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Base-Promoted Transannulation of Heterocyclic Enamines and 2,3-Epoxypropan-1-ones: Regio- and Stereoselective Synthesis of Fused Pyridines and Pyrroles

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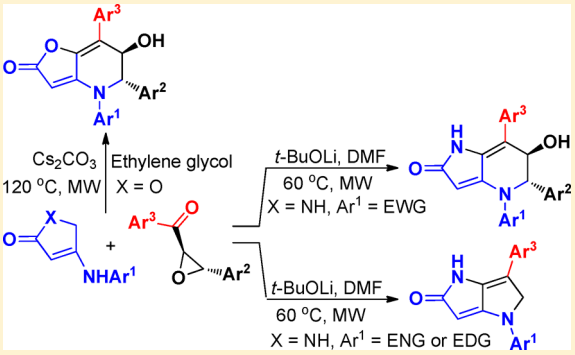
Supporting Information

ABSTRACT: Base-promoted transannulation of heterocyclic enamines and 2,3-epoxypropan-1-ones has been successfully achieved, providing a new access to structurally diverse fused pyridines and pyrroles with excellent regio- and stereoselectivity. Treatment with *N*-aryl 4-aminofuran-2(5*H*)-ones and 2,3-epoxypropan-1-ones under microwave heating resulted in functional furo[3,2-*b*]pyridines in good yields. The *N*-aryl 4-aminopyrrol-2(5*H*)-ones bearing an electron-withdrawing group engaged in the reaction afforded pyrrolo[3,2-*b*]pyridines, whereas their counterparts with an electron-neutral or an electron-donating group underwent a different reaction pathway to form pyrrolo[3,2-*b*]pyrroles through C−C bond cleavage.



INTRODUCTION

Oxa-aza-containing bicyclic skeletons are omnipresent in a wide range of naturally and unnaturally occurring products with important biological activities.[1] Among these products, furo[3,2-*b*]pyridine scaffolds combining a π-electron rich furan ring and a π-electron deficient pyridine ring have captured special interest owing to their synthetic potential. This potential arises from their substituent diversity as well as their interesting biological properties. For instance, they can serve as SYK inhibitors[2] (Figure 1, type I), therapeutic sodium channel blockers,[3] FXa inhibitors,[4] nicotinic acetylcholine receptors,[5] and retroviral protease inhibitors.[6] Furo[3,2-*b*]pyridine derivatives commonly exist in a wide range of natural alkaloids, represented by kopsilactone[7] (Figure 1, type II) and isofebrifugine[8] (type III). In addition to their biological benefits, such heterocycles have proven to be versatile synthons, and have been efficiently employed in the total synthesis of natural products and the preparation of bioactive molecules.[9] With these attributes in mind, the scientific community devotes a great effort in finding new synthetic methods for the synthesis of furo[3,2-*b*]pyridines and their structural analogues.

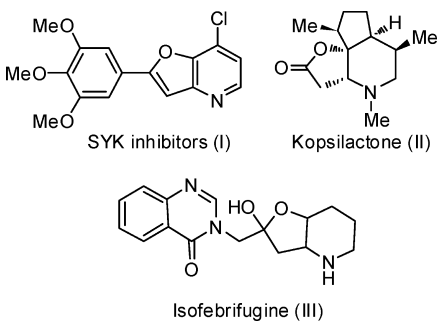


Figure 1. Biologically important furo[3,2-*b*]pyridine derivatives.

A survey of the literature revealed that substantial synthetic methods for the formation of functional furo[3,2-*b*]pyridines have been developed, which involved carbanionic ring closure,[10] photocyclization of 3-furanyl-3-aminoalkene imines,[11] heteroaromatic C-H insertion of alkylidenecarbenes,[12] metal-catalyzed heteroannulation of alkynes,[13] and other methods.[14] Nevertheless, most of these approaches suffered from many drawbacks such as a limited substrate scope, multistep sequences, metal catalysts, and laborious workup. Therefore, the exploration of new and more efficient synthetic strategies, especially metal-free pathways, to access functionalized furo[3,2-*b*]pyridines is critical to the pharmaceutical and fine chemical industries.

N-substituted 4-aminofuran-2(5*H*)-ones possessing C,N-nucleophilic sites are versatile heterocyclic enamine (aza-ene)

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feedstocks in organic, medicinal, and materials chemistry.[15] In particular, the heterocyclization of *N*-substituted 4-aminofuran-2(5*H*)-ones with a,b-nucleophilic centers has been investigated extensively over the past few decades, resulting in well-developed procedures[16] (Figure 2, eq 1). However, *in sharp*

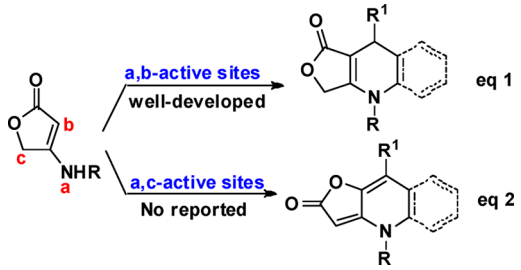


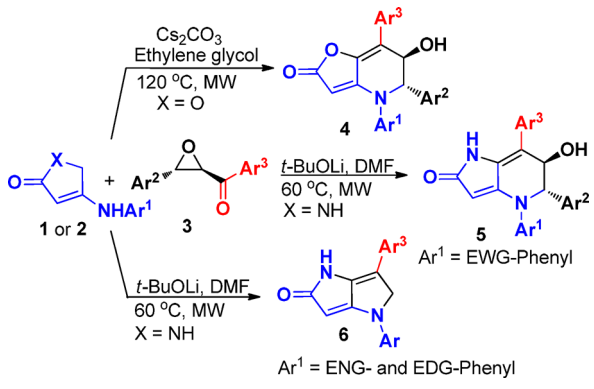
Figure 2. Profiling applications of 4-aminofuran-2(5*H*)-ones.

contrast, the simultaneous functionalization of a,c-active sites on a 4-aminofuran-2(5H)-one ring generating aza-heterocyces has not been reported so far, although its great potential in C−N bond and C−C bond formation (eq 2). Due to the inductive effect of the oxygen atom and the carbonyls on the furan ring, we conceived that deprotonation at the c-position could provide a suitable nucleophile, which would enable the construction of important multifunctional aza-heterocycles. Considering this challenging project and the great demand for the construction of aza-heterocycles, we designed a series of furo[3,2-*b*]pyridines via a regioselective transannulation between *N*-aryl 4-aminofuran-2(5*H*)-ones and 1,3-diaryl-2,3-epoxypropan-1-ones under microwave (MW) heating. Using 4-aminopyrrol-2(5*H*)-ones **2** as replacement for 4-aminofuran-2(5*H*)-ones **1**, this formal (3 + 3) cycloaddition reaction gave two different products depending on the electronic properties of the substituents on the aniline moiety of the 4-aminopyrrol-2(5*H*)-ones. The *N*-aryl 4-aminopyrrol-2(5*H*)-ones **2** bearing an electron-withdrawing group (EWG) afforded a high yield of the desired pyrrolo[3,2-*b*]pyridines, whereas electron-neutral (ENG) and -donating (EDG) substituents preferred a different reaction pathway, forming new polyfunctionalized pyrrolo[3,2-*b*]-pyrroles through C−C bond cleavage (Scheme 1).

