Selective Synthesis of New Tetracyclic Coumarin-fused Pyrazolo [3,4-*b*]pyridines and Pyrazolo[3,4-*b*]pyridin-6(7*H*)-ones

Meilin Liu, Guodong Yin,* Can Zhu, and Chaochao Yao

Hubei Collaborative Innovation Center for Rare Metal Chemistry, Hubei Key Laboratory of Pollutant Analysis and Reuse Technology, Hubei Normal University, Huangshi 435002, China

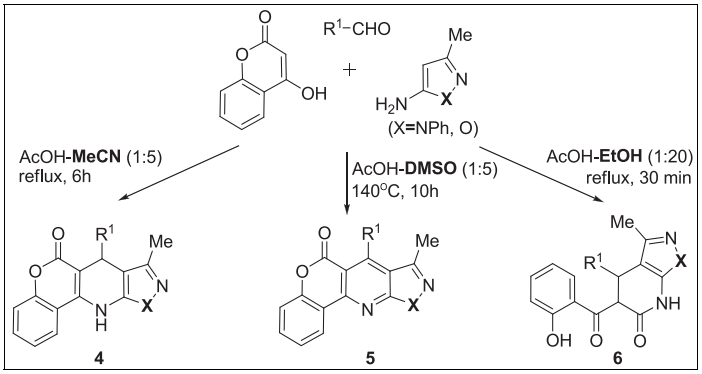
*E-mail: gdyin_hbnu@163.com

Additional Supporting Information may be found in the online version of this article.

Received February 3, 2015

DOI 10.1002/jhet.2473

Published online 00 Month 2015 in Wiley Online Library (wileyonlinelibrary.com).



A three-component reaction for the synthesis of new coumarin-fused tetracyclic system from 4-hydroxycoumarin, aldehydes, and 5-aminopyrazoles/5-aminoisoxazole is described. In the presence of acetic acid, 4,7-dihydro-1H-pyrazolo[3,4-*b*]pyridines (**4**) and pyrazolo[3,4-*b*]pyridines (**5**) were obtained in acetonitrile and dimethylsulfoxide medium, respectively. The reaction gave rise to 4,5-dihydro-1H-pyrazolo[3,4-*b*]pyridin-6(7*H*)-ones (**6**) in acetic acid–ethanol combination system, which involved the C–O bond cleavage. 4-Hydroxy-6-methyl-2H-pyran-2-one and acenaphthylene-1,2-dione were also examined, affording the corresponding C–O bond cleavage products. Mechanism indicates that the reaction is reversible in acetic acid–ethanol combination system.

INTRODUCTION

Ever-increasing attention has been paid in recent years to the functionalized pyrazolo[3,4-*b*]pyridines [1], which are widely present in numerous natural products and biologically active molecules [2]. For example, anxiolytic drugs cartazolate, etazolate, and tracazolate are pyrazolo[3,4-*b*]pyridine derivatives [3]. In addition, coumarin chemistry has captured the continuous attention of chemists and pharmacists for their biological activities [4]. Many synthetic drugs, warfarin, phenprocoumon, and brodifacoum, contain coumarin fragment [5].

The development of new multicomponent reactions has become an active and challenging topic in modern synthetic chemistry because it is a preferred approach to design and discover biologically active compounds [6,7]. Literature survey a variety of functionalized polycyclic pyrazolo[3,4-*b*]pyridine derivatives that have been reported [8–12]. However, several routes have thus far been reported for the construction of coumarin-fused pyrazolo[3,4-*b*]pyridines [13]. Boruah and coworkers reported the synthesis of coumarin-fused pyrazolo[3,4-*b*] pyridines via a palladium-catalyzed reaction of 3-bromo-2-oxo-2H-chromene-4-carbaldehyde and 5-aminopyrazoles under microwave irradiation [14]. Wang described the reaction to prepare tetracyclic pyrazolo[3,4-*b*]pyridine-based coumarin chromophores from 3-acetyl coumarin derivatives and 5-aminopyrazoles. They also found that these polycyclic compounds exhibited high fluorescence quantum yields and good electrochemical, thermal, and photochemical stabilities [15]. Ji and coworkers illustrated an example for the synthesis of 8-carboxylnaphthyl-functionalized pyrazolo[3,4-*b*]pyridine involving the C–C bond cleavage reaction [16]. Recently, it was found that iodine and *n*-tetrabutylammonium tribromide could catalyze synthesis of dihydrochromeno[4,3-*b*]pyrazolo[4,3-*e*] pyridin-6(7*H*)-ones involving three-component reaction of aromatic aldehydes, 4-hydroxycoumarin, and 3-aminopyrazoles, respectively [17,18]. However, the aliphatic aldehydes show the poor yields of the expected products. In continuation with our previous work [19] in minimizing the efforts in construction of coumarin-fused heterocyclic frameworks, we herein report a solvent-tunable selective synthesis of new tetracyclic system by the three-component reactions of 4-hydroxycoumarin (**1**), aldehydes (**2**), and 5-aminopyrazoles (**3**). Coumarin-fused 4,7-dihydro-1H-pyrazolo[3,4-*b*]pyridines were obtained in refluxing

acetonitrile in the presence of acetic acid. When acetonitrile was replaced by dimethylsulfoxide, the reactions gave the corresponding aromatization products tetracyclic pyrazolo [3,4-*b*]pyridines. Moreover, C–O bond cleavage products 4,5-dihydro-1H-pyrazolo[3,4-*b*]pyridin-6(7*H*)-ones were obtained when the reactions were carried out in acetic acid–ethanol combination system.

RESULTS AND DISCUSSION

Our studies commenced with the reaction of **1**, **2a,** and **3a** in refluxing acetonitrile without any catalyst, and the desired **4a** was isolated in 32% yield with the formation of a small amount of aromatization product **5a**. The structures of **4a** and **5a** were confirmed by means of ^{1}H NMR, ^{13}C NMR, HRMS, and IR spectra. The former was further clarified by X-ray single-crystal diffraction analysis (Fig. 1) [20]. When the reaction was carried out in the presence of $ZrCl_4$, $InCl_3$, $FeCl_3$, *L*-proline, trifluoroacetic acid, iodine, and acetic acid within different solvents, it was found that **4a** was obtained in 95% yield in acetic acid and acetonitrile combination system (1:5). Next, we were expecting to obtain aromatization product **5a** as the major product. In consideration of the oxidization and high boiling point of dimethylsulfoxide, the reaction was heated in dimethylsulfoxide at 140°C in the presence of acetic acid. We were pleased to find that **5a** was isolated in 82% yield only with a trace amount of **4a** (Table 1).

With these results in hand, a variety of substituted aldehydes were subsequently investigated under the aforementioned optimal conditions, and the results are summarized in Scheme 1. It was observed that **2a** substrates bearing 4-substituted or 2-substituted electron-donating groups (–Me, –OMe, –*t*-Bu, and $–NMe_2$) gave the corresponding products **4b–4f** in 65–86% yields. Hydroxyl group substrate was well tolerated in the reaction, leading to the final product **4g** in 89% yield. Substrates bearing withdrawing groups (–Br and $–NO_2$) also delivered **4h** and **4i** in good to excellent yield. To our delight, heteroaromatic substrates (furan, thiophene, and pyridine) also furnished **4j–4l** in 78–82% yields. Aliphatic aldehyde (R^1=Me) gave a slightly low yield with isolation of **4m** in 55% yield. Note that 3-methylisoxazol-5-amine (**3b**) was also suitable for this transformation to afford **4n** in 76% yield.

