

Hydrogen Bond-Assisted 6π -Azaelectrocyclization of Penta-2,4-dienamides: Synthesis of Dihydropyridin-2(3H)-ones

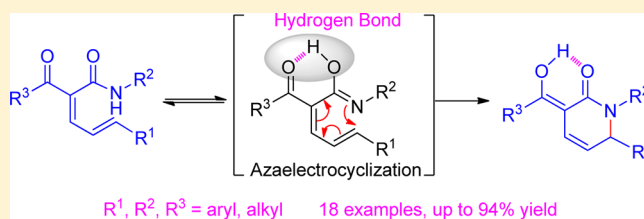
Xu Liu,[†] Ning Zhang,^{*,†} Jiming Yang,[†] Yongjiu Liang,[†] Rui Zhang,^{†,‡} and Dewen Dong^{*,†,‡}

[†]Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun, 130022, China

[‡]Changzhou Institute of Energy Storage Materials & Devices, Changzhou, 213000, China

S Supporting Information

ABSTRACT: A facile and efficient synthesis of substituted dihydropyridin-2(3H)-ones is developed from penta-2,4-dienamides, in which an intramolecular C–N bond was formed through thermal 6π -azaelectrocyclization. The intramolecular hydrogen bonding-assisted cyclization reaction opens access to a variety of dihydropyridin-2(3H)-ones.



INTRODUCTION

Pyridin-2(1H)-ones and their analogues, a prominent class of nitrogen heterocyclic compounds, have provoked great interest in chemical and biological fields.^{1–9} These structural motifs can serve as efficient catalysts in a variety of proton-dependent reactions² and valuable ligands in coordination chemistry.³ Furthermore, pyridin-2(1H)-ones are versatile intermediates in the synthesis of a wide range of aza-heterocycles such as indolizidine,⁴ quinolizidine,⁴ quinoline⁵ and isoquinoline derivatives.⁶ On the other hand, pyridin-2(1H)-one is key unit in a variety of naturally occurring alkaloids,⁷ biologically active molecules,⁸ and pharmacologically active compounds, such as cerpegin⁹ and camptothecin.¹⁰ To date, a variety of synthetic approaches have been well established to access pyridin-2(1H)-ones and their analogues, which comprise the modification of the preconstructed heterocyclic ring by pyridinium salt chemistry¹¹ and *N*-alkylation,¹² and the construction of heterocyclic skeletons from appropriately substituted open-chain precursors via metal-catalyzed *sp*² C–H bond amination,¹³ ring closing metathesis,¹⁴ and Diels–Alder reaction.¹⁵ In spite of the successful pioneering work, the aforementioned reactions may suffer from either tedious synthetic procedures or utilization of toxic or expensive metal catalyst in the synthesis. Thus, the development of efficient and convenient synthetic approaches for such nitrogen-containing heterocycles is demanded.¹⁶

6π -Electrocyclization,¹⁷ one of the well-known concerted pericyclic reactions,¹⁸ represents an elegant annulation approach for the synthesis of heterocycles and has gained great interest in the synthesis of pyridines,¹⁹ chromene,²⁰ nicotinamide²¹ and pyridinium bisretinoid.²² Recently, Katsumura and co-workers reported the synthesis of dihydropyridin-2(3H)-ones via a Pd-catalyzed 6-endo type cyclization of *N*-sulfonyldienamide.²³ Soon after, they revealed that analogous reactions could successfully proceed in the absence of transition metal catalysts following a thermal 6π -azaelectrocyclization mechanism. The presence of *N*-*p*-tosyl and ester groups in the *N*-sulfonyl-dienamide precursors was proved essential to ensure and accelerate the cyclic reaction, which,

however, would impair the substituent versatility in the dihydropyridin-2(3H)-one ring.