RESULTS AND DISCUSSION

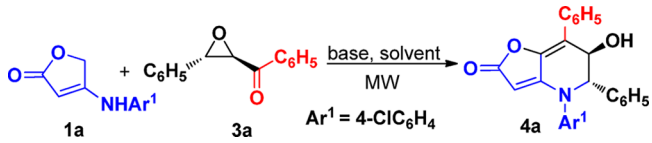
To develop metal-free conditions for the regioselective transannulation, we started our study by preparing *N*-aryl 4-aminofuran-2(5*H*)-ones and 1,3-diaryl-2,3-epoxypropan-1-ones

Scheme 1. Synthesis of Substituted Fused Pyridines and Pyrroles



in our laboratory according to the literature procedure.[17] In order to optimize the reaction conditions, *N*-4-chlorophenyl 4-aminofuran-2(5*H*)-one **1a** and 1,3-diphenyl-2,3-epoxypropan-1-one **3a** were investigated as model substrates using different bases for the synthesis of functional furo[3,2-*b*]pyridines (Table 1).

Table 1. Optimization of Conditions for Forming Product 4a under MW



entry	base (equiv)	solvent	temp (°C)	yield[a] /%
1	Et_3N (1.0)	ethylene glycol	100	trace
2	EtONa (1.0)	ethylene glycol	100	trace
3	NaOH (1.0)	ethylene glycol	100	31
4	K_2CO_3 (1.0)	ethylene glycol	100	52
5	Cs_2CO_3 (1.0)	ethylene glycol	100	74
6	Cs_2CO_3 (1.0)	EtOH	100	69
7	Cs_2CO_3 (1.0)	CH_3CN	100	32
8	Cs_2CO_3 (1.0)	DMF	100	12
9	Cs_2CO_3 (1.0)	ethylene glycol	80	70
10	Cs_2CO_3 (1.0)	ethylene glycol	120	81
11	Cs_2CO_3 (1.0)	ethylene glycol	130	79

[a]Isolated yield.

As shown in Table 1, the reaction afforded only trace product in the presence of Et_3N and EtONa (1.0 equiv) in ethylene glycol (EG) at 100 °C for 15 min. The desired product **4a** was isolated in poor yield (31%) using NaOH as a base promoter. The use of K_2CO_3 gave higher yield (up to 52%). To our delight, the desired product **4a** was obtained in 74% yield in the presence of Cs_2CO_3 (1.0 equiv) (Table 1, entry 5). Taking Cs_2CO_3 as the optimized base, we varied other parameters. Other polar solvents such as EtOH, acetonitrile, and DMF were inferior to ethylene glycol in terms of reaction yields. Next, the reaction temperature was investigated. Raising the temperature slightly to 120 °C proved more efficient, affording the expected product **4a** in 81% yield. Further lowering or raising of the reaction temperature did not significantly change the yield (entries 9 and 11).

The scope for *N*-aryl enamines was investigated first under the optimized conditions [Cs_2CO_3 (1.0 equiv), EG, 120 °C, MW] (Scheme 2). First, the effects of *N*-substituents on 4-aminofuran-2(5*H*)-ones were investigated by employing different aryl groups bearing a variety of electron-withdrawing (chloro and bromo) or electron-donating groups (such as methyl and methoxyl). Among them, *N*-substituents bearing withdrawing groups showed the higher reactivity than their electron-donating counterparts. For instance, 4-((4-bromophenyl)amino)furan-2(5H)-one **1b** with a bromo group reacted with 1,3-diphenyl-2,3-epoxypropan-1-ones **3a**, affording the corresponding product **4b** in 82% yield. The presence of a methyl group on the phenyl ring of substrate **1f** resulted in the desired product **4f** in 66% yield. The exact structure of product **4j** was unequivocally determined by single-crystal X-ray analysis. These experimental facts indicated that the electronic nature of the *N*-substituents seemed to exert a delicate effect on the reactivity. Then, a series of 1,3-diaryl-2,3-epoxypropan-1-ones with electronically poor substituents linked to the Ar^2 ring

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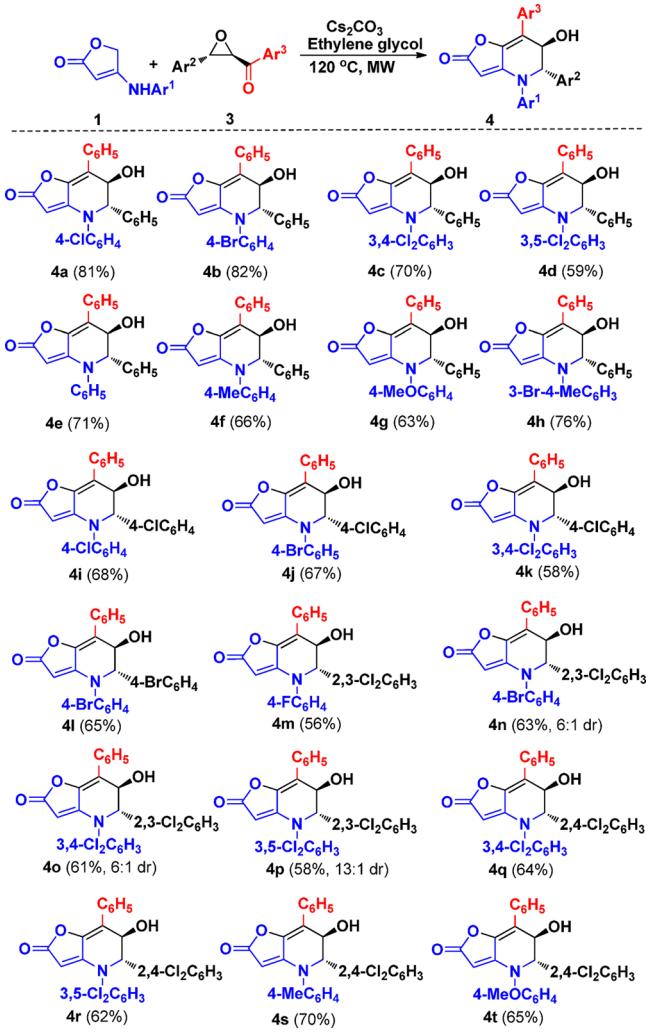
Scheme 2. Synthesis of Functional Furo[3,2-*b*]pyridines[a,b]

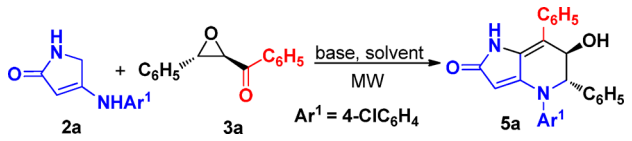


[a]Reaction conditions: **1** (1.0 mmol), **3** (1.0 mmol), Cs_2CO_3 (1.0 mmol), ethylene glycol (1.5 mL), 120 °C, MW. [b]Isolated yield based on substrate **1**.

were utilized in the transannulation, generating the desired furo[3,2-*b*]pyridines containing two stereogenic centers in generally high yields and excellent diastereoselectivity (only one isomer except **4n**−**4p**). Among them, bulky 2-subsituted Ar^2 groups lowered the yield of the cycloaddition reaction relative to those obtained with 2-unsubsituted analogues, which indicated that the steric hindrance exerted some influence on the reactivity of the substrates. These examples showed the efficiency and applicability of this strategy to the simultaneous functionalization of the a,c-active sites on the 4-aminofuran-2(5*H*)-one ring.