Then, the acetic acid–dimethylsulfoxide combination was employed for the synthesis of **5**. As shown in Scheme 2, it was found that the representative aldehydes in which R^1 is a phenyl ring bearing methyl, methoxy, and nitro substituents could smoothly react with **1** and **3a** to give the corresponding products **5b–5e** in 80–87% yields. 2-Thienylaldehyde and acetaldehyde also furnished **5f** and **5g** in 90% and 78% yields, respectively.

When the mixture of **1**, **2a,** and **3a** was heated in acetic acid–ethanol (1:20) for 30 min, an unexpected insoluble white solid was obtained in 74% yield, which was identified as the C–O bond cleavage product **6a** and further clarified by X-ray single-crystal diffraction analysis (Fig. 1) [21]. We then extended the substrates to other substituted aldehydes for the preparation of the structurally diverse pyrazolo[3,4-*b*]pyridin-6(7*H*)-ones, and the corresponding products **6b–6f** were also isolated in 63–75% yields (Scheme 3).

Moreover, 4-hydroxy-6-methyl-2H-pyran-2-one (**7**) was employed to react with **2a** and **3a** in acetic acid–acetonitrile at reflux for 4 h, and product **8** was isolated in 55% yield. It should be noted that **8** was also obtained in 64% yield in acetic acid–ethanol system (Scheme 4). Acenaphthylene-1,2-dione (**9**) was reacted with **1** and **3a** in acetic acid–acetonitrile or acetic acid–ethanol medium, resulting in **10** [22] in 56% and 85% yields (Scheme 5).

To our surprise, heating the ethanol solution of **6a** at reflux for 4 h, the unexpected C–C bond cleavage product **11** was obtained in 98% yield. However, in the presence of acetic acid, **11** was only obtained in 35% yield with the formation of coumarin-fused products **4a** (25%) and **5a** (38%) (Scheme 6).

A plausible reaction mechanism is postulated in Scheme 7. First, the Knoevenagel reaction of **1** and **2a** in the presence of acetic acid gives the intermediate **A**, which is reacted with **3a** through the Michael-type

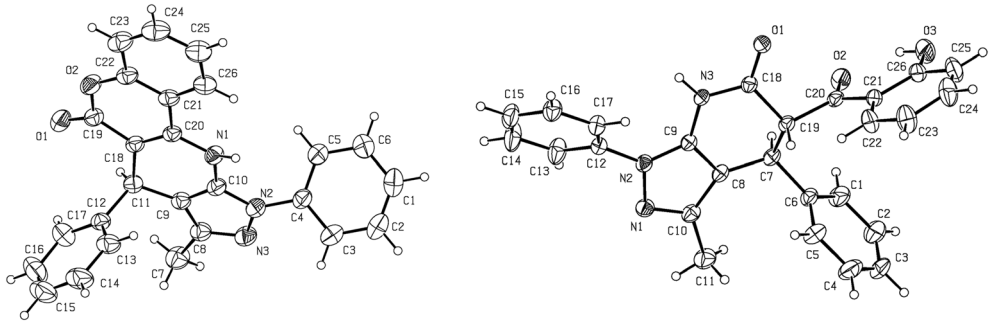
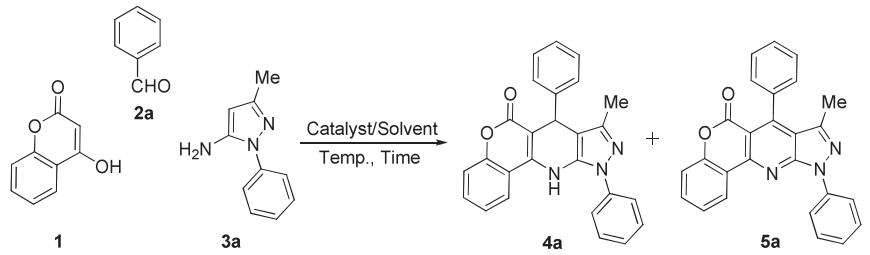


Figure 1. X-ray structures of **4a** and **6a**.

Table 1

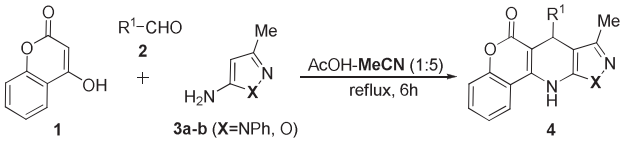
Optimization of the reaction conditions for the synthesis of **4a/5a**[a].



Entry	Catalyst/solvent[b]	Temperature (°C)	Time (h)	Yield (%)[c] 4a	5a
1	None/MeCN	Reflux	10	32	4
2	$ZrCl_4$/MeCN	Reflux	10	75	—
3	$InCl_3$/MeCN	Reflux	10	80	—
4	$FeCl_3$/MeCN	Reflux	10	46	15
5	*L*-proline/MeCN	Reflux	10	47	8
6	TFA/MeCN (1:10)	Reflux	6	85	—
7	I_2/MeCN	Reflux	6	40	—[d]
8	AcOH	120	10	89	5
9	AcOH/MeCN (1:10)	Reflux	6	82	—[d]
10	AcOH/MeCN (1:20)	Reflux	6	71	—[d]
11[e]	AcOH/MeCN (1:5)	Reflux	6	95	—
12[e]	AcOH/MeCN (1:5)	50	12	54	—
13	AcOH/MeCN (1:5)	25	12	32	—
14	AcOH/DCM (1:5)	Reflux	10	75	12
15	AcOH/toluene (1:5)	Reflux	10	49	21
16	AcOH/DMSO (1:5)	Reflux	10	—[d]	82
17	AcOH/DMSO (1:5)	Reflux	10	—[d]	75
18	AcOH/DMSO (1:2)	Reflux	10	20	55
19	AcOH/DMSO (1:1)	Reflux	10	15	48

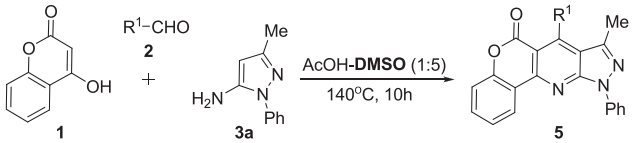
[a]All reactions were performed with **1** (0.5 mmole), **2a** (0.5 mmole), and **3a** (0.5 mmole) in an appropriate solvent (6 mL).
[b]20 mol% of catalyst was employed in these reactions unless mentioned; values in parentheses were the volume ratio of catalyst/solvent.
[c]Isolated yield.
[d]Trace amount of product.
[e]Unexpected insoluble white solid was formed.

Scheme 1. Synthesis of coumarin-fused 4,7-dihydro-1H-pyrazolo-[3,4-*b*] pyridines (**4**).



