reflux	6	71
16	CuSO <sub>4</sub> (20)	EtOH	reflux	5	76
17	CuSO <sub>4</sub> (25)	EtOH	reflux	5	74
18	CuSO <sub>4</sub> (20)	EtOH	20	12	43
19	CuSO <sub>4</sub> (20)	EtOH	40	12	56
20	CuSO <sub>4</sub> (20)	EtOH	60	8	62

<sup>a</sup>Yield was determined by HPLC-MS

CuSO<sub>4</sub> was tested (Table 1, entries 5 and 14-17). A 20 mol% loading of CuSO<sub>4</sub> was sufficient to promote the reaction. The reaction was then conducted at different temperature, such as: 20, 40, 60 °C, and refluxing temperature, to determine the optimum temperature for this transformation. All these experiments were conducted in ethanol catalyzed by CuSO<sub>4</sub> (20 mol%) (Table 1, entries 5 and 18-20). So the best temperature for this transformation was at refluxing temperature. Based on all these experiments, the optimum reaction conditions were identified as using ethanol as solvent and 20 mol% CuSO<sub>4</sub> as the catalyst at refluxing temperature for several hours.

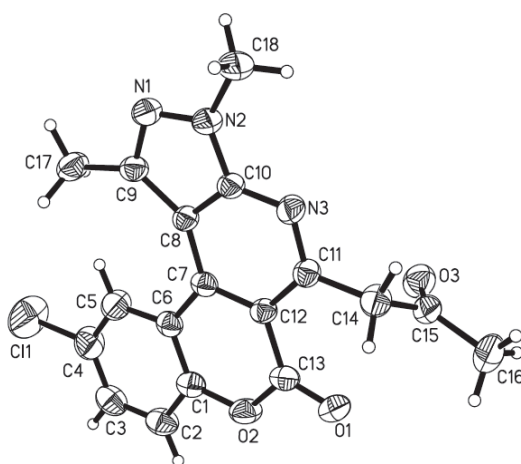
The optimized reaction conditions were then tested for library construction with substituted salicylaldehydes and pyrazol-5-amines. The results are summarized in Table 2. It was found that there were no remarkable effect of the electronic effect of the substituted groups of salicylaldehydes and pyrazol-5-amines to the yields.

**Table 2.** The Synthesis of functionalized chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridine derivatives **4**



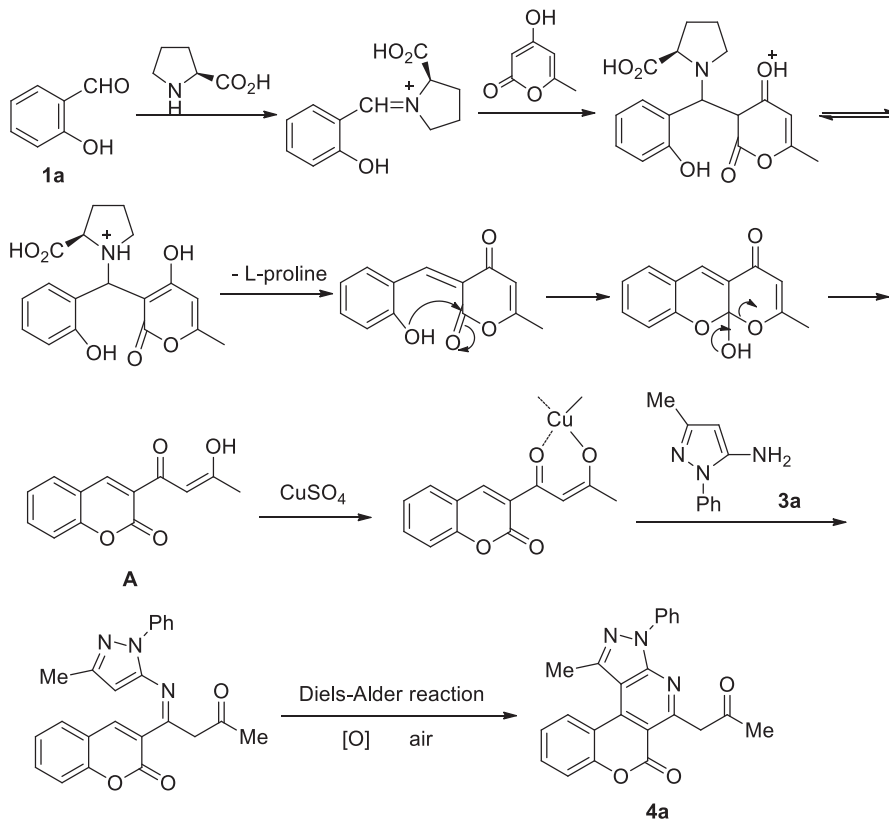
Entry	Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Time (h)	Yield (%)
1	<b>4a</b>	H	Ph	Me	5	78
2	<b>4b</b>	5-Cl	Ph	Me	6	62
3	<b>4c</b>	3-MeO	Ph	Me	20	55
4	<b>4d</b>	4-MeO	Ph	Me	18	56
5	<b>4e</b>	5-Cl	Ph	Ph	20	46
6	<b>4f</b>	3-MeO	Ph	Ph	24	45
7	<b>4g</b>	4-MeO	Ph	Ph	24	45
8	<b>4h</b>	5-Cl	Me	Me	6	57
9	<b>4i</b>	H	Me	Ph	14	71
10	<b>4j</b>	5-Br	Me	Ph	17	68
11	<b>4k</b>	5-MeO	Me	Ph	15	61
12	<b>4l</b>	3,5-Cl <sub>2</sub>	Me	Ph	10	59