After our success with functional furo[3,2-*b*]pyridines **4**, we turned our attention to evaluating the feasibility of the synthesis of pyrrolo[3,2-*b*]pyridines **5**. The cycloaddition reaction between *N*-4-chlorophenyl 4-aminopyrrol-2(5*H*)-one **2a** and 1,3-diphenyl-2,3-epoxypropan-1-one **3a** was conducted under the conditions described above. The expected pyrrolo[3,2-*b*]pyridines **5a** could not be obtained. Instead, a black gelatinous liquid was observed, most likely due to the decomposition of 4-aminopyrrol-2(5*H*)-one **2a** as a result of the high temperature. Lowering the reaction temperature from 120 to 50 °C failed to give the product **5a**. Next, we adjusted bases and solvents for the optimized conditions (Table 2). The use of 1.0 equiv of Cs_2CO_3, NaOH, and Et_3N as well as EtONa

Table 2. Optimization of Conditions for Forming Product 5a



entry	base (equiv)	solvent	temp (°C)	yield (%)
1	Cs_2CO_3 (1.0)	ethylene glycol	120	no
2	Cs_2CO_3 (1.0)	ethylene glycol	50	no
3	Cs_2CO_3 (1.0)	DMF	50	trace
4	Et_3N (1.0)	DMF	50	trace
5	NaOH (1.0)	DMF	50	trace
6	EtONa (1.0)	DMF	50	12
7	*t*-BuOK (1.0)	DMF	50	52
8	*t*-BuOLi (1.0)	DMF	50	61
9	*t*-BuOLi (1.0)	CH_3CN	50	60
10	*t*-BuOLi (1.0)	EtOH	50	41
11	*t*-BuOLi (1.0)	DMF	60	82
12	*t*-BuOLi (1.0)	DMF	40	50

in DMF was met with little success (Table 2, entries 2−6). Stronger bases such as *t*-BuOK and *t*-BuOLi were then tried, and 1.0 equiv of *t*-BuOK gave the target product **5a** in 52% yield (entry 7). Exchanging *t*-BuOK for *t*-BuOLi (1.0 equiv) led to a slightly higher yield (61% yield, entry 8). After careful optimizations, we found that *t*-BuOLi (1.0 equiv) in DMF at 60 °C was the most suitable condition for the cycloaddition reaction, affording the expected product in the best yield of 82% (entry 11).

With the established optimal conditions, we were eager to investigate the substrate scope of 4-aminopyrrol-2(5*H*)-one **2a** and 1,3-diaryl-2,3-epoxypropan-1-ones **3**. As shown in Scheme 3, this protocol tolerates a broad range of 1,3-diaryl-2,3-epoxypropan-1-ones, leading to a highly diastereoselective synthesis of structurally diverse pyrrolo[3,2-*b*]pyridines in generally good yields. In detail, 1,3-diaryl-2,3-epoxypropan-1-ones **3** carrying either electronically poor, neutral, or rich groups could successfully participate in the [3 + 3] cycloaddition with 4-aminopyrrol-2(5*H*)-one **2** with electron-withdrawing substituents in overall acceptable yields (up to 82%) and high stereoselectivity (only one isomer except **5c**). However, the bulk steric hindrance related to 1,3-diaryl-2,3-epoxypropan-1-ones decreased this reactive behavior, leading to relatively lower yields for products **5e**−**5g**. Furthermore, 4-aminopyrrol-2(5*H*)-ones **2** bearing electron-neutral or electron-rich groups were examined by the reactions with 1,3-diaryl-2,3-epoxypropan-1-ones **3** under the optimal conditions. Unexpectedly, the target pyrrolo[3,2-*b*]pyridines **5** were not obtained. Instead, the reaction underwent another direction to form new polyfunctionalized pyrrolo[3,2-*b*]pyrroles **6** through C−C bond cleavage (Scheme 4). Next, we set out to vary the substituents of 4-aminopyrrol-2(5*H*)-ones **2** and treated these derivatives to the treatment with 1,3-diphenyl-2,3-epoxypropan-1-one **3a**. Both methyl and methoxy functional groups in the 4-aminopyrrol-2(5*H*)-ones delivered the corresponding pyrrolo[3,2-*b*]pyrroles **6b**−**c** with good yields (Scheme 4, eq 1). Finally, single-crystal X-ray diffraction analysis of **6b** was carried out for further structural confirmation. This above observation illustrates that the

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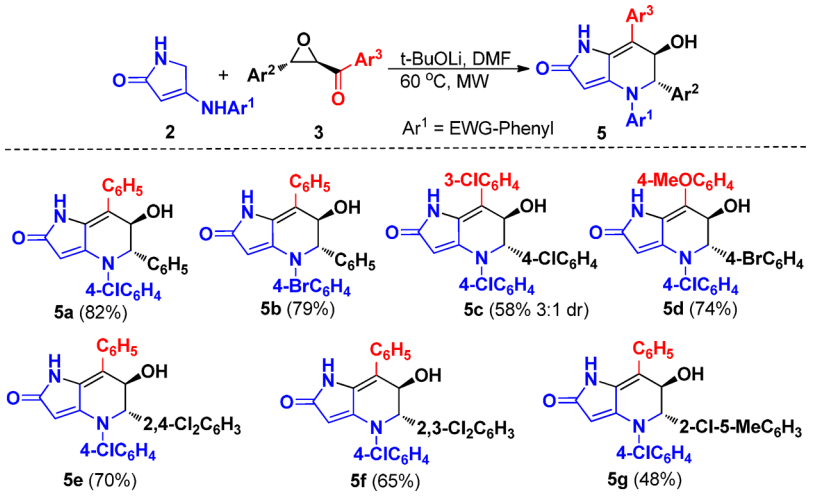
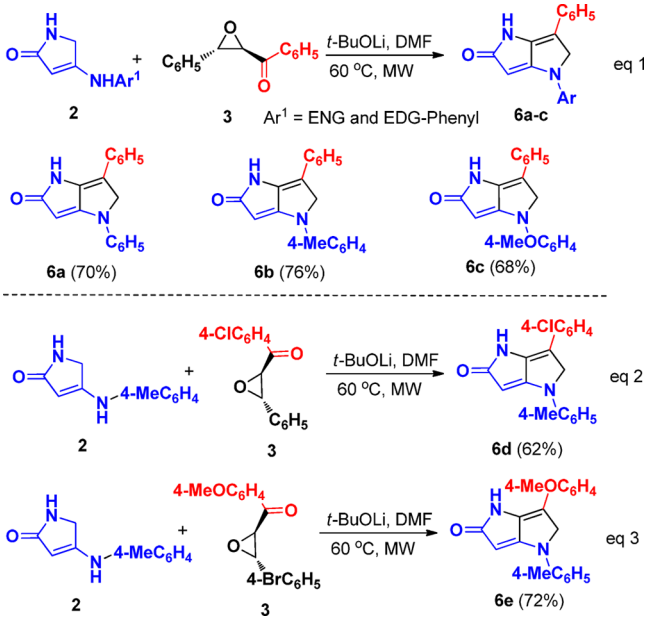
Scheme 3. Synthesis of Functional Pyrrolo-Fused Pyridines 5[a,b]



[a]Reaction conditions: **2** (1.0 mmol), **3** (1.0 mmol), *t*-BuOLi (1.0 mmol), DMF (1.5 mL), 60 °C, MW. [b]Isolated yield based on substrate **2**.