Recently, we achieved the synthesis of quinolin-2(1H)-ones and 2,5-dihydrofurans from penta-2,4-dienamides mediated by concentrated H₂SO₄ and hypervalent iodine reagent, respectively.²⁴ It should be noted that these penta-2,4-dienamides exhibit a promising structural feature as a potential oxatriene or azatriene, which, subjected to suitable electrocyclization conditions, might lead to the construction of the skeleton of heterocycles. In light of this, we examined their reaction behavior under varied conditions and, to the end, developed an efficient, diastereoselective synthesis of dihydropyridin-2(3H)-ones via 6π -electrocyclization of such penta-2,4-dienamides. Herein, we wish to report our experimental results and the reaction mechanism involved.

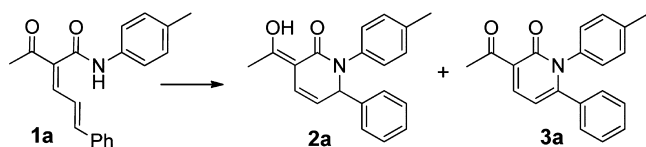
RESULTS AND DISCUSSION

The substrates, penta-2,4-dienamides **1**, were prepared by Knoevenagel condensation of commercially available β -oxo amides with cinnamaldehydes in the presence of piperidine in high yields according to the procedure described in literature.^{24,25} Then, 2-acetyl-5-phenyl-*N*-(*p*-tolyl)penta-2,4-dienamide **1a** was selected as a model compound for the investigation. The reaction of **1a** was attempted in toluene under reflux. As indicated by TLC, the reaction occurred and furnished a product along with some starting material remaining intact after workup and purification by column chromatography of the resulting mixture. The product was characterized as 3-(1-hydroxy ethylidene)-6-phenyl-1-(*p*-tolyl)-1,6-dihydro-pyridin-2(3H)-one **2a** (Table 1, entry 1a). It was noted that the reaction conversion was still low even with prolonged reaction time (Table 1, entry 1b).

To optimize the reaction conditions, the thermal cyclic reaction of **1a** was conducted in other solvents. When **1a** was subjected into xylene at 130 °C, the reaction proceeded smoothly to afford

Received: January 31, 2013

Published: February 27, 2013

Table 1. Reactions of **1a** under Different Conditions^a

entry	solvent	temp (°C)	time (h)	yield ^b (%)	
				2a	3a
1a	toluene	reflux	6.0	36 ^c	0
1b	toluene	reflux	12.0	65	0
1c	xylene	130	12.0	91	5
1d	mesitylene	140	12.0	83	10
1e	phenyl ether	130	12.0	78	12
1f	DMF	130	12.0	complex mixture	

^aReaction conditions: **1a** (2.0 mmol), solvent (10.0 mL). ^bIsolated yield. ^c53% of **1a** was recovered.

2a in 91% yield. Meanwhile, 3-acetyl-6-phenyl-1-(*p*-tolyl)pyridin-2(1*H*)-one **3a** was isolated as a byproduct, which was most likely derived from the oxidation of **2a** by air (Table 1, entry 1c). The employment of mesitylene at increased reaction temperature resulted in much more oxidized product **3a** (Table 1, entry 1d). The reaction of **1a** performed in diphenyl ether furnished **2a** in 78% yield (Table 1, entry 1e), whereas in DMF it formed a complex mixture (Table 1, entry 1f). The findings indicated that polar solvents might not be suitable as reaction media for the electrocyclizations, which was consistent with the results reported by Katsumura.²⁶

Under the optimal conditions as for **2a** in entry 1c, Table 1, a range of reactions of substrates **1** were carried out to determine the scope of the dihydropyridin-2(3*H*)-one synthesis, and some of the results are summarized in Table 2. It was found that the