The structures of all the products were identified by their IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS spectra. The structure of compound **4h** was further confirmed by X-ray diffraction analysis. The molecular structure of the product **4h** is shown in Figure 1.



**Figure 1.** The crystal structure of compound **4h**

Based on the references,<sup>14b,16</sup> the proposed mechanism for the synthesis of compound **4a** is shown in Scheme 1. The intermediate **A** was formed by the condensation reactions of salicylaldehyde (**1a**) with 4-hydroxy-6-methyl-2*H*-pyran-2-one (**2**) catalyzed by L-proline. The intermediate **A** then reacted with 3-methyl-1-phenylpyrazol-5-amine (**3a**) to form imine catalyzed by CuSO<sub>4</sub>. The desired product **4a** was obtained by the Diels-Alder and oxidation in air from the imine.



**Scheme 1.** The proposed mechanism for one-pot domino reaction

In conclusion, we have developed a facile and efficient protocol for the construction of functionalized chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridine derivatives via a novel one-pot three-component reaction of salicylaldehydes, 4-hydroxy-6-methyl-2*H*-pyran-2-one and pyrazol-5-amines catalyzed by CuSO<sub>4</sub> in ethanol. This protocol has the advantages of mild reaction conditions, easily accessible starting materials, and wide range of substrates, which makes it a useful and attractive method for the synthesis of the complex chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridines in synthetic and medicinal chemistry. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

## EXPERIMENTAL

IR spectra were recorded on a Varian F-1000 spectrometer in KBr with absorptions in cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz or 300 MHz) and <sup>13</sup>C NMR (100 MHz or 75 MHz) spectra were recorded on a Varian Inova-300 MHz and Varian Inova-400 MHz in CDCl<sub>3</sub> solution. *J* values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard TMS. High-resolution mass spectra (HRMS) for all the compounds were determined on Bruker MicrOTOF-QII mass spectrometer with ESI resource. X-Ray diffraction analysis was recorded on a Rigaku Mercury CCD/AFC diffractometer.

**Starting Materials.** All chemicals used in this study were commercially available.

**Typical experimental procedure for the synthesis of chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridine derivatives 4.** A mixture of salicylaldehydes **1** (1 mmol), 4-hydroxy-6-methyl-2*H*-pyran-2-one **2** (1 mmol) and L-proline (0.10 mmol) in EtOH (10 mL) was stirred at 80 °C for 1 h. Then pyrazol-5-amines **3** (1 mmol) and CuSO<sub>4</sub> (0.20 mmol) was added to the reactor and stirred at 80 °C for 4-48 h. After completion of the reaction confirmed by TLC (eluent acetone/petroleum ether (PE), V/V = 1:3), the reaction mixture was concentrated in vacuo to remove the solvent. The product purified by column chromatography (PE-acetone = 5:1) to afford the pure product **4**.