Scheme 4. Synthesis of Functional Pyrrolo-Fused Pyrroles 6[a,b]

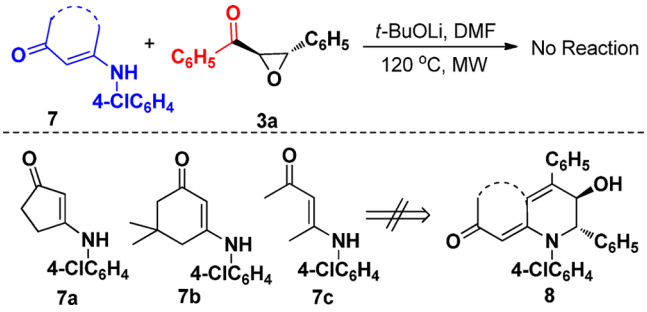


[a]Reaction conditions: **2** (1.0 mmol), **3** (1.0 mmol), *t*-BuOLi (1.0 mmol), DMF (1.5 mL), 60 °C, MW. [b]Isolated yield based on substrate **2**.

electronic nature of the substituents on the 4-aminopyrrol-2(5*H*)-ones may control chemoselectivity of the reaction. In order to gain insight regarding the C−C bond cleavage, some control experiments were performed under the optimal reaction conditions using different substituents linked to the benzene ring of 1,3-diaryl-2,3-epoxypropan-1-one **3**. (4-Chlorophenyl)-(3-phenyloxiran-2-yl)methanone and (3-(4-bromophenyl)-oxiran-2-yl)(4-methoxyphenyl)methanone were reacted with 4-(*p*-tolylamino)-1*H*-pyrrol-2(5*H*)-one, respectively, transforming readily into 4-chlorophenyl and 4-methoxyphenyl substituted pyrrolo[3,2-*b*]pyrroles **6d** (62%) and **6e** (72%) (Scheme 4, eqs 2 and 3). This suggested that the C−C bond cleavage occurred in the oxirane ring. In general, this new transannulation gives new examples for the formation of richly decorated fused pyrrol-2(5*H*)-ones, which are ubiquitous structural units in a substantial number of bioactive compounds.

After the formation of functional products **4**−**6**, we devoted our efforts to further probe the generality of the new transannulation. Instead of heterocyclic enamines **1** or **2**, carbocyclic or acyclic enamines **7a**−**c** were employed to react with substrate **3a**, respectively (Scheme 5). Unfortunately,

Scheme 5. Exploration of Reaction Scope



almost all of the starting material was recovered and the desired product **8** was not detected at all. It is obvious that these carbocyclic or acyclic enamines **7a**−**c** showed poor reactivity in the cycloaddition reaction.

On the basis of our experimental observations and literature precedents, plausible mechanistic pathways to products **4**−**6** are illustrated in Schemes 6 and 7. Initially, nucleophilic addition of heterocyclic enamines **1** or **2** (Ar^1 = EWG) to the *β*-position of oxiranes **3** in the presence of base generates intermediate **A**, followed by H-transfer and intramolecular Knoevenagel condensation, to afford the final fused pyridines **4** and **5** (Scheme 6). Heterocyclic enamines **2** carrying electron-donating (EDG) and electron-neutral (ENG) aryl rings may enhance C5 nucleophilicity of the pyrrol-2(5*H*)-one ring, thereby favoring aldol-type reaction of oxiranes **3**. In view of this consideration, the *N*-position of heterocyclic enamines **2c**−**e** (Ar^1 = EDG or ENG) is activated by strong base, which undergoes 1,3-H transfer to form intermediate **C**. Intermediate **C** facilitates aldol-type reaction of oxiranes **3**, providing adduct intermediate **D**. Next, the *N*-position of adduct intermediate **D**

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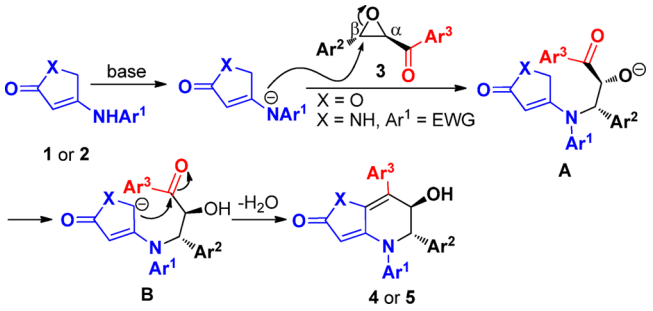
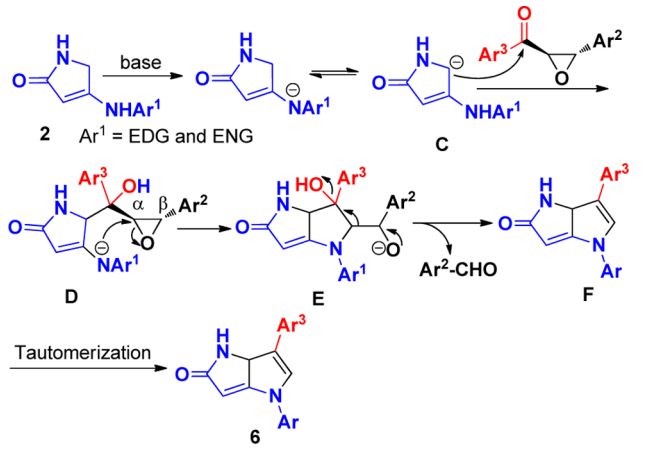
Scheme 6. Plausible Mechanistic Pathways to Products 4−5



Scheme 7. Plausible Mechanistic Pathways to Products 6



attacks selectively on the α-position of oxiranes **3** in an intramolecular manner, giving rise to intermediate **E**. Intermediate **E** releases an aryl aldehyde and a hydroxyl anion to yield pyrrolo[3,2-*b*]pyrrole intermediate **F**, which converted into the final pyrrolo[3,2-*b*]pyrroles **6** through tautomerization (Scheme 7). In both reactions, the key steps of bifurcate transannulations to different products involve nucleophilic addition of heterocyclic enamines to different positions of oxiranes **3**, despite that the detailed reason for these divergent additions is not yet clear to us.

In summary, we have established a new and versatile base-promoted transannulation of heterocyclic enamines and 2,3-epoxypropan-1-ones, allowing the conversion of simple starting materials into substituted fused pyridines and pyrroles with excellent regio- and stereoselectivity. The formal [3 + 3] cycloaddition simultaneously installs a C−N and a C−C bond through a key C−O bond cleavage process, enabling the efficient synthesis of diverse furo[3,2-*b*]pyridines and pyrrolo-[3,2-*b*]pyridines with biological relevance. The latter provides a new insight into the [3 + 2] heterocyclization, depending on the electronic properties of the substituents on the aniline moiety of the 4-aminopyrrol-2(5*H*)-ones, which represents a special example for forming pyrrolo[3,2-*b*]pyrroles through a C−O bond and a C−C bond cleavage process. Further study of the mechanism of these divergent transformations and evaluation of their biological activity are in progress.

EXPERIMENTAL SECTION

General. Microwave irradiation was carried out with Initiator 2.5 Microwave Synthesizers from Biotage, Uppsala, Sweden. The reaction temperatures were measured by an infrared detector during microwave heating.

General Procedure for the Synthesis of 4. *Example for the Synthesis of* ***4a****.* 4-((4-Chlorophenyl)amino)furan-2(5H)-one (**1a**, 1.0 mmol, 209 mg) was introduced in a 10 mL Initiator reaction vial; 1,3-diphenyl-2,3-epoxypropan-1-ones (**3a**, 1.0 mmol, 224 mg) and Cs_2CO_3 (1.0 mmol, 326 mg) as well as ethylene glycol (1.5 mL) were then successively added. Subsequently, the reaction vial was capped and then prestirred for 20 s. The mixture was irradiated (time, 20 min; temperature, 120 °C; absorption level, high; fixed hold time) until TLC (petroleum ether/acetone V/V = 3/1) revealed that conversion of the starting material **1a** was complete. The system was diluted with cold water (40 mL). The solid product was collected by Büchner filtration and purified by flash column chromatography (silica gel, mixtures of petroleum ether/ethyl acetate) to afford the pure product **4a**.