4a (R^1=C_6H_5, X=NPh, 95%)
4b (R^1=4-MeC_6H_4, X=NPh, 86%)
4c (R^1=4-$MeOC_6H_4$, X=NPh, 84%)
4d (R^1=2-$MeOC_6H_4$, X=NPh, 72%)
4e (R^1=4-^{t}BuC_6H_4, X=NPh, 81%)
4f (R^1=4-$Me_2NC_6H_4$, X=NPh, 65%)
4g (R^1=3-HOC_6H_4, X=NPh, 89%)
4h (R^1=4-BrC_6H_4, X=NPh, 78%)
4i (R^1=4-$O_2NC_6H_4$, X=NPh, 92%)
4j (R^1=2-furyl, X=NPh, 82%)
4k (R^1=2-thienyl, X=NPh, 80%)
4l (R^1=2-pyridyl, X=NPh, 78%)
4m (R^1=Me, X=NPh, 55%)
4n (R^1=C_6H_5, X=O, 76%)

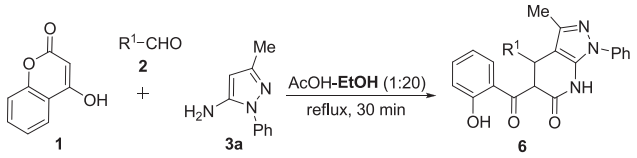
Scheme 2. Synthesis of coumarin-fused pyrazolo[3,4-*b*]pyridines (**5**).



5a (R^1=C_6H_5, 82%)
5b (R^1=4-MeC_6H_4, 85%)
5c (R^1=4-$MeOC_6H_4$, 84%)
5d (R^1=2-$MeOC_6H_4$, 80%)
5e (R^1=4-$O_2NC_6H_4$, 87%)
5f (R^1=2-thienyl, 90%)
5g (R^1=Me, 78%)

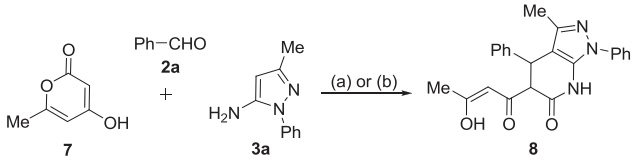
addition reaction to deliver the intermediate **B** [23]. One pathway is that the amino group attacks the ketone carbonyl group, furnishing the intramolecular cyclization intermediate **C** after loss of water, followed by proton transfer to give **4a** [11]. Aromatization product **5a** was obtained from **4a** at high temperature in the presence of dimethylsulfoxide and air. The other pathway is that the amino group attacks the ester carbonyl group in

Scheme 3. Synthesis of pyrazolo[3,4-*b*]pyridin-6(7*H*)-ones (**6**).



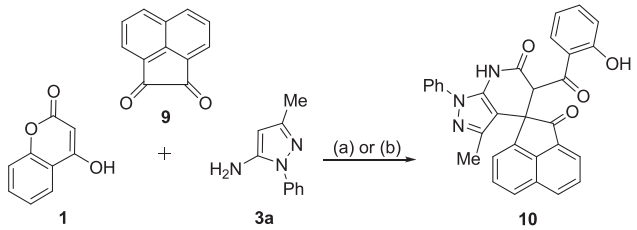
6a (R^1=C_6H_5, 74%) **6d** (R^1=4-^{t}BuC_6H_4, 71%)
6b (R^1=4-MeC_6H_4, 75%) **6e** (R^1=4-BrC_6H_4, 72%)
6c (R^1=4-MeOC_6H_4, 63%) **6f** (R^1=2-thienyl, 66%)

Scheme 4



(a) AcOH-MeCN (1:5), reflux, 4h, 55%
(b) AcOH-EtOH (1:20), reflux,4h, 64%

Scheme 5



(a) AcOH-MeCN (1:5), reflux, 4h, 56%
(b) AcOH-EtOH (1:20), reflux,4h, 85%

acetic acid–ethanol medium to give **6a** [24], which could be converted to the C–C bond cleavage product **11** in refluxing ethanol [25]. The experimental results in Scheme 7 indicate that the formation of **6a** from intermediate **B** is reversible in acetic acid–ethanol combination system.

CONCLUSION

In summary, we have described a solvent-tunable three-component reaction for the selective synthesis of new coumarin-fused tetracyclic system from 4-hydroxycoumarin, aldehydes, and 5-aminopyrazoles/5-aminoisoxazole. The possible reaction mechanism was postulated. All these reported compounds were characterized by means of ^{1}H NMR, ^{13}C NMR, HRMS, and IR spectra. The structures of **4a** and **6a** were further clarified by X-ray single-crystal diffraction analysis. The prominent advantages of this approach are easily available starting materials, wide scope of substrates, and excellent yields.

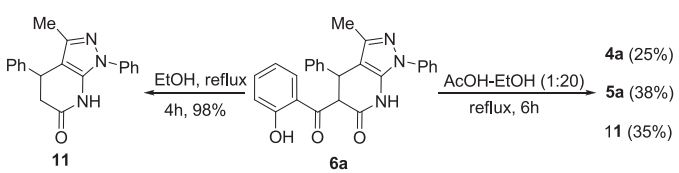
EXPERIMENTAL

All the chemicals were commercially available and used without further purification. All the organic solvents were dried and freshly distilled before use. ^{1}H and ^{13}C NMR were recorded in $CDCl_3$ or DMSO-d_6 using Bruker AV 300-MHz spectrometers at 300 and 75 MHz (Bruker, Germany), respectively. Chemical shifts are reported relative to tetramethylsilane (TMS) (internal standard). High-resolution mass spectra were recorded using a Bruker ultrafleXtreme MALDI-TOF/TOF (HCCA matrix) (Bruker). IR spectra were obtained as KBr pellet samples using a Nicolet 5700 FTIR spectrometer (Thermo, USA). Flash column chromatography was performed on silica gel (200–300 meshes). Melting points were determined using an uncorrected X-4 apparatus (Shanghai Precision & Scientific Instrument Co., Ltd., China). The X-ray crystal structure determination was performed using a Bruker SMART APEX CCD system (Bruker).

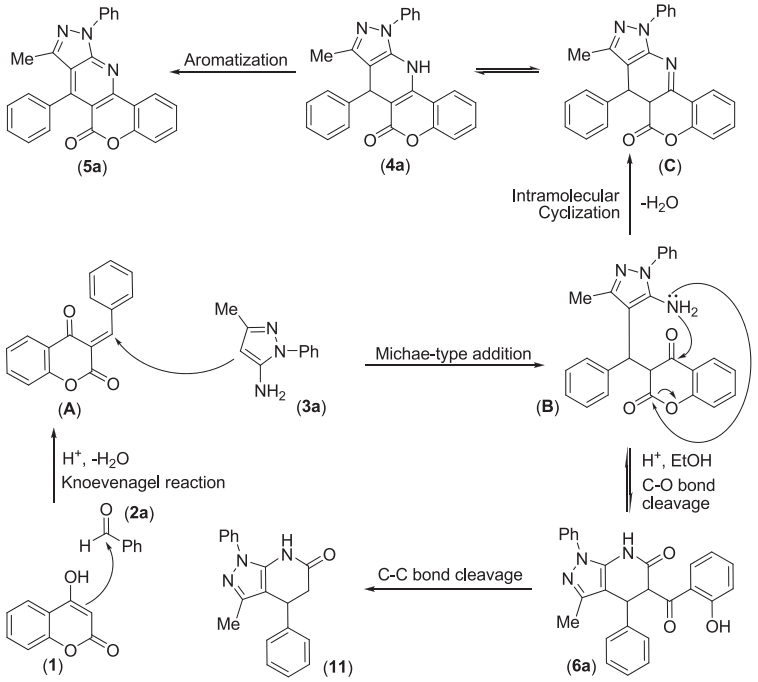
General one-pot procedure for the synthesis of 4. A mixture of **1** (0.5 mmole), **2** (0.5 mmole), and **3** (0.5 mmole) was heated in AcOH/MeCN (1:5, 6 mL) under reflux. After the reaction was completed (6 h, monitored by thin layer chromatography (TLC)), the mixture was slowly cooled at room temperature and purified by column chromatography using petroleum ether–ethyl acetate as the eluent to deliver the desired products **4**.