Table 2. Synthesis of Substituted Dihydropyridin-2(3*H*)-ones **2**^a

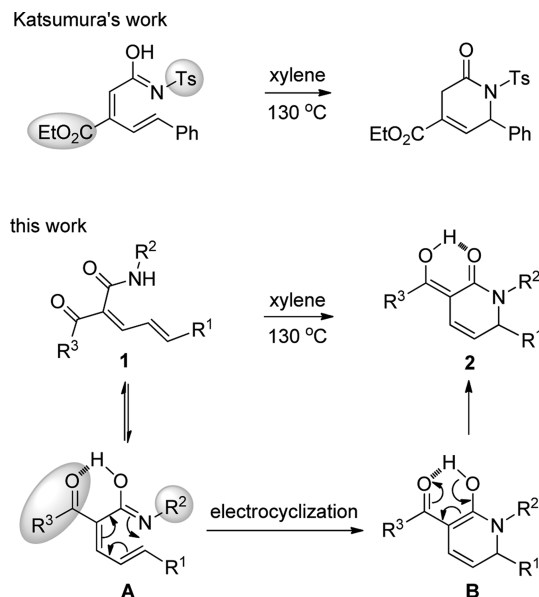
entry	R ¹	R ²	R ³	2	yield ^b (%)
1a	Ph	4-MeC ₆ H ₄	Me	2a	91
1b	4-MeOC ₆ H ₄	4-MeC ₆ H ₄	Me	2b	82
1c	2-MeOC ₆ H ₄	4-MeC ₆ H ₄	Me	2c	87
1d	4-MeC ₆ H ₄	4-MeC ₆ H ₄	Me	2d	89
1e	4-ClC ₆ H ₄	4-MeC ₆ H ₄	Me	2e	84
1f	Me	Ph	Me	2f	86
1g	4-MeOC ₆ H ₄	2-MeC ₆ H ₄	Me	2g	86 (61:39) ^c
1h	4-MeOC ₆ H ₄	4-ClC ₆ H ₄	Me	2h	87
1i	4-MeOC ₆ H ₄	2-ClC ₆ H ₄	Me	2i	94 (86:14) ^c
1j	4-MeOC ₆ H ₄	4-MeOC ₆ H ₄	Me	2j	85
1k	Ph	2-MeC ₆ H ₄	Me	2k	85 (65:35) ^c
1l	Ph	4-ClC ₆ H ₄	Me	2l	82
1m	Ph	2-ClC ₆ H ₄	Me	2m	87 (86:14) ^c
1n	Ph	4-MeOC ₆ H ₄	Me	2n	90
1o	Ph	Ph	Me	2o	91
1p	Ph	Bn	Me	2p	79
1q	Ph	Ph	Pr	2q	88
1r	Ph	4-MeC ₆ H ₄	Ph	2r	83

^aReagents and conditions: **1** (5.0 mmol), xylene (20 mL), reflux, 10.0–16.5 h. ^bIsolated yield. ^cThe data in parentheses are diastereomeric ratios (dr) determined by ¹H NMR.

reactions of **1b–f** bearing varied electron-donating and electron-withdrawing aryl groups or alkyl group R¹ proceeded smoothly in xylene at 130 °C to afford the corresponding substituted dihydropyridin-2(1*H*)-ones **2b–f** in high yields (Table 2, entries 1b–1f). The versatility of this cyclization was further evaluated by performing the reaction of penta-2,4-dienamides **1g–p** containing a variety of aryl amide or alkyl amide groups R² (Table 2, entries 1g–1p). The dihydropyridin-2(3*H*)-one synthesis was also proved to be suitable for penta-2,4-dienamides **1q** and **1r** with different acyl groups, i.e., COR³ (Table 2, entries 1q and 1r). The dihydropyridin-2(3*H*)-ones **2** were characterized by means of NMR (¹H, ¹³C) spectra and elemental analysis. The structure of **2i** was further confirmed by the X-ray single crystal analysis.

It was reported that enantioselective synthesis of dihydropyridin-2(3*H*)-ones could be realized via a Pd-catalyzed 6-*endo*cyclization of dienamides induced by chiral ligands.²² In the present work, we achieved diastereoselective synthesis of dihydropyridin-2(3*H*)-ones **2g**, **2i**, **2k** and **2m** without any catalyst or chiral ligands. The configuration of these compounds was identified by means of NMR spectral and single crystal analysis (Table 2, entries 1g, 1i, 1k and 1m). The slightly inferior diastereoselectivity as observed in **2g**, **2i**, **2k** and **2m** is very likely attributed to the steric hindrance of R² and/or the electronic effect of the 2-substitution in the phenyl ring.²⁷