*4-(4-Chlorophenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4a**).* Yellow solid (336 mg, 81% yield): mp 201−203 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.38−7.33 (m, 7H), 7.28 (s, 1H), 6.39 (d, J = 7.6 Hz, 1H), 5.38 (s, 1H), 5.22 (s, 1H), 4.84 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.9, 154.8, 142.3, 142.2, 137.8, 133.8, 130.6, 130.1, 129.5, 129.1, 128.6, 128.4, 126.5, 124.9, 112.4, 82.3, 71.4, 70.3; IR (KBr, ν) 3351, 2341, 1737, 1606, 1494, 1216, 1011, 847, 695 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{19}ClNO_3$ 416.1053, found 416.1068.

*4-(4-Bromophenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4b**).* Yellow solid (375 mg, 82% yield): mp 212−214 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.37−7.33 (m, 5H), 7.27 (d, J = 8.8 Hz, 3H), 6.37 (d, J = 7.6 Hz, 1H), 5.39 (s, 1H), 5.22 (s, 1H), 4.84 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.9, 154.6, 142.7, 142.2, 137.8, 133.8, 133.0, 129.5, 129.1, 128.6, 128.4, 126.5, 125.2, 118.8, 112.5, 82.4, 71.4, 70.3; IR (KBr, ν) 3381, 2341, 1741, 1615, 1488, 1251, 1072, 872, 698 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{19}BrNO_3$ 462.0526, found 462.0520.

*4-(3,4-Dichlorophenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydrofuro-[3,2-b]pyridin-2(4H)-one (**4c**).* White solid (314 mg, 70% yield): mp 223−225 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (m, 3H), 7.53 (d, J = 2.8 Hz, 1H), 7.44−7.29 (m, 9H), 6.39 (d, J = 7.6 Hz, 1H), 5.50 (s, 1H,), 5.29 (s, 1H), 4.85 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.8, 154.4, 143.4, 142.0, 137.6, 133.8, 132.4, 132.0, 129.6, 129.2, 129.1, 128.7, 128.6, 128.5, 126.5, 125.0, 123.4, 112.8, 83.4, 71.3, 70.1; IR(KBr, ν) 3358, 2361, 1737, 1603, 1475, 1288, 1037, 895, 695 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Cl_2NO_3$ 450.0658, found 450.0654.

*4-(3,5-Dichlorophenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydrofuro-[3,2-b]pyridin-2(4H)-one (**4d**).* Pale white solid (265 mg, 59% yield): mp 237−239 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.2 Hz, 2H), 7.52 (s, 1H), 7.45−7.39 (m, 3H), 7.37 (d, J = 2.0 Hz, 3H), 7.32 (d, J = 1.6 Hz, 4H), 6.34 (d, J = 8.0 Hz, 1H,), 5.57 (s, 1H), 5.32 (s, 1H), 4.86 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.7, 154.2, 145.7, 142.0, 137.5, 135.3, 133.7, 129.6 129.2, 129.1, 128.7, 128.5, 126.5, 126.2, 121.9, 112.9, 84.1, 71.3, 70.0; IR (KBr, ν) 3391, 2361, 1730, 1572, 1447, 1212, 1044, 811, 852, 692 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Cl_2NO_3$ 450.0658, found 450.0657.

*6-Hydroxy-4,5,7-triphenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4e**).* Pale white solid (271 mg, 71% yield): mp 243−245 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 7.6 Hz, 2H), 7.43 (d, J = 7.6 Hz, 4H), 7.37−7.32 (m, 7.0 Hz, 7H), 7.27 (d, J = 7.2 Hz, 2H), 6.36 (d, J = 7.6 Hz, 1H), 5.28 (s, 1H), 5.23 (s, 1H), 4.83 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 155.0, 143.4, 142.3, 138.1, 133.9, 130.1, 129.5, 129.1, 129.0, 128.6, 128.3, 126.7, 126.6, 123.1, 112.2, 81.5, 71.5, 70.4; IR (KBr, ν) 3369, 2342, 1738, 1614, 1493, 1274, 1048, 869, 695 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{20}NO_3$ 382.1438, found 382.1439.

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*6-Hydroxy-5,7-diphenyl-4-(p-tolyl)-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4f**)*. Pale white solid (261 mg, 66% yield): mp 246−248 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.6 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.38−7.30 (m, 5H), 7.29−7.20 (m, 5H), 6.35 (d, J = 7.2 Hz, 1H), 5.18 (s, 2H), 4.80 (d, J = 7.6 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 155.2, 142.3, 140.9, 138.1, 136.3, 134.0, 130.6, 129.4, 129.1, 129.0, 128.6, 128.3, 126.6, 123.4, 112.1, 80.9, 71.4, 70.6, 21.0; IR (KBr, ν) 3691, 2361, 1742, 1599, 1509,1436, 1034, 867, 699 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{22}NO_3$ 396.1564, found 396.1564.

*6-Hydroxy-4-(4-methoxyphenyl)-5,7-diphenyl-5,6-dihydrofuro-[3,2-b]pyridin-2(4H)-one (**4g**)*. White solid (255 mg, 63% yield): mp 239−241 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.6 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.36−7.31 (m, 5H), 7.26 (d, J = 9.2 Hz, 3H), 6.99 (d, J = 9.2 Hz, 2H), 6.35 (d, J = 7.6 Hz, 1H), 5.12 (s, 1H), 5.04 (s, 1H), 4.78 (d, J = 7.2 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 158.0, 155.7, 142.2, 138.0, 136.1, 134.0, 129.4, 129.1, 129.0, 128.6, 128.3, 126.7, 125.4, 115.3, 112.0, 80.2, 71.5, 71.0, 55.8; IR (KBr, ν) 3375, 2342, 1740, 1599, 1510, 1247, 1032, 865, 759, 669 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{22}NO_4$ 412.1543, found 412.1543.

*4-(3-Bromo-4-methylphenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4h**)*. White solid (359 mg, 76% yield): mp 240−242 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.6 Hz, 2H), 7.50 (d, J = 2.0 Hz, 1H), 7.44−7.39 (m, 3H), 7.38−7.32 (m, 5H), 7.30−7.25 (m, 2H), 6.34 (d, J = 7.6 Hz, 1H), 5.29 (s, 1H), 5.22 (s, 1H), 4.82 (d, J = 7.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.8, 154.9, 142.4, 142.1, 137.7, 136.0, 133.9, 132.3, 129.5, 129.1, 128.6, 128.4, 126.8, 126.6, 124.8, 122.8, 112.5, 82.0, 71.4, 70.4, 22.4; IR (KBr, ν) 3374, 2342, 1742, 1590, 1494, 1212, 1039, 775, 693 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{21}BrNO_3$ 476.0683, found 476.0687.

*4,5-Bis(4-chlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4i**)*. Pale white solid (305 mg, 68% yield): mp 209−211 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 7.2 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.42 (t, J = 6.4 Hz, 4H), 7.38−7.31 (m, 5H), 6.41 (s, 1H), 5.38 (s, 1H), 5.24 (s, 1H), 4.81 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.8, 154.6, 142.1, 136.8, 133.7, 133.1, 130.7, 130.2, 129.5, 129.1, 128.6, 128.6, 125.0, 112.4, 82.6, 71.1, 69.6; IR (KBr, ν) 3379, 2341, 1736, 1585, 1492, 1255, 1092, 781, 688 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Cl_2NO_3$ 450.0663, found 450.0660.