8-Methyl-7,10-diphenyl-10,11-dihydrochromeno[4,3-b]pyrazolo [4,3-e]pyridin-6(7H)-one (4a). White solid, mp 223–224°C; IR (KBr) 750, 1028, 1204, 1447, 1537, 1699, 3406 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.06 (s, 3H), 5.32 (s, 1H), 7.14–7.61 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 12.3, 37.9, 102.8, 103.4, 113.3, 117.8, 119.8, 122.7, 123.9, 126.7, 127.7, 128.26, 128.29, 130.2, 131.7, 135.1, 138.0, 141.6, 144.9, 147.5, 152.7, 161.2; HRMS: *m/z* calcd for $C_{26}H_{20}N_3O_2$: 406.1550, found: 406.1562 $[M+H]^+$.

Scheme 6



Scheme 7. The proposed reaction mechanism.



8-Methyl-10-phenyl-7-(p-tolyl)-10,11-dihydro-chro-meno[4,3-b] pyrazolo[4,3-e]pyri-din-6(7H)-one (4b). White solid, mp 227–228°C; IR (KBr) 844, 1033, 1211, 1453, 1539, 1711, 3431 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.07 (s, 3H), 2.28 (s, 3H), 5.26 (s, 1H), 7.06 (d, $J = 7.9$ Hz, 2H), 7.20–7.23 (m, 2H), 7.29–7.60 (m, 9H); ^{13}C NMR ($CDCl_3$): δ 12.3, 21.0, 37.4, 102.9, 103.5, 113.3, 117.7, 119.9, 122.6, 123.8, 127.6, 128.1, 128.9, 130.2, 131.6, 135.1, 136.2, 138.0, 141.5, 142.0, 147.4, 152.6, 161.2; HRMS: *m/z* calcd for $C_{27}H_{22}N_3O_2$: 420.1707, found: 420.1707 $[M+H]^+$.

7-(4-Methoxyphenyl)-8-methyl-10-phenyl-10,11-dihydro-chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4c). White solid, mp 217–219°C; IR (KBr) 758, 1032, 1250, 1454, 1539, 1710, 3430 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.04 (s, 3H), 3.74 (s, 3H), 5.20 (s, 1H), 6.78 (d, $J = 8.5$ Hz, 2H), 7.24–7.60 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 12.2, 36.9, 55.2, 102.9, 103.5, 113.4, 113.6, 117.6, 120.1, 122.7, 123.8, 127.6, 129.3, 130.1, 131.6, 135.1, 137.3, 138.0, 141.4, 147.4, 152.5, 158.2, 161.3; HRMS: *m/z* calcd for $C_{25}H_{20}N_3O$: 436.1656, found: 436.1656 $[M+H]^+$.

7-(2-Methoxyphenyl)-8-methyl-10-phenyl-10,11-dihydro-chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4d). White solid, mp 171–174°C; IR (KBr) 757, 1023, 1246, 1542, 1696, 3448 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.07 (s, 3H), 3.84 (s, 3H), 5.67 (s, 1H), 6.83–6.89 (m, 2H), 7.12–7.22 (m, 3H), 7.30–7.33(m, 1H), 7.39–7.44 (m, 2H), 7.50–7.58 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 12.1, 32.1, 55.9, 102.5, 103.4, 111.3, 113.3, 117.7, 119.7, 120.8, 122.6, 123.8, 127.5, 127.8, 129.8, 130.2, 131.5, 133.5, 135.2, 138.1, 142.4, 147.5, 152.7, 156.7, 161.0; HRMS: *m/z* calcd for $C_{27}H_{22}N_3O_3$: 436.1656, found: 436.1647 $[M+H]^+$.

7-(4-(tert-Butyl)phenyl)-8-methyl-10-phenyl-10,11-dihydro-chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4e). Yellow solid, mp 247–248°C; IR (KBr) 758, 1034, 1211, 1534, 1626, 1712, 3441 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.24 (s, 9H), 2.04 (s, 3H), 5.14 (s, 1H), 7.23–7.60 (m, 13H). ^{13}C NMR ($CDCl_3$): δ 12.2, 31.2, 34.2, 37.1, 102.6, 103.5, 113.4, 117.3, 120.4, 122.7, 123.7, 125.0, 127.4, 127.6, 129.9, 131.4, 135.3, 137.9, 141.9, 147.2, 149.1, 152.4, 161.4. HRMS: *m/z* calcd for $C_{30}H_{28}N_3O_2$: 462.2176, found: 462.2178 $[M+H]^+$.

7-(4-(Dimethylamino)phenyl)-8-methyl-10-phenyl-10,11-dihydro-chromeno[4,3-b]pyrazolo[4,3-e] pyridin-6(7H)-one (4f). Yellow solid, mp 260–261°C; IR (KBr) 765, 1033, 1214, 1533, 1709, 3444 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.09 (s, 3H), 2.89 (s, 6H), 5.25 (s, 1H), 6.65–6.67 (m, 2H), 7.07 (s, 1H), 7.18–7.22 (m, 1H), 7.30–7.61 (m, 9H); ^{13}C NMR ($CDCl_3$): δ 12.3, 36.7, 40.9, 103.4, 103.7, 112.7, 113.5, 117.7, 119.7, 122.6, 123.8, 127.6, 129.0, 130.2, 131.5, 135.1, 138.1, 141.0, 147.6, 152.6, 161.3; HRMS: *m/z* calcd for $C_{28}H_{25}N_4O_2$: 449.1972, found: 449.1972 $[M+H]^+$.

7-(3-Hydroxyphenyl)-8-methyl-10-phenyl-10,11-dihydro-chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4g). Yellow solid, mp 159–160°C; IR (KBr) 765, 1043, 1211, 1450, 1537, 1671, 3291 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.97 (s, 3H), 5.09 (s, 1H), 6.54–6.57 (m, 1H), 6.66–6.74 (m, 2H), 7.05 (t, $J = 7.8$ Hz, 1H), 7.35–7.44 (m, 3H), 7.55–7.69 (m, 5H), 8.04–8.07 (m, 1H), 9.27 (s, 1H), 10.02 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 12.1, 101.4,

104.1, 113.4, 114.0, 114.8, 116.5, 118.7, 122.6, 123.7, 126.7, 129.0, 129.4, 131.8, 136.0, 138.8, 143.8, 145.9, 147.6, 152.0, 157.2, 160.6; HRMS: *m/z* calcd for $C_{26}H_{20}N_3O_3$: 422.1499, found: 422.1499 $[M+H]^+$.

7-(4-Bromophenyl)-8-methyl-10-phenyl-10,11-dihydrochromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4h). White solid, mp 239–240°C; IR (KBr) 753, 1050, 1393, 1538, 1696, 3428 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.05 (s, 3H), 5.29 (s, 1H), 7.18–7.25 (m, 2H), 7.27–7.61 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 12.3, 37.5, 102.3, 102.8, 113.1, 117.8, 119.8, 120.6, 122.7, 124.0, 127.8, 130.1, 130.3, 131.4, 131.9, 135.0, 137.9, 141.6, 143.9, 147.4, 152.7, 161.1; HRMS: *m/z* calcd for $C_{26}H_{19}BrN_3O_2$: 484.0655, found: 484.0655 $[M+H]^+$.