**1-Methyl-5-(2-oxopropyl)-3-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one 4a:** white solid; mp 203-205 °C. IR (KBr) 2960, 1726, 1594, 1547, 1507, 1443, 1248, 772 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DCl<sub>3</sub>) δ 8.31 (d, *J* = 7.6 Hz, 1H, ArH), 8.19 (d, *J* = 6.8 Hz, 2H, ArH), 7.63 (t, *J* = 6.8 Hz, 1H, ArH), 7.53 (t, *J* = 6.8 Hz, 2H, ArH), 7.42-7.35 (m, 3H, ArH), 4.62 (s, 2H, CH<sub>2</sub>), 2.93 (s, 3H, CH<sub>3</sub>), 2.43 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.1, 160.3, 159.3, 152.6, 151.6, 143.0, 142.6, 138.5, 133.0, 129.4, 129.2, 127.0, 124.0, 122.3, 117.6, 116.7, 110.8, 109.7, 54.9, 30.6, 19.3; HRMS Calculated for C<sub>23</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>Na: [M+Na]<sup>+</sup> 406.1168, found: 406.1169.

**10-Chloro-1-methyl-5-(2-oxopropyl)-3-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one 4b:** white solid; mp 235-238 °C; IR (KBr) 2959, 1734, 1608, 1278, 1180, 1021, 829, 753, 689 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.37 (s, 1H, ArH), 8.18 (d, *J* = 8.0 Hz, 2H, ArH), 7.61-7.52 (m, 3H, ArH), 7.38 (d, *J*

= 8.0 Hz, 2H, ArH), 4.63 (s, 2H, CH<sub>2</sub>), 2.98 (s, 3H, CH<sub>3</sub>), 2.43 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 205.0, 159.9, 159.4, 151.7, 151.0, 142.8, 141.4, 138.5, 132.8, 129.6, 129.3, 128.9, 127.2, 122.6, 119.0, 118.0, 110.9, 109.5, 54.9, 30.6, 19.5; HRMS Calculated for C<sub>23</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>3</sub>: [M]<sup>+</sup> 417.0880, found: 417.0877.

**8-Methoxy-1-methyl-5-(2-oxopropyl)-3-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one**

**4c** : white solid; mp 247-249 °C; IR (KBr) 2936, 1739, 1545, 1506, 1181, 1024, 968, 833, 789, 681 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.19 (d, *J* = 8.0 Hz, 2H, ArH), 7.87 (d, *J* = 8.0 Hz, 1H, ArH), 7.53 (t, *J* = 8.0 Hz, 2H, ArH), 7.36 (t, *J* = 7.6 Hz, 2H, ArH), 7.20 (d, *J* = 6.8 Hz, 1H, ArH), 4.63 (s, 2H, CH<sub>2</sub>), 4.01 (s, 3H, CH<sub>3</sub>O), 2.93 (s, 3H, CH<sub>3</sub>), 2.43 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.2, 159.4, 157.2, 148.0, 145.8, 143.4, 138.6, 129.2, 127.0, 125.0, 123.7, 122.5, 120.8, 117.5, 114.7, 110.0, 108.1, 101.9, 56.6, 54.8, 30.6, 19.4; HRMS Calculated for C<sub>24</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>: [M]<sup>+</sup> 413.1376, found: 413.1380.

**9-Methoxy-1-methyl-5-(2-oxopropyl)-3-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one**

**4d** : white solid; mp 213-216 °C; IR (KBr) 3097, 1721, 1559, 1487, 1389, 1248, 1143, 969, 783, 738, 693 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.24-8.17 (m, 3H, ArH), 7.52 (t, *J* = 8.0 Hz, 2H, ArH), 7.35 (t, *J* = 7.6 Hz, 1H, ArH), 6.97 (d, *J* = 8.8 Hz, 1H, ArH), 6.88 (s, 1H, ArH), 4.59 (s, 2H, CH<sub>2</sub>), 3.93 (s, 3H, CH<sub>3</sub>O), 2.91 (s, 3H, CH<sub>3</sub>), 2.42 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.2, 160.6, 159.5, 154.6, 151.7, 143.0, 138.6, 130.6, 129.2, 128.9, 122.5, 112.2, 109.9, 109.4, 109.3, 101.3, 56.1, 54.9, 30.6, 19.4; HRMS Calculated for C<sub>24</sub>H<sub>18</sub>N<sub>3</sub>O<sub>4</sub>: [M-H]<sup>-</sup> 412.1297, found: 412.1348.