*4-(4-Bromophenyl)-5-(4-chlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4j**)*. Yellow solid (330 mg, 67% yield): mp 200−202 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.45−7.41 (m, 4H), 7.39−7.32 (m, 3H), 7.26 (d, J = 8.8 Hz, 2H), 6.39 (d, J = 7.6 Hz, 1H), 5.39 (s, 1H), 5.24 (s, 1H), 4.82 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.9, 154.5, 142.7, 142.2, 137. 3, 133.8, 133.2, 132.5, 132.0, 129.2, 129.0, 128.7, 125.3, 121.8, 119.0, 112.5, 82.8, 71.2, 69.7; IR (KBr, ν) 3348, 2330, 1721, 1618, 1490, 1210, 1011, 854, 702 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}BrClNO_3$ 496.0133, found 496.0132.

*5-(4-Chlorophenyl)-4-(3,4-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4k**)*. Pale yellow solid (280 mg, 58% yield): mp 219−221 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74−7.68 (m, 3H), 7.55 (s, 1H), 7.44−7.41 (m, 4H), 7.37 (d, J = 8.8 Hz, 3H), 7.29 (d, J = 8.8 Hz, 1H), 6.37 (d, J = 8.0 Hz, 1H), 5.50 (s, 1H), 5.30 (s, 1H), 4.83 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.7, 154.2, 143.2, 142.0, 136.6, 133.7, 133.1, 132.4, 132.0, 129.5, 129.2, 129.1, 128.8, 128. 7, 128.6, 125.2, 123.5, 112.8, 83.7, 71.1, 69.4; IR (KBr, ν) 3387, 2361, 1733, 1604, 1415, 1287, 1117, 783, 691 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{17}Cl_3NO_3$ 486.0243, found 486.0243.

*4,5-Bis(4-bromophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4l**)*. White yellow solid (372 mg, 65% yield): mp 222−224 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.4 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.37−7.24 (m, 5H), 6.41 (d, J = 7.6 Hz, 1H), 5.40 (s, 1H), 5.23 (s, 1H), 4.82 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.8, 154.4, 142.5, 142.1, 137.2, 133.7, 133.1, 132.4, 129.1, 128.9, 128.6, 125.2, 121.7, 118.9, 112.4, 82.7, 71.1, 69.6; IR (KBr, ν) 3364, 1719, 1624, 1433, 1307, 1261, 1011, 837, 720, 691 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Br_2NO_3$ 539.9633, found 539.9629.

*5-(2,3-Dichlorophenyl)-4-(4-fluorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4m**)*. Pale white solid (262 mg, 56% yield): mp 213-215 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72−7.62 (m, 3H), 7.43−7.36 (m, 9H), 6.76 (s, 1H), 5.43 (s, 1H), 5.23 (s, 1H), 4.76 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.7, 160.0 ($^1J_{CF}$ = 243.4 Hz), 155.3, 142.0, 139.3, 137.0, 133.7, 133.3, 131.0, 130.2 ($^3J_{CF}$ = 7.1 Hz), 129.5 129.2, 128.6, 126.5, 126.2, 126.1, 117.3 ($^2J_{CF}$ = 22.9 Hz), 112.2, 82.2, 68.9, 68.9; IR(KBr, ν) 3385, 2341, 1732, 1606, 1413, 1218, 1055, 864, 692 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{17}Cl_2FNO_3$ 468.0564, found 468.0556.

*4-(4-Bromophenyl)-5-(2,3-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4n**)*. White solid (332 mg, 63% yield): mp 239−241 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 8.8 Hz, 3H), 7.61 (s, 1H), 7.46−7.40 (m, 3H), 7.40−7.34 (m, 2H), 7.26 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 7.6 Hz, 1H), 5.44 (s, 1H), 5.38 (s, 1H), 4.77 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.7, 154.6, 142.3, 142.0, 136.9, 133.7, 133.3, 132.7, 131.0, 130.1, 129.5, 129.2, 128.6, 126.4, 125.5, 123.2, 119.5, 112.3, 83.2, 68.8, 68.6; IR (KBr, ν) 3376, 2360, 1734, 1602, 1414, 1286, 1052, 896, 692 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{17}BrCl_2NO_3$ 529.9742, found 529.9736.

*4,5-Bis(2,3-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro-[3,2-b]pyridin-2(4H)-one (**4o**)*. White solid (315 mg, 61% yield): mp 236−238 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 8.0 Hz, 3H), 7.65−7.61 (m, 2H), 7.42 (d, J = 8.0 Hz, 3H), 7.37−7.32 (m, 2H), 7.25 (d, J = 6.4 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 5.49 (s, 1H), 5.46 (s, 1H), 4.79 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.6, 154.4, 142.9, 141.8, 136.6, 133.6, 133.3, 132.6, 132.4, 131.1, 130.2, 129.6, 129.5, 129.3, 129.2, 128.9, 128.6, 125.8, 121.0, 112.5, 84.0, 68.9, 68.6; IR (KBr, ν) 3350, 2338, 1732, 1574, 1475, 1283,1096, 864, 688 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{16}Cl_4NO_3$ 519.9852, found 519.9851.

*5-(2,3-Dichlorophenyl)-4-(3,5-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4p**)*. Yellow solid (300 mg, 58% yield): mp 232−234 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 7.3 Hz, 2H), 7.63 (d, J = 6.4 Hz, 1H), 7.58 (s, 1H), 7.42 (d, J = 8.0 Hz, 3H), 7.36 (d, J = 2.0 Hz, 4H), 6.69 (d, J = 7.6 Hz, 1H), 5.52 (s, 1H), 5.49 (s, 1H), 4.81 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.5, 154.2, 145.2, 141.7, 136.5, 135.6, 133.5, 133.3, 131.1, 130.1, 129.6, 129.3, 129.2, 128., 127.1, 126.5, 122.7, 112.7, 84.6, 68.8, 68.5; IR (KBr, ν) 3424, 2361, 1735, 1605, 1409, 1297,1117, 874, 689 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{16}Cl_4NO_3$ 519.9852, found 519.9854.

*5-(2,4-Dichlorophenyl)-4-(3,4-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4q**)*. White solid (331 mg, 64% yield): mp 228−230 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 9.2 Hz, 4H), 7.61 (s, 1H), 7.44 (t, J = 7.6 Hz, 3H), 7.36 (t, J = 7.6 Hz, 2H), 7.26 (d, J = 8.8 Hz, 1H), 6.72 (d, J = 7.6 Hz, 1H), 5.50 (s, 1H), 5.39 (s, 1H), 4.76 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.6, 154.4, 142.9, 141.8, 134.3, 133.6, 133.2, 133.2, 132.6, 132.4, 130.5, 129.6, 129.3, 129.2, 129.2, 128.8, 128.6, 125.8, 123.8, 112.5, 84.0, 68.9, 67.6; IR (KBr, ν) 3352, 1776, 1467, 1333, 1048, 836, 700, 654 cm^{-1}; HRMS

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(APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{16}Cl_4NO_3$ 519.9852, found 519.9861.