8-Methyl-7-(4-nitrophenyl)-10-phenyl-10,11-dihydrochromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4i). Yellow solid, mp 207–209°C; IR (KBr) 755, 1039, 1349, 1533, 1674, 3426 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.96 (s, 3H), 5.37 (s, 1H), 7.17– 7.55 (m, 11H), 8.07 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 12.3, 38.1, 101.4, 102.0, 112.9, 117.9, 120.0, 122.7, 123.7, 124.2, 128.0, 129.3, 130.4, 132.3, 135.1, 137.7, 142.1, 146.7, 147.2, 151.9, 152.7, 161.1; HRMS: *m/z* calcd for $C_{26}H_{19}N_4O_4$: 451.1401, found: 451.1404 $[M+H]^+$.

7-(Furan-2-yl)-8-methyl-10-phenyl-10,11-dihydrochromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4j). Yellow solid, mp 225–227°C; IR (KBr) 760, 1213, 1258, 1531, 1673, 3437 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.22 (s, 3H), 5.50 (s, 1H), 6.20 (d, J = 3.2 Hz, 1H), 6.27–6.29 (m, 1H), 7.20–7.59 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 12.1, 31.5, 99.3, 100.6, 105.8, 110.3, 113.2, 117.8, 119.8, 122.7, 124.0, 127.8, 130.2, 132.0, 135.2, 137.9, 141.5, 142.4, 147.5, 152.7, 155.9, 161.2; HRMS: *m/z* calcd for $C_{24}H_{18}N_3O_3$: 396.1343, found: 396.1346 $[M+H]^+$.

8-Methyl-10-phenyl-7-(thiophen-2-yl)-10,11-dihydro-chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4k). White solid, mp 206–208°C; IR (KBr) 758, 1032, 1255, 1537, 1692, 3429 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.19 (s, 3H), 5.71 (s, 1H), 6.88–6.91 (m, 1H), 7.06 (d, J = 3.0 Hz, 1H), 7.11–7.13 (m, 1H), 7.22 (s, 1H), 7.30–7.37 (m, 3H), 7.43–7.51 (m, 1H), 7.52–7.54 (m, 1H), 7.57–7.61 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 12.2, 32.4, 102.2, 102.8, 113.2, 117.9, 119.8, 122.7, 124.0, 124.3, 124.8, 126.7, 127.8, 130.3, 131.9, 135.1, 137.9, 141.2, 147.5, 149.2, 152.6, 161.4; HRMS: *m/z* calcd for $C_{24}H_{18}N_3O_2S$: 412.1114, found: 412.1109 $[M+H]^+$.

8-Methyl-10-phenyl-7-(pyridin-2-yl)-10,11-dihydrochromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4l). White solid, mp 252–254°C; IR (KBr) 760, 1044, 1260, 1535, 1696, 3434 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.05 (s, 3H), 5.43 (s, 1H), 7.04–7.11 (m, 3H), 7.28–7.41 (m, 5H), 7.53 (d, J = 8.1 Hz, 2H), 7.63–7.68 (m, 1H), 8.27–8.28 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 12.5, 40.9, 101.1, 102.0, 113.4, 117.3, 120.8, 121.8, 123.5, 123.6, 124.1, 128.0, 129.7, 131.5, 136.1, 136.3, 138.1, 143.6, 147.0, 149.2, 152.3, 161.5, 162.4.; HRMS: *m/z* calcd for $C_{25}H_{19}N_4O_2$: 407.1503, found: 407.1503 $[M+H]^+$.

7,8-Dimethyl-10-phenyl-10,11-dihydrochromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(7H)-one (4m). Yellow solid, mp 207–209°C; IR (KBr) 754, 1014, 1215, 1527, 1662, 3448 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.45 (d, J = 6.6 Hz, 3H), 2.32 (s, 3H), 4.27 (q, J = 6.6 Hz, 1H), 6.98 (s, 1H), 7.30–7.45 (m, 4H), 7.52–7.61 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 12.3, 23.1, 26.8, 103.9, 104.3, 113.3, 117.7, 119.6, 122.6, 123.9, 127.6, 130.2, 131.6, 134.8, 138.0, 142.1, 147.0, 152.5, 161.7; HRMS: *m/z* calcd for $C_{21}H_{18}N_3O_2$: 344.1394, found: 344.1384 $[M+H]^+$.

8-Methyl-7-phenyl-7,11-dihydro-6H-chromeno[4,3-b]isoxazolo[4,5-e]pyridin-6-one (4n). White solid, mp 254–256°C; IR (KBr) 757, 1063, 1264, 1514, 1666, 3447 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.91 (s, 3H), 5.17 (s, 1H), 7.15–7.22 (m, 1H), 7.27 (d, J = 4.2 Hz, 4H), 7.38–7.47 (m, 2H), 7.63–7.69 (m, 1H), 8.21 (d, J = 7.2 Hz, 1H), 11.5 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 9.8, 37.3, 95.2, 100.5, 113.3, 116.8, 123.1, 124.2, 126.6, 127.8, 128.3, 132.2, 143.1, 145.4, 152.2, 158.4, 159.1, 160.2; HRMS: *m/z* calcd for $C_{20}H_{15}N_2O_3$: 331.1077, found: 331.1078 $[M+H]^+$.

General one-pot procedure for the synthesis of 5. A mixture of **1** (0.5 mmole), **2** (0.5 mmole) and **3a** (0.5 mmole) was heated in AcOH/DMSO (1:5, 6 mL) at 140°C. After the reaction was completed (10 h, monitored by TLC), the mixture was slowly cooled at room temperature and purified by column chromatography using petroleum ether–ethyl acetate as the eluent to deliver the desired product **5**.

8-Methyl-7,10-diphenylchromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(10H)-one (5a). Yellow solid, mp 253–255°C; IR (KBr) 754, 1082, 1193, 1497, 1644, 1733 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.92 (s, 3H), 7.30–7.41 (m, 5H), 7.53–7.61 (m, 6H), 8.37 (d, J = 7.7 Hz, 2H), 8.68 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 14.3, 109.8, 116.9, 117.4, 119.7, 121.0, 124.4, 125.7, 126.2, 127.1, 128.1, 128.4, 129.1, 132.4, 136.4, 138.9, 145.8, 150.9, 152.1, 152.5, 152.9, 159.5; HRMS: *m/z* calcd for $C_{26}H_{18}N_3O_2$: 404.1394, found: 404.1380 $[M+H]^+$.

8-Methyl-10-phenyl-7-(p-tolyl)chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(10H)-one (5b). White solid, mp 250–251°C; IR (KBr) 758, 1079, 1194, 1499, 1561, 1599, 1734 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.97 (s, 3H), 2.49 (s, 3H), 7.22 (d, J = 8.0 Hz, 2H), 7.32–7.43 (m, 5H), 7.54–7.62 (m, 3H), 8.36–8.39 (m, 2H), 8.68–8.71 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 14.4, 21.5, 110.0, 116.9, 117.6, 119.7, 121.0, 124.4, 125.7, 126.1, 127.0, 128.8, 129.1, 132.4, 133.3, 138.1, 138.9, 145.9, 150.9, 152.1, 152.9, 153.0, 159.5; HRMS: *m/z* calcd for $C_{27}H_{20}N_3O_2$: 418.1550, found: 418.1548 $[M+H]^+$.