**10-Chloro-5-(2-oxopropyl)-1,3-diphenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one**

**4e** : white solid; mp 202-204 °C; IR (KBr) 3048, 1720, 1608, 1540, 1502, 1355, 1312, 1247, 1198, 1162, 1023, 762, 702, 672 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.27 (d, *J* = 7.6 Hz, 2H, ArH), 7.56-7.50 (m, 7H, ArH), 7.41 (d, *J* = 6.4 Hz, 2H, ArH), 7.33 (s, 1H, ArH), 7.28 (s, 1H, ArH), 4.69 (s, 2H, CH<sub>2</sub>), 2.46 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.0, 160.3, 159.7, 151.6, 150.9, 147.3, 141.1, 138.5, 134.0, 132.7, 131.4, 129.8, 129.6, 129.3, 129.1, 128.9, 127.5, 122.9, 118.1, 116.7, 111.3, 107.8, 54.9, 30.6; HRMS Calculated for C<sub>28</sub>H<sub>18</sub>ClN<sub>3</sub>O<sub>3</sub>: [M]<sup>+</sup> 479.1037, found: 479.1065.

**8-Methoxy-5-(2-oxopropyl)-1,3-diphenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one**

**4f**: gray solid; mp 253-256 °C; IR (KBr) 2852, 1734, 1548, 1497, 1250, 1161, 1128, 863, 830, 757, 701 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.28 (d, *J* = 7.6 Hz, 2H, ArH), 7.57-7.38 (m, 8H, ArH), 6.99 (d, *J* = 6.8 Hz, 1H, ArH), 6.93 (d, *J* = 8.0 Hz, 1H, ArH), 6.66 (t, *J* = 8.0 Hz, 1H, ArH), 4.69 (s, 2H, CH<sub>2</sub>), 3.96 (s, 3H, CH<sub>3</sub>O), 2.46 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.2, 160.0, 159.8, 147.6, 147.3, 142.7, 138.7, 134.4, 129.7, 129.3, 129.2, 128.7, 127.3, 123.1, 122.9, 122.7, 116.5, 114.6, 111.4, 108.1, 56.5, 54.9, 29.9; HRMS Calculated for C<sub>29</sub>H<sub>20</sub>N<sub>3</sub>O<sub>4</sub>: [M-H]<sup>-</sup> 474.1454, found: 474.1510.

**9-Methoxy-5-(2-oxopropyl)-1,3-diphenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one**

**4g**: gray solid; mp 150-152 °C; IR (KBr) 2919, 1730, 1539, 1488, 1381, 1275, 1156, 1006, 902, 851, 768, 701

cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.27 (d, *J* = 7.6 Hz, 2H, ArH), 7.56-7.39 (m, 8H, ArH), 7.44 (t, *J* = 8.0 Hz, 1H, ArH), 6.81 (d, *J* = 8.4 Hz, 1H, ArH), 6.27 (d, *J* = 8.8 Hz, 1H, ArH), 4.65 (s, 2H, CH<sub>2</sub>), 3.83 (s, 3H, CH<sub>3</sub>O), 2.46 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.2, 163.4, 160.6, 159.8, 154.6, 151.8, 147.5, 145.9, 142.7, 138.7, 134.4, 132.8, 129.7, 129.2, 128.9, 127.3, 122.8, 111.3, 109.9, 109.0, 107.5, 100.7, 56.0, 55.0, 30.6; HRMS Calculated for C<sub>29</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>: [M]<sup>+</sup> 475.1532, found: 475.1521.

**10-Chloro-1,3-dimethyl-5-(2-oxopropyl)chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one 4h**: gray solid; mp 166-168 °C; IR (KBr) 2943, 1718, 1561, 1474, 1385, 1357, 1278, 1248, 1205, 1169, 1096, 970, 778, 675 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.33 (s, 1H, ArH), 7.54 (d, *J* = 8.4 Hz, 1H, ArH), 7.32 (d, *J* = 8.4 Hz, 1H, ArH), 4.57 (s, 2H, CH<sub>2</sub>), 4.12 (s, 3H, CH<sub>3</sub>), 2.87 (s, 3H, CH<sub>3</sub>), 2.42 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.0, 160.0, 158.9, 152.0, 150.9, 141.3, 141.2, 132.6, 129.4, 128.6, 118.9, 118.0, 109.8, 107.6, 54.7, 34.1, 30.5, 19.4; HRMS Calculated for C<sub>18</sub>H<sub>14</sub>ClN<sub>3</sub>O<sub>3</sub>: [M]<sup>+</sup> 355.0724, found: 355.0722.