*5-(2,4-Dichlorophenyl)-4-(3,5-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4r**).* Pale white solid (321 mg, 62% yield): mp 224−226 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75−7.67 (m, 3H), 7.59 (s, 1H), 7.44 (t, J = 7.6 Hz, 3H), 7.36 (d, J = 8.4 Hz, 4H), 6.69 (d, J = 7.6 Hz, 1H), 5.55 (s, 1H), 5.41 (s, 1H), 4.77 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.5, 154.2, 145.2, 141.8, 135.6, 134.4, 133.5, 133.1, 133.0, 130.5, 129.3, 129.2, 128.9, 128.6, 127.1, 122.6, 112.6, 84.7, 68.9, 67.6; IR (KBr, ν) 3371, 2259, 1737, 1679, 1468, 1297, 1097, 854, 694 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{16}Cl_4NO_3$ 519.9852, found 519.9844.

*5-(2,4-Dichlorophenyl)-6-hydroxy-7-phenyl-4-(p-tolyl)-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4s**).* White solid (324 mg, 70% yield): mp 220−222 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73−7.69 (m, 3H), 7.47−7.42 (m, 3H), 7.37−7.33 (m, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 6.72 (d, J = 7.6 Hz, 1H), 5.38 (s, 1H), 5.18 (s, 1H), 4.71 (d, J = 7.6 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.8, 155.2, 142.1, 140.4, 137.0, 134.1, 133.8, 133.7, 133.2, 130.8, 130.4, 129.2, 128.7, 128.6, 123.7, 112.0, 81.7, 69.0, 67.8, 21.0; IR (KBr, ν) 3308, 2342, 1735, 1654, 1431, 1271, 1039, 883, 682 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{20}Cl_2NO_3$ 464.0815, found 464.0819.

*5-(2,4-Dichlorophenyl)-6-hydroxy-4-(4-methoxyphenyl)-7-phenyl-5,6-dihydrofuro[3,2-b]pyridin-2(4H)-one (**4t**).* Yellow solid (311 mg, 65% yield): mp 236−239 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.6 Hz, 2H), 7.69 (s, 1H), 7.48−7.42 (m, 3H), 7.40−7.34 (m, 2H), 7.27 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.72 (d, J = 7.6 Hz, 1H), 5.35 (s, 1H), 5.06 (s, 1H), 4.70 (d, J = 7.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.8, 158.3, 155.7, 142.0, 135.6, 134.1, 133.8, 133.6, 133.3, 130.3, 129.2, 129.2, 129.1, 128.7, 128.5, 125.7, 115.5, 111.9, 81.1, 69.0, 68.1, 55.8; IR (KBr, ν) 3396, 2341, 1727, 1595, 1425, 1219, 1042, 879, 696 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{20}Cl_2NO_4$ 480.0764, found 480.0733.

General Procedure for the Synthesis of 5. *Example for the Synthesis of **5a**.* 4-((4-Chlorophenyl)amino)-1*H*-pyrrol-2(5*H*)-one (**2a**, 1.0 mmol, 208 mg) was introduced in a 10 mL Initiator reaction vial; 1,3-diphenyl-2,3-epoxypropan-1-one (**3a**, 1.0 mmol, 224 mg) and *t*-BuOLi (1.0 mmol, 80 mg) as well as DMF (1.5 mL) were then successively added. Subsequently, the reaction vial was capped and then prestirred for 20 s. The mixture was irradiated (time, 30 min; temperature, 60 °C; absorption level, high; fixed hold time) until TLC (petroleum ether/ethyl acetate V/V = 4/1) revealed that conversion of the starting material **2a** was complete. After the reaction mixture was cooled to room temperature, water (20 mL) was added into the reaction system, resulting in a black viscous liquid isolated from the solution through liquid separation and extraction by using ethyl acetate. The organic phase was concentrated by vacuum distillation and was purified by flash column chromatography (silica gel, mixtures of petroleum ether/ethyl acetate) to afford the desired pure product **5a** as a yellow solid.

*4-(4-Chlorophenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5a**).* Yellow solid (339 mg, 82% yield): mp 242−244 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (s, 1H), 7.46−7.40 (m, 4H), 7.38−7.29 (m, 7H), 7.28−7.23 (m, 3H), 6.06 (d, J = 7.2 Hz, 1H), 5.15 (d, J = 1.2 Hz, 1H), 5.04 (s, 1H), 4.52 (dd, J_1 = 2.0 Hz, J_2 = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 150.3, 143.6, 139.1, 136.9, 132.7, 129.8, 129.3, 129.1, 129.0, 128.1, 128.0, 127.9, 126.6, 124.4, 112.1, 89.0, 72.7, 70.1; IR (KBr, ν) 3048, 2912, 2869, 1748, 1672, 838, 750, 612 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{20}ClN_2O_2$ 415.1213, found 415.1217.

*4-(4-Bromophenyl)-6-hydroxy-5,7-diphenyl-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5b**).* Yellow solid (362 mg, 79% yield): mp 238−240 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (s, 1H), 7.60−7.54 (m, 2H), 7.44−7.38 (m, 2H), 7.36−7.25 (m, 7H), 7.25−7.16 (m, 3H), 6.06 (d, J = 7.2 Hz, 1H), 5.15 (d, J = 1.2 Hz, 1H), 5.04 (s, 1H), 4.52 (dd, J_1 = 2.0 Hz, J_2 = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 150.2, 144.0, 139.1, 136.9, 132.7, 132.7, 129.3, 129.0, 128.1, 128.1, 127.9, 126.6, 124.7, 117.2, 112.2, 89.1, 72.7, 70.0; IR (KBr, ν) 3042, 2918, 2879, 1740, 1677, 826, 750, 613 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{20}BrN_2O_2$ 459.0708, found 459.0707.

*7-(3-Chlorophenyl)-4,5-bis(4-chlorophenyl)-6-hydroxy-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5c**).* Yellow solid (280 mg, 58% yield): mp 221−223 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.62 (s, 1H), 7.46−7.42 (m, 4H), 7.37−7.32 (m, 5H), 7.29−7.23 (m, 3H), 6.15 (d, J = 7.6 Hz, 1H), 5.16 (s, 1H), 5.04 (d, J = 12.8 Hz,1H), 4.48 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.6, 150.0, 143.3, 138.9, 137.9, 133.7, 133.7, 132.7, 130.8, 129.9, 129.4, 128.2, 128.1, 127.8, 126.8, 124.6, 110.4, 89.4, 79.4, 72.3, 69.3; IR (KBr, ν) 3554, 3061, 1638, 1492, 858, 764, 623 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Cl_3N_2O_2$ 483.0434, found 483.0439.

*5-(4-Bromophenyl)-4-(4-chlorophenyl)-6-hydroxy-7-(4-methoxyphenyl)-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5d**).* Yellow solid (386 mg, 74% yield): mp 247−249 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.34 (s, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 4H), 6.91 (d, J = 8.4 Hz, 2H), 6.04 (d, J = 7.2 Hz, 1H), 5.13 (s, 1H), 5.01 (s, 1H), 4.47 (d, J = 6.8 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.4, 159.1, 150.0, 143.5, 138.7, 132.2, 131.5, 129.9, 129. 6, 129.1, 129.0, 128.9, 124.4, 121.2, 114.5, 112.1, 89.1, 72.4, 69.4, 55.6; IR (KBr, ν) 3553, 3064, 1656, 1434, 874, 716, 623 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{21}BrClN_2O_3$ 523.0424, found 523.0415.