7-(4-Methoxyphenyl)-8-methyl-10-phenylchromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(10H)-one (5c). White solid, mp 225–227°C; IR (KBr) 751, 1183, 1249, 1503, 1602, 1736 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.02 (s, 3H), 3.93

(s,3H), 7.07 (d, $J = 8.7$ Hz, 2H), 7.25 (s, 1H), 7.27–7.28 (m, 1H), 7.33–7.44 (m, 3H), 7.56–7.63 (m, 3H), 8.38 (d, $J = 7.8$ Hz, 2H), 8.70–8.73 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 14.6, 55.3, 110.1, 113.6, 116.9, 117.8, 119.8, 121.1, 124.4, 125.7, 126.2, 128.4, 128.6, 129.1, 132.4, 138.9, 145.9, 151.0, 152.2, 152.7, 152.9, 159.6, 159.7; HRMS: *m/z* calcd for $C_{27}H_{20}N_3O_3$: 434.1499, found: 434.1489 $[M+H]^+$.

7-(2-Methoxyphenyl)-8-methyl-10-phenylchromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(10H)-one (5d). Yellow solid, mp 254–256°C; IR (KBr) 754, 1080, 1245, 1499, 1640, 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 3H), 3.75 (s, 3H), 7.07–7.15 (m, 3H), 7.33–7.44 (m, 3H), 7.49–7.63 (m, 4H), 8.40 (d, $J = 8.0$ Hz, 2H), 8.73 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 14.0, 55.7, 110.7, 110.8, 116.9, 117.6, 119.9, 120.5, 121.1, 124.3, 125.4, 125.7, 126.1, 128.4, 129.1, 130.1, 132.3, 139.0, 145.8, 149.8, 151.3, 152.1, 152.9, 156.0, 159.4; HRMS: *m/z* calcd for $C_{27}H_{20}N_3O_3$: 434.1499, found: 434.1499 $[M+H]^+$.

8-Methyl-7-(4-nitrophenyl)-10-phenylchromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(10H)-one (5e). Yellow solid, mp 270–272°C; IR (KBr) 760, 1085, 1202, 1346, 1506, 1564, 1601, 1733 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.95 (s, 3H), 7.33–7.46 (m, 3H), 7.53–7.63 (m, 5H), 8.36 (d, $J = 7.7$ Hz, 2H), 8.42 (d, $J = 8.7$ Hz, 2H), 8.68–8.71 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 14.5, 109.4, 116.6, 117.0, 119.3, 121.1, 123.5, 124.7, 125.7, 126.6, 128.4, 129.2, 132.9, 138.6, 143.4, 144.8, 147.9, 149.4, 150.9, 152.2, 152.7, 159.6. HRMS: *m/z* calcd for $C_{26}H_{17}N_4O_4$: 449.1244, found: 449.1448 $[M+H]^+$.

8-Methyl-10-phenyl-7-(thiophen-2-yl)chromeno[4,3-b]pyrazolo[4,3-e]pyridin-6(10H)-one (5f). Yellow solid, mp 260–262°C; IR (KBr) 760, 1074, 1190, 1251, 1496, 1563, 1737 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.14 (s, 3H), 7.09–7.11 (m, 1H), 7.22–7.24 (m, 1H), 7.34–7.44 (m, 3H), 7.56–7.63 (m, 4H), 8.37 (d, $J = 7.7$ Hz, 2H), 8.68–8.71 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 13.7, 111.3, 116.9, 121.1, 124.5, 125.7, 126.3, 126.86, 126.93, 127.1, 129.1, 132.6, 135.4, 138.8, 145.5, 145.8, 150.8, 152.1, 152.8, 159.0; HRMS: *m/z* calcd for $C_{24}H_{16}N_3O_2S$: 410.0958, found: 410.0959 $[M+H]^+$.

7,8-Dimethyl-10-phenylchromeno[4,3-b]pyrazolo [4,3-e]pyridin-6(10H)-one (5g). Yellow solid, mp 236–237°C; IR (KBr) 759, 1088, 1249, 1497, 1574, 1723 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.87 (s, 3H), 3.27 (s, 3H), 7.33–7.40 (m, 3H), 7.56–7.61 (m, 3H), 8.34–8.37 (m, 2H), 8.60–8.63 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 16.6, 18.5, 110.6, 116.6, 117.9, 119.7, 120.9, 124.4, 125.6, 126.1, 129.0, 132.3, 138.9, 145.1, 150.9, 152.2, 152.5, 152.8, 160.9; HRMS: *m/z* calcd for $C_{21}H_{16}N_3O_2$: 342.1237, found: 342.1232 $[M+H]^+$.

General one-pot procedure for the synthesis of 6. A mixture of **1** (0.5 mmole), **2** (0.5 mmole) and **3a** (0.5 mmole) was heated in AcOH/EtOH (1:20, 6 mL) under reflux. After the reaction was completed (30 min, monitored by TLC), insoluble solid was formed, which was filtrated and washed with a small amount of anhydrous ethanol to give the product **6**.

5-(2-Hydroxybenzoyl)-3-methyl-1,4-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridin-6(7H)-one (6a). White solid, mp 222–223°C; IR (KBr) 756, 918, 1252, 1494, 1680, 3170, 3454 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.81 (s, 3H), 4.59 (d, $J = 6.9$ Hz, 1H), 4.81 (d, $J = 6.9$ Hz, 1H), 6.87– 6.92 (m, 1H), 6.99–7.02 (m, 1H), 7.23–7.25 (m, 2H), 7.27–7.40 (m, 6H), 7.44–7.50 (m, 3H), 7.62–7.65 (m, 1H), 8.78 (br, 1H), 11.9 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.5, 40.4, 57.2, 101.2, 118.8, 118.9, 119.2, 123.2, 127.4, 127.8, 127.9, 129.2, 129.8, 130.4, 136.3, 137.1, 140.6, 147.0, 163.2, 167.1, 200.7; HRMS: *m/z* calcd for $C_{26}H_{22}N_3O_3$: 424.1656, found: 424.1659 $[M+H]^+$.

5-(2-Hydroxybenzoyl)-3-methyl-1-phenyl-4-(p-tolyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridin-6(7H)-one (6b). White solid, mp 217–218°C; IR (KBr) 745, 918, 1156, 1246, 1498, 1676, 3230, 3442 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.81 (s, 3H), 2.30 (s, 3H), 4.55 (d, $J = 6.8$ Hz, 1H), 4.78 (d, $J = 6.8$ Hz, 1H), 6.89 (t, $J = 7.5$ Hz, 1H), 7.00 (d, $J = 8.3$ Hz, 1H), 7.12–7.25 (m, 5H), 7.31–7.52 (m, 5H), 7.64 (d, $J = 7.9$ Hz, 1H), 8.94 (s, 1H), 11.91 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.5, 21.0, 39.9, 57.3, 101.4, 118.8, 119.2, 123.1, 127.3, 127.8, 129.6, 129.8, 130.4, 136.3, 137.0, 137.1, 137.4, 137.5, 147.0, 163.1, 167.5, 200.9; HRMS: *m/z* calcd for $C_{27}H_{24}N_3O_3$: 438.1812, found: 438.1818 $[M+H]^+$.