**3-Methyl-5-(2-oxopropyl)-1-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one 4i**: cyan solid; mp 237-240 °C; IR (KBr) 2917, 1721, 1589, 1555, 1470, 1383, 1253, 1201, 1166, 851, 827, 687 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.49-7.41 (m, 6H, ArH), 7.33 (t, *J* = 8.4 Hz, 2H, ArH), 6.71 (t, *J* = 7.6 Hz, 1H, ArH), 4.66 (s, 2H, CH<sub>2</sub>), 4.28 (s, 3H, CH<sub>3</sub>), 2.47 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.3, 160.6, 159.2, 152.6, 152.1, 146.3, 142.5, 134.6, 132.8, 131.5, 129.6, 129.0, 128.8, 123.2, 116.8, 115.8, 110.5, 106.2, 54.8, 34.5, 30.6; HRMS Calculated for C<sub>23</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>Na: [M+Na]<sup>+</sup> 406.1168, found: 406.1160.

**10-Bromo-3-methyl-5-(2-oxopropyl)-1-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one 4j**: yellow solid; mp 218-220 °C; IR (KBr) 2991, 1724, 1546, 1512, 1444, 1306, 1257, 1167, 918, 826, 694 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.53-7.47 (m, 7H, ArH), 7.20 (d, *J* = 7.6 Hz, 1H, ArH), 4.66 (s, 2H, CH<sub>2</sub>), 4.28 (s, 3H, CH<sub>3</sub>), 2.47 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.2, 160.1, 159.3, 152.0, 151.4, 146.3, 141.0, 135.5, 134.3, 129.7, 129.5, 129.1, 118.4, 117.4, 116.2, 110.5, 106.1, 54.8, 34.6, 30.6; HRMS Calculated for C<sub>23</sub>H<sub>16</sub>BrN<sub>3</sub>O<sub>3</sub>: [M]<sup>+</sup> 461.0375, found: 461.0376.

**10-Methoxy-3-methyl-5-(2-oxopropyl)-1-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one 4k**: yellow solid; mp 176-178 °C; IR (KBr) 2988, 1722, 1603, 1591, 1556, 1502, 1473, 1444, 1390, 1351, 1201, 1156, 1025, 903, 826, 781, 749, 695 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55 (d, *J* = 6.8 Hz, 2H, ArH), 7.49-7.44 (m, 3H, ArH), 7.28 (s, 1H, ArH), 7.03 (d, *J* = 8.4 Hz, 1H, ArH), 6.90 (s, 1H, ArH), 4.67 (s, 2H, CH<sub>2</sub>), 4.29 (s, 3H, CH<sub>3</sub>), 2.90 (s, 3H, CH<sub>3</sub>O), 2.48 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR: (75 MHz, CDCl<sub>3</sub>) δ 205.3, 160.8, 159.3, 155.0, 152.2, 146.9, 146.0, 142.5, 134.8, 129.7, 129.1, 128.9, 122.3, 118.1, 116.1, 112.7, 110.6, 105.7, 54.8, 54.7, 34.6, 30.6; HRMS Calculated for C<sub>24</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>: [M]<sup>+</sup> 413.1376, found: 413.1371.

**8,10-Dichloro-3-methyl-5-(2-oxopropyl)-1-phenylchromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridin-6(3*H*)-one**

**4l**: yellow solid; mp 176-178 °C; IR (KBr) 3065, 1732, 1559, 1537, 1524, 1450, 1399, 1262, 1012, 788, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53-7.42 (m, 7H, ArH), 4.67 (s, 2H,  $\text{CH}_2$ ), 4.29 (s, 3H,  $\text{CH}_3$ ), 2.48 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR: (75 MHz,  $\text{CDCl}_3$ )  $\delta$  205.1, 159.4, 152.1, 147.0, 146.2, 143.7, 140.7, 134.1, 133.7, 132.5, 129.9, 129.7, 129.5, 129.1, 128.6, 127.2, 122.5, 117.9, 110.5, 106.2, 102.4, 54.8, 34.7, 30.6; HRMS Calculated for  $\text{C}_{23}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_3$ :  $[\text{M}]^+$  451.0490, found: 451.0486.

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