*4-(4-Chlorophenyl)-5-(2,4-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5e**).* Yellow solid (337 mg, 70% yield): mp 227−229 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.50 (s, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.50−7.46 (m, 3H), 7.41 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.28−7.15 (m, 4H), 6.41 (d, J = 7.2 Hz, 1H), 5.23 (s, 1H), 5.12 (s, 1H), 4.43 (dd, J_1 = 2.0 Hz, J_2 = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.4, 150.2, 143.1, 136.8, 134.8, 133.9, 133.0, 132.6, 130.3, 130.1, 129.9, 129.2, 129.1, 128.6, 128.1, 124.8, 111.9, 89.5, 70.1, 67.4; IR (KBr, ν) 3552, 3070, 1638, 1492, 869, 749, 622 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Cl_3N_2O_2$ 483.0434, found 483.0429.

*4-(4-Chlorophenyl)-5-(2,3-dichlorophenyl)-6-hydroxy-7-phenyl-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5f**).* Yellow solid (313 mg, 65% yield): mp 202−204 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.50 (s, 1H), 7.61 (d, J = 6.8 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.44−7.38 (m, 3H), 7.37−7.33 (m, 2H), 7.28−7.16 (m, 4H), 6.43 (d, J = 7.2 Hz, 1H), 5.30 (s, 1H), 5.14 (s, 1H), 4.45 (dd, J_1 = 2.0 Hz, J_2 = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.4, 150.2, 143.2, 138.4, 136.8, 133.1, 132.6, 130.7, 130.1, 123.0, 129.9, 129.3, 129.1, 128.1, 126.5, 124.7, 111.9, 89.5, 70.1, 68.3; IR (KBr, ν) 3554, 3058, 1684, 1492, 874, 778, 624 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{25}H_{18}Cl_3N_2O_2$ 483.0434, found 483.0435.

*4-(4-Bromophenyl)-5-(2-chloro-5-methylphenyl)-6-hydroxy-7-phenyl-5,6-dihydro-1H-pyrrolo[3,2-b]pyridin-2(4H)-one (**5g**).* Yellow solid (243 mg, 48% yield): mp 230−232 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.45 (s, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.43−7.34 (m, 5H), 7.29−7.23 (m, 3H), 7.17 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 6.42 (d, J = 7.2 Hz, 1H), 5.20 (s, 1H), 5.01 (s, 1H), 4.42 (d, J = 7.2 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.6, 150.7, 141.6, 139.8, 136.8, 135.9, 135.7, 133.3, 132.7, 130.7, 130.3, 129.1, 128.1, 127.5, 123.1, 121.0, 111.6, 88.3, 70.2, 69.8, 20.9; IR (KBr, ν) 3516, 3027, 1639, 1025, 827, 766, 630 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{26}H_{21}BrClN_2O_2$ 507.0475, found 507.0475.

General Procedure for the Synthesis of 6. *Example for the Synthesis of **6a**.* 4-Phenylamino-1*H*-pyrrol-2(5*H*)-one (**2c**, 1.0 mmol, 174 mg) was introduced in a 10 mL Initiator reaction vial; 1,3-diphenyl-2,3-epoxypropan-1-one (**3a**, 1.0 mmol, 224 mg) and *t*-BuOLi

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(1.0 mmol, 80 mg) as well as DMF (1.5 mL) were then successively added. Subsequently, the reaction vial was capped and then prestirred for 20 s. The mixture was irradiated (time, 25 min; temperature, 60 °C; absorption level, high; fixed hold time) until TLC (petroleum ether/ethyl acetate V/V = 2/1) revealed that conversion of the starting material **2c** was complete. After the reaction mixture was cooled to room temperature, water (20 mL) was added into the reaction system, resulting in a black viscous liquid isolated from the solution through liquid separation and extraction by using ethyl acetate. The organic phase was concentrated by vacuum distillation and was purified by flash column chromatography (silica gel, mixtures of petroleum ether/ethyl acetate) to afford the desired pure product **6a** as a white solid.

*4,6-Diphenyl-3,4-dihydropyrrolo[3,2-b]pyrrol-2(1H)-one (**6a**).* White solid (192 mg, 70% yield): mp 206−208 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.26 (s, 1H), 7.68 (d, J = 7.6 Hz, 2H), 7.46−7.30 (m, 7H), 7.10 (t, J = 6.8 Hz, 1H), 5.23 (d, J = 28.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.2, 157.6, 140.9, 134.0, 132.0, 130.0, 129.3, 128.0, 127.2, 122.7, 116.5, 112.3, 83.9, 60.5; IR (KBr, ν) 3041, 2034, 1698, 1441, 1149, 826, 750 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{18}H_{15}N_2O$ 275.1184, found 275.1187.

*6-Phenyl-4-(p-tolyl)-3,4-dihydropyrrolo[3,2-b]pyrrol-2(1H)-one (**6b**).* White solid (219 mg, 76% yield): mp 212−214 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.21 (s, 1H), 7.66 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.33−7.24 (m, 5H), 5.17 (d, J = 14.4 Hz, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.2, 157.7, 138.6, 134.0, 132.1, 131.8, 130.4, 129.2, 127.9, 127.2, 116.5, 112.0, 83.2, 60.6, 20.7; IR (KBr, ν) 3034, 2028, 1695, 1441, 1147, 828, 766 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{19}H_{17}N_2O$ 289.1341, found 289.1338.

*6-(4-Methoxyphenyl)-4-phenyl-3,4-dihydropyrrolo[3,2-b]pyrrol-2(1H)-one (**6c**).* White solid (207 mg, 68% yield): mp 208−210 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.19 (s, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.35−7.30 (m, 3H), 7.02 (d, J = 8.8 Hz, 2H), 5.14 (d, J = 10.4 Hz, 3H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.3, 157.9, 132.2, 129.2, 129.1, 127.1, 125.6, 121.1, 119.6, 118.0, 115.3, 115.0, 111.9, 60.8, 55.8; IR (KBr, ν) 3158, 2126, 1659, 1452, 1293, 826, 764 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{19}H_{17}N_2O_2$ 305.1290, found 305.1289.

*6-(4-Chlorophenyl)-4-(p-tolyl)-3,4-dihydropyrrolo[3,2-b]pyrrol-2(1H)-one (**6d**).* White solid (199 mg, 62% yield): mp 201−203 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.23 (s, 1H), 8.28 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 7.30−7.20 (m, 5H), 5.12 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.1, 155.5, 137.0, 134.9, 132.0, 131.8, 130.8, 130.1, 129.4, 128.9, 117.9, 113.1, 91.3, 83.6, 20.8; IR (KBr, ν) 3059, 2061, 1683, 1437, 1148, 819, 760 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{19}H_{16}ClN_2O$ 323.0951, found 323.0948.

*6-(4-Methoxyphenyl)-4-(p-tolyl)-3,4-dihydropyrrolo[3,2-b]pyrrol-2(1H)-one (**6e**).* White solid (229 mg, 72% yield): mp 211−213 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (d, J = 17.6 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.29−7.21 (m, 4H), 6.99 (d, J = 8.8 Hz, 2H), 5.13 (d, J = 18.8 Hz, 3H), 3.81 (d, J = 1.6 Hz, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.1, 159.2, 159.0, 157.7, 138.7, 130.4, 124.7, 117.8, 116.4, 114.8, 114.6, 112.4, 83.2, 60.6, 55.7, 20.7; IR (KBr, ν) 3049, 2035, 1694, 1430, 1153, 827, 764 cm^{-1}; HRMS (APCI-TOF) m/z calcd for $[M + H]^+$ $C_{20}H_{19}N_2O_2$ 319.1447, found 319.1445.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all pure products, and X-ray crystal data (CIF) for **4j** and **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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