5-(2-Hydroxybenzoyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-4,5-dihydro-1H-pyrazolo[3,4-b] pyridin-6(7H)-one (6c). White solid, mp 193–194°C; IR (KBr) 758, 1251, 1504, 1674, 3417, 3595 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.84 (s, 3H), 3.78 (s, 3H), 4.58 (d, $J = 6.9$ Hz, 1H), 4.81 (d, $J = 6.9$ Hz, 1H), 6.83–6.93 (m, 3H), 7.00 (d, $J = 8.3$ Hz, 1H), 7.18 (d, $J = 8.6$ Hz, 2H), 7.32–7.36 (m, 1H), 7.43–7.52 (m, 5H), 7.66 (d, $J = 8.1$ Hz, 1H), 8.24 (s, 1H), 11.90 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.5, 39.6, 55.3, 57.5, 101.6, 114.5, 118.87, 118.91, 119.2, 123.1, 128.0, 128.5, 129.9, 130.4, 132.5, 136.1, 137.1, 137.2, 147.1, 159.0, 163.2, 167.0, 200.8; HRMS: *m/z* calcd for $C_{27}H_{24}N_3O_4$: 454.1761, found: 454.1761 $[M+H]^+$.

4-(4-(tert-Butyl)phenyl)-5-(2-hydroxybenzoyl)-3-methyl-1-phenyl-4,5-dihydro-1H-pyrazolo[3,4-b] pyridin-6(7H)-one (6d). White solid, mp 242–243°C; IR (KBr) 751, 1249, 1499, 1675, 3227, 3444 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.31 (s, 9H), 1.93 (s, 3H), 4.54 (d, $J = 5.0$ Hz, 1H), 4.85 (d, $J = 5.0$ Hz, 1H), 6.94 (t, $J = 7.2$ Hz, 1H), 7.03 (d, $J = 8.5$ Hz, 1H), 7.19 (d, $J = 8.3$ Hz, 2H), 7.34–7.43 (m, 3H), 7.50–7.55 (m, 5H), 7.74 (d, $J = 7.3$ Hz, 1H), 8.02 (s, 1H), 11.89 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.4, 31.3, 34.5, 39.9, 57.6, 101.4, 118.4, 119.0, 119.2, 123.1, 126.1, 126.8, 128.0, 129.9, 130.4, 136.3, 137.1, 137.2,

137.7, 147.1, 150.8, 163.3, 166.9, 200.7; HRMS: *m/z* calcd for $C_{30}H_{30}N_3O_3$: 480.2282, found: 480.2313 $[M+H]^+$.

4-(4-Bromophenyl)-5-(2-hydroxybenzoyl)-3-methyl-1-phenyl-4,5-dihydro-1H-pyr-azolo[3,4-b]pyridin-6(7H)-one (6e). White solid, mp 220–221°C; IR (KBr) 753, 1074, 1247, 1317, 1493, 1678, 3238, 3447 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.81 (s, 3H), 4.61 (d, $J=7.6$Hz, 1H), 4.77 (d, $J=7.6$ Hz, 1H), 6.87–6.93 (m, 1H), 6.99–7.02 (m, 1H), 7.14–7.17 (m, 2H), 7.31–7.32 (m, 1H), 7.37–7.54 (m, 7H),7.59–7.62 (m, 1H), 8.64 (s, 1H), 11.86 (s, 1H);^{13}C NMR ($CDCl_3$): δ 12.6, 39.7, 56.8, 100.8, 118.9, 119.0, 119.3, 121.7, 123.1, 128.0, 129.3, 129.7, 130.2, 132.3, 136.3, 137.0, 137.3, 139.5, 146.8, 163.1, 167.0, 200.3; HRMS: *m/z* calcd for $C_{26}H_{21}BrN_3O_3$: 502.0761, found: 502.0767 $[M+H]^+$.

5-(2-Hydroxybenzoyl)-3-methyl-1-phenyl-4-(thiophen-2-yl)-4,5-dihydro-1H-pyrazolo[3,4-b] pyridin-6(7H)-one (6f). Yellow solid, mp 226–227°C; IR (KBr) 757, 1075, 1251, 1338, 1495, 1681, 3233, 3439 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.99 (s, 3H), 4.92 (s, 2H), 6.90–6.98 (m, 3H), 7.00–7.03 (m, 1H), 7.20–7.22 (m, 1H), 7.29–7.35 (m, 1H), 7.40–7.55 (m, 5H), 7.75–7.79 (m, 1H), 8.43 (s, 1H), 11.84 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.3, 35.5, 58.1, 101.2, 118.6, 119.0, 119.4, 123.2, 125.1, 125.3, 127.1, 128.0, 129.8, 130.3, 136.1, 137.0, 137.3, 144.2, 146.9, 163.2, 166.5, 200.1; HRMS: *m/z* calcd for $C_{24}H_{20}N_3O_3S$: 430.1220, found: 430.1221 $[M+H]^+$.

One-pot procedure for the synthesis of 8 and **10**. Products **8** and **10** were synthesized as analogous procedure for **4** and **6**.

(*Z*)-5-(3-Hydroxybut-2-en-1-yl)-3-methyl-1,4-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-*b*]pyridi*n*-6(7*H*)-one (8). White solid; mp 229–230°C; IR (KBr) 757, 1076, 1324, 1603, 1674, 3226, 3436 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.93 (s, 3H), 2.02 (s, 3H), 3.70 (d, $J=5.8$ Hz, 1H), 4.64 (d, $J=5.8$ Hz, 1H), 5.58 (s, 1H), 7.20–7.24 (m, 2H), 7.28–7.39 (m, 4H), 7.45–7.49 (m, 4H), 8.16 (s, 1H), 15.07 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.4, 23.8, 38.6, 60.3, 100.0, 101.7, 122.9, 127.4, 127.5, 127.9, 129.0, 129.9, 136.2, 137.2, 140.9, 147.2, 167.2, 188.5, 190.4; HRMS: *m/z* calcd for $C_{23}H_{22}N_3O_3$: 388.1656, found: 388.1662 $[M+H]^+$.

5′-(2-hydroxybenzoyl)-3′-methyl-1′-phenyl-5′,7′-dihydro-2H-spiro [acenaphthylene-1,4′-pyrazolo[3,4-*b*]pyridine]-2,6′(1′H)-dione (10). Yellow solid; mp 269–270°C; IR (KBr) 759, 1304, 1490, 1562, 1633, 1715, 3257, 3440 cm^{-1}; ^1H NMR (DMSO-d_6): δ 0.86 (s, 3H), 6.41 (s, 1H), 6.88 (d, $J=7.7$ Hz, 2H), 7.36–7.69 (m, 8H), 7.88–8.05 (m, 4H), 8.31 (d, $J=8.1$ Hz, 1H), 10.99 (s, 1H), 11.20 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 11.3, 52.2, 58.1, 102.8, 117.6, 119.3, 120.4, 121.8, 122.1, 122.7, 125.2, 127.1, 128.7, 128.9, 129.3, 130.2, 131.4, 131.5, 132.4, 136.3, 137.8, 138.1, 139.3, 141.2, 144.1, 160.0, 168.1, 197.9,201.6; HRMS: *m/z* calcd for $C_{31}H_{22}N_3O_4$: 500.1605, found: 500.1616 $[M+H]^+$.