Over the past decades, extensive experimental and theoretical work had demonstrated that the substituents in the triene precursors had a distinct effect on facilitating the electrocyclization.^{28,29} This “substituent-driven activation” was clarified by Katsumura and co-workers on rapid 6*π*-azaelectrocyclization of dienamides to substituted pyridines and chiral piperidines (Scheme 1). The cyclization was realized by the remarkable

Scheme 1. Katsumura's Work and a Plausible Mechanism for the 6*π*-Azaelectrocyclization of Penta-2,4-dienamides **1**

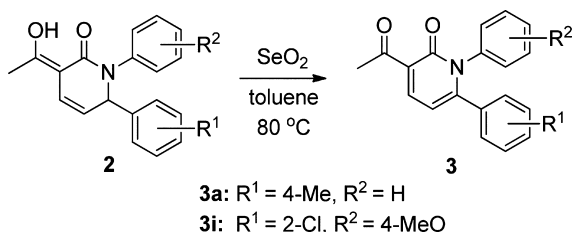
substituent effect due to the enhancement of the HOMO–LUMO interaction in the 6*π*-electron system, which mainly derived from the C-4 ester substituent and the additional electron-withdrawing group at the nitrogen.^{23,26} In contrast, our present cyclic reaction of penta-2,4-dienamides, carrying an electron-withdrawing acyl group at C-3 position and an aryl or alkyl group

at the nitrogen, proceeded smoothly without any catalyst. The results imply that the activation to the electrocyclization of 1-azatrienes might not merely originate from the electronic effect of the substituents or their position. For further investigation, we synthesized 2-(1-hydroxyethyl)-*N*,5-diphenylpenta-2,4-dienamide **1s** and *N*,5-diphenylpenta-2,4-dienamide **1t** bearing CH(OH)-CH₃ and H at C-3 position, respectively, and subjected them to the identical conditions described above. However, no reaction was observed in both cases, which suggested that the acyl group at C-3 position might play a special role in the cyclization.

On the basis of the observations above and the work reported in literature,³⁰ we propose that the intramolecular hydrogen bond within the imidic acid **A**,^{26,31} a tautomer of penta-2,4-dienamide **1**, is the main driving force for the cyclization as shown in Scheme 1. The hydrogen bond can stabilize the structure of **A** and keep the azadiene N=C—C=C in a *cis* conformation, both favoring the subsequent 6 π -aza-electrocyclization to give the intermediate **B**. Furthermore, the acyl group can form hydrogen bonds to stabilize the product **2**, which is generated from **B** through a 1,5-*H* migration.³²

It should be mentioned that pyridin-2(1*H*)-one **3a** was obtained during the screening of the optimal conditions. We next intended to synthesize this kind of heterocycle under oxidative conditions. Thus, dihydropyridin-2(3*H*)-ones **2a** and **2i** were selected and subjected to toluene in the presence of SeO₂ (1.2 equiv) at 80 °C for 1.5 h. The corresponding pyridin-2(1*H*)-ones **3a** and **3i** were obtained in 86 and 91% yields, respectively (Scheme 2). Obviously, this transformation can broaden the choices for the synthesis of 2-pyridone analogues.

Scheme 2. Synthesis of Substituted Pyridin-2(1*H*)-ones **3**



CONCLUSION

In summary, a facile and efficient synthesis of substituted dihydropyridin-2(3*H*)-ones is developed from elaborately designed penta-2,4-dienamides, through which an intramolecular C—N bond was formed via an intramolecular hydrogen bonding-assisted 6 π -aza-electrocyclization. The simple execution, readily available substrates, good yields, high diastereoselectivity and synthetic potential of the products make this protocol highly desirable. Expanding the scope of the methodology and further exploration of the mechanism are currently under investigation in our laboratory.

EXPERIMENTAL SECTION

Materials and Methods. All reagents were purchased from commercial sources and used without further treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ¹H NMR and ¹³C NMR spectra were recorded at 300 MHz and at 400 and 100 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded in the range of 400–4000 cm⁻¹. Petroleum ether (PE) was the fraction boiling in the range 60–90 °C. All melting points were determined in open capillary tubes and are uncorrected.

Synthesis. Typical Procedure for the Synthesis of Substituted Penta-2,4-dienamides **1 (**1b** as an example).** To a 100 mL round-bottomed flask was added 3-oxo-*N*-(*p*-tolyl)butanamide (0.955 g, 5.0 mmol), 3-(4-methoxyphenyl)acrylaldehyde (0.811 g, 5.0 mmol), piperidine (0.1 mmol) and ethanol (30 mL). Then the mixture was heated under reflux for 3.5 h and cooled to room temperature. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic phase was washed with water (3 × 30 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 10:1) to give 92% yield of **1b**: 1.543 g, orange solid; mp 84–85 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.33 (s, 3H), 2.52 (s, 3H), 3.85 (s, 3H), 6.89 (d, *J* = 9.0 Hz, 2H), 7.06–7.16 (m, 3H), 7.53 (d, *J* = 1.5 Hz, 2H), 7.56 (d, *J* = 2.4 Hz, 2H), 7.60 (d, *J* = 11.7 Hz, 1H), 8.19–8.28 (m, 1H), 10.25 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 20.7, 27.4, 55.2, 114.2, 120.3, 123.1, 128.4, 129.3, 130.0, 133.6, 135.4, 147.4, 151.8, 161.3, 162.8, 199.7. Anal. Calcd for C₂₁H₂₁NO₃: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.49; H, 6.42; N, 4.03.

Substrates **1a**, **1f**, **1g**, **1k**, **1l**, **1n**, **1o**, **1q**, **1r** and **1t** are known compounds. For the spectral and analytical data of **1a**, **1g**, **1k**, **1l**, **1n**, **1o**, **1q**, **1r**, and **1t**, see ref 24a, and for **1f**, see ref 33.

1c: 1.560 g, yield 93%, orange solid; mp 129–131 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.32 (s, 3H), 2.51 (s, 3H), 3.87 (s, 3H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.53–7.58 (m, 3H), 7.63 (d, *J* = 11.4 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 8.24–8.33 (dd, *J*₁ = 15.6 Hz, *J*₂ = 11.4 Hz, 1H), 10.14 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 20.8, 27.4, 55.4, 110.9, 120.3, 120.7, 124.5, 125.2, 127.9, 129.3, 130.0, 131.5, 133.6, 135.5, 142.0, 152.0, 157.8, 162.8, 199.8. Anal. Calcd for C₂₁H₂₁NO₃: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.63; H, 6.39; N, 4.31.

1d: 1.421 g, yield 89%, white solid; mp 136–137 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.33 (s, 3H), 2.37 (s, 3H), 2.51 (s, 3H), 7.10 (d, *J* = 15.0 Hz, 1H), 7.14–7.19 (m, 4H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.54–7.60 (m, 3H), 8.21–8.30 (dd, *J*₁ = 15.0 Hz, *J*₂ = 11.4 Hz, 1H), 10.20 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 20.8, 21.4, 27.5, 120.4, 124.4, 128.3, 129.3, 129.5, 132.9, 133.8, 135.4, 140.7, 147.0, 147.5, 151.6, 162.7, 199.9; IR (KBr, cm⁻¹): 3265, 1670, 1635, 1593, 1570, 1242, 802, 739. Anal. Calcd for C₂₁H₂₁NO₂: C, 78.97; H, 6.63; N, 4.39. Found: C, 79.22; H, 6.49; N, 4.56.

1e: 1.495 g, yield 88%, orange solid; mp 141–144 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.33 (s, 3H), 2.54 (s, 3H), 7.08 (d, *J* = 15.0 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 3.3 Hz, 2H), 7.54 (d, *J* = 15.0 Hz, 1H), 8.27–8.36 (dd, *J*₁ = 15.0 Hz, *J*₂ = 10.4 Hz, 1H), 10.16 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 20.8, 27.5, 120.4, 125.8, 129.0, 129.3, 129.4, 131.2, 134.0, 134.1, 135.3, 135.9, 145.3, 150.4, 162.4, 199.9. Anal. Calcd for C₂₀H₁₈ClNO₂: C, 70.69; H, 5.34; N, 4.12. Found: C, 70.51; H, 5.40; N, 3.97.

1h: 1.619 g, 91%, orange solid; mp 129–131 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.55 (s, 3H), 3.86 (s, 3H), 7.15 (d, *J* = 15.0 Hz, 1H), 7.31 (d, *J* = 9.0 Hz, 2H), 7.60 (t, *J* = 3.0 Hz, 3H), 7.64–7.69 (m, 2H), 8.28–8.37 (q, *J* = 12.0 Hz, 1H), 10.59 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 27.5, 55.3, 114.4, 121.6, 123.2, 128.1, 128.4, 128.8, 128.9, 130.2, 136.7, 148.4, 153.5, 161.6, 162.8. Anal. Calcd for C₂₀H₁₈ClNO₃: C, 67.51; H, 5.10; N, 3.94. Found: C, 67.27; H, 5.23; N, 3.72.

1i: 1.672 g, 94%, orange solid; mp 120–121 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.57 (s, 3H), 3.86 (s, 3H), 6.92 (d, *J* = 8.7 Hz, 2H), 7.03–7.09 (m, 1H), 7.16 (d, *J* = 15.3 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.40–7.42 (m, 1H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.69 (d, *J* = 11.4 Hz, 1H), 8.24–8.33 (q, *J* = 4.2 Hz, 1H), 8.53 (d, *J* = 8.1 Hz, 1H), 10.91 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 27.3, 55.2, 114.3, 122.1, 123.2, 123.7, 124.4, 127.2, 128.1, 128.3, 129.1, 130.1, 135.3, 148.4, 153.6, 161.5, 162.8, 199.9. Anal. Calcd for C₂₀H₁₈ClNO₃: C, 67.51; H, 5.10; N, 3.94. Found: C, 67.32; H, 5.01; N, 3.77.

1j: 1.599 g, 91%, orange solid; mp 114–115 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.55 (s, 3H), 3.81 (s, 3H), 3.85 (s, 3H), 6.89 (t, *J* = 3.0 Hz, 2H), 6.91 (t, *J* = 3.0 Hz, 2H), 7.12 (d, *J* = 15.0 Hz, 1H), 7.58 (d, *J* = 9.0 Hz, 4H), 7.64 (d, *J* = 12.0 Hz, 1H), 8.25–8.34 (q, *J* = 12.0 Hz, 1H), 10.28 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 27.6, 55.4, 55.5, 114.1, 114.4, 122.2, 123.6, 128.6, 129.0, 130.2, 131.3, 147.7, 152.8, 156.4,

161.5, 162.6, 200.4. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.44; H, 6.15; N, 4.17.

1m: 1.401 g, 86%, yellow solid; mp 114–116 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.58 (s, 3H), 7.07 (t, $J = 7.5$ Hz, 1H), 7.19 (d, $J = 15.6$ Hz, 1H), 7.30 (q, $J = 4.5$ Hz, 2H), 7.41 (t, $J = 3.6$ Hz, 4H), 7.63 (t, $J = 3.6$ Hz, 2H), 7.68 (d, $J = 11.1$ Hz, 1H), 8.30–8.51 (dd, $J_1 = 15.6$ Hz, $J_2 = 11.1$ Hz, 1H), 8.52 (d, $J = 8.1$ Hz, 1H), 10.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 122.0, 124.4, 125.0, 125.5, 127.1, 128.1, 128.6, 128.9, 129.4, 130.0, 135.0, 135.2, 147.7, 152.2, 162.4, 199.8; IR (KBr, cm^{-1}): 3085, 1673, 1579, 1441, 1377, 977, 745. Anal. Calcd for $C_{19}H_{16}ClNO_2$: C, 70.05; H, 4.95; N, 4.30. Found: C, 70.29; H, 4.86; N, 4.18.

1p: 1.298 g, 85%, white solid; mp 75–77 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 4.60 (d, $J = 6.0$ Hz, 2H), 7.08 (d, $J = 16.0$ Hz, 1H), 7.26–7.33 (m, 2H), 7.34–7.36 (m, 6H), 7.48–7.53 (m, 3H), 7.99–8.06 (dd, $J_1 = 20.0$ Hz, $J_2 = 12.0$ Hz, 1H), 8.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.4, 43.4, 125.2, 127.4, 127.7, 128.2, 128.7, 128.9, 130.1, 131.6, 135.7, 138.3, 146.3, 149.4, 164.9, 199.2; IR (KBr, cm^{-1}): 3481, 3292, 1663, 1634, 1607, 1580, 1539, 731, 692. Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 79.02; H, 6.41; N, 4.45.

Typical Procedure for the Synthesis of 1s. To a 100 mL round-bottomed flask was added 2-acetyl-N,5-diphenylpenta-2,4-dienamide **1o** (1.457 g, 5.0 mmol), $NaBH_4$ (0.227 g, 6.0 mmol) and ethanol (20 mL). Then the mixture was stirred at room temperature for 5 min. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL) and extracted with dichloromethane (3 \times 30 mL). The combined organic phase was washed with water (3 \times 30 mL) and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 9:1) to give 76% yield of **1s** as white solid (1.113 g): mp 123–125 °C; 1H NMR (300 MHz, $CDCl_3$) δ 1.50 (d, $J = 6.6$ Hz, 1H), 2.89 (s, 1H), 4.62 (q, $J = 6.6$ Hz, 1H), 6.52 (d, $J = 11.1$ Hz, 1H), 6.73 (d, $J = 15.6$ Hz, 1H), 7.13 (t, $J = 7.2$ Hz, 1H), 7.23–7.37 (m, 5H), 7.45 (d, $J = 7.2$ Hz, 2H), 7.58–7.66 (m, 3H), 8.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 71.9, 120.2, 124.4, 124.6, 127.1, 128.6(1), 128.6(2), 129.0, 136.0, 136.4, 137.7, 139.0, 166.0. Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.25; H, 7.13; N, 5.04.

Typical Procedure for the Synthesis of Substituted Dihydropyridin-2(3H)-ones 2 (2a as an example). To a 50 mL round bottomed flask was added **1a** (1.527 g, 5.0 mmol) and xylene (10.0 mL). The mixture was heated to reflux for 13.0 h. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL) and extracted with dichloromethane (3 \times 20 mL). The combined organic phase was washed with water and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 12:1) to give 91% yield of **2a** (1.389 g): white solid; mp 177–178 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.15 (s, 3H), 2.28 (s, 3H), 5.36 (d, $J = 3.9$ Hz, 1H), 5.42–5.46 (dd, $J_1 = 3.9$ Hz, $J_2 = 9.9$ Hz, 1H), 6.40–6.43 (dd, $J_1 = 0.9$ Hz, $J_2 = 9.9$ Hz, 1H), 6.81 (d, $J = 8.1$ Hz, 2H), 7.06 (d, $J = 8.1$ Hz, 2H), 7.13–7.16 (m, 2H), 7.25–7.28 (m, 3H), 14.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 21.0, 67.7, 98.2, 117.9, 120.6, 127.5, 127.8, 128.0, 128.6, 129.7, 137.3, 137.4, 140.8, 168.9, 170.3; IR (KBr, cm^{-1}): 3126, 1663, 1618, 1593, 1491, 1448, 1285, 816, 768, 706. Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.91; H, 6.20; N, 4.33.

2b: 1.375 g, yield 82%, white solid; mp 129–130 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.28 (s, 3H), 3.77 (s, 3H), 5.30 (d, $J = 3.9$ Hz, 1H), 5.39–5.44 (dd, $J_1 = 9.9$ Hz, $J_2 = 3.9$ Hz, 1H), 6.40 (d, $J = 9.9$ Hz, 1H), 6.77 (d, $J = 3.0$ Hz, 2H), 6.80 (d, $J = 3.0$ Hz, 2H), 7.05 (t, $J = 7.5$ Hz, 4H), 14.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 21.0, 55.2, 67.