Synthesis of 3-methyl-1,4-diphenyl-4,5-dihydro-1H-pyrazolo [3,4-*b*]pyridin-6(7*H*)-one (11). A solution of **3a** (0.5 mmole) was heated in EtOH (4 mL) under reflux. After the reaction was completed (4 h, monitored by TLC), the mixture was slowly cooled at room temperature and purified by column chromatography using petroleum ether–ethyl acetate as eluent to deliver **11** as the white solid; mp 148–149°C; IR (KBr) 766, 1074, 1330, 1680, 3449 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.96 (s, 3H), 2.87 (dd, $J_1=16.3$ Hz, $J_2=6.5$ Hz, 1H), 3.08 (dd, $J_1=16.3$ Hz, $J_2=7.3$ Hz, 1H), 4.24 (t, $J=6.8$ Hz, 1H), 7.22–7.25 (m, 2H), 7.28–7.41 (m, 3H), 7.46–7.53 (m, 4H), 7.76 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.5, 35.5, 40.6, 102.7, 122.9, 127.1, 127.2, 127.8, 128.9, 129.9, 137.3, 137.4, 142.2, 146.9, 169.6; HRMS: *m/z* calcd for $C_{19}H_{18}N_3O$: 304.1444, found: 304.1447 $[M+H]^+$.

Acknowledgments. We gratefully acknowledge support from the Educational Commission of Hubei Province (D20142501).

REFERENCES AND NOTES

[1] Allais, C.; Grassot, J. M.; Rodriguez, J.; Constantieux, T. Chem Rev 2014, 114, 10829.

[2] Barreiro, E. J.; Camara, C. A.; Verli, H.; Brazil-Más, L.; Castro, N. G.; Cintra, W. M.; Aracava, Y.; Rodrigues, C. R.; Fraga, C. A. M. J Med Chem 2003, 46, 1144.

[3] (a) Williams, M. J Med Chem 1983, 26, 619; (b) Placheta, P.; Karobath, M. Eur J Pharmacol 1980, 62, 225; (c) Patel, J. B.; Malick, J. B. Eur J Pharmacol 1982, 78, 323.

[4] Patil, P. O.; Bari, S. B.; Firke, S. D.; Deshmukh, P. K.; Donda, S. T.; Patil, D. A. Bioorg Med Chem 2013, 21, 2434.

[5] Ahmad, V. U.; Ullah, F.; Hussain, J.; Farooq, U.; Zubair, M.; Khan, M. T. H.; Choudhary, M. I. Chem Pharm Bull 2004, 52, 1458.

[6] Dömling, A.; Wang, W.; Wang, K. Chem Rev 2012, 112, 3083.

[7] Jiang, B.; Rajale, T.; Wever, W.; Tu, S. J.; Li, G. G. Chem Asian J 2010, 5, 2318.

[8] Jiang, B.; Liu, Y. P.; Tu, S. J. Eur J Org Chem 2011, 3026.

[9] Hao, W. J.; Xu, X. P.; Bai, H. W.; Wang, S. Y.; Ji, S. J. Org Lett 2012, 14, 4894.

[10] Gunasekaran, P.; Indumathi, S.; Perumal, S. RSC Adv 2013, 3, 8318.

[11] (a) Manpadi, M.; Uglinskii, P. Y.; Rastogi, S. K.; Cotter, K. M.; Wong, Y. S. C.; Anderson, L. A.; Ortega, A. J.; Van-slambrouck, S.; Steelant, W. F. A.; Rogelj, S.; Tongwa, P.; Antipin, M. Y.; Magedov, I. V.; Kornienko, A. Org Biomol Chem 2007, 5, 3865; (b) Bazgir, A.; Ahadi, S.; Ghahremanzadeh, R.; Khavasi, H. R.; Mirzaei, P. Ultrasonics Chem 2010, 17, 447; (c) Tu, X. J.; Hao, W. J.; Ye, Q.; Wang, S. S.; Jiang, B.; Li, G.; Tu, S. J. J Org Chem 2014, 79, 11110.

[12] (a) Beutner, G. L.; Kuethe, J. T.; Kim, M. M.; Yasuda, N. J Org Chem 2009, 74, 789; (b) Lee, S.; Park, S. B. Org Lett 2009, 11, 5214.

[13] Iaroshenko, V. O.; Erben, F.; Mkrtchyan, S.; Hakobyan, A.; Vilches-Herrera, M.; Dudkin, S.; Bunescu, A.; Villinger, A.; Sosnovskikh, V. Y.; Langer, P. Tetrahedron 2011, 67, 7946.

[14] Shekarrao, K.; Kaishap, P. P.; Saddanapu, V.; Addlagatta, A.; Gogoi, S.; Boruah, R. C. RSC Adv 2014, 4, 24001.

[15] Chen, J. H.; Liu, W. M.; Ma, J. J.; Xu, H. T.; Wu, J. S.; Tang, X. L.; Fan, Z. Y.; Wang, P. F. J Org Chem 2012, 77, 3475.

[16] Hao, Y.; Xu, X. P.; Chen, T.; Zhao, L. L.; Ji, S. J. Org Biomol Chem 2012, 10, 724.

[17] Pal, S.; Khan, M. N.; Karamthulla, S.; Choudhury, L. H. RSC Adv 2013, 3, 15705.

[18] Ghosh, A.; Khan, A. T. Tetrahedron Lett 2014, 55, 2006.

[19] Yin, G. D.; Ren, T. B.; Rao, Y.; Zhou, Y. F.; Li, Z.; Shu, W. M.; Wu, A. X. J Org Chem 2013, 78, 3132.

[20] Crystal data of **4a** (CCDC 1037057). $C_{24}H_{19}N_3O_2 \cdot 2C_2H_6O$, M = 497.58, triclinic, a = 11.270(4), b = 12.125(4), c = 12.411(5) Å, α = 111.185(8)°, β = 103.908(9)°, γ = 109.487(9)°, U = 1359.3(8) Å^3, T = 296(2) K, space group P-1, Z 2, 6921 reflections measured, 3115 unique (R_{int} = 0.0605) which were used in all calculations. The final wR (F_2) was 0.2101 (all data).

[21] Crystal data of **6a** (CCDC 1037058). $C_{26}H_{21}N_3O_3$, M = 423.46, monoclinic, a = 16.8092(15), b = 6.6511(7), c = 21.0780(19) Å, α = 90°, β = 112.272(2)°, γ = 90°, U = 2180.7(4) Å^3, T = 296(2) K, space group P2(1)/n, Z = 4, 4468 reflections measured, 3399 unique (R_{int} = 0.0418) which were used in all calculations. The final wR(F_2) was 0.1185 (all data).

[22] Ahadi, S.; Ghahremanzadeh, R.; Mirzaei, P. Bazgir, A. Tetrahedron 2009, 65, 9316.

[23] Jiang, B.; Zhang, G.; Ma, N.; Shi, F.; Tu, S. J.; Kaur, P.; Li, G. G. Org Biomol Chem 2011, 9, 3834.

[24] Shi, F.; Zhang, J. Y.; Tu, S. J.; Jia, R. H.; Zhang, Y.; Jiang, B.; Jiang, H. J Heterocyclic Chem 2007, 44, 1013.

[25] Ma, N.; Jiang, B.; Zhang, G. Tu, S. J.; Wever, W.; Li, G. G. Green Chem 2010, 12, 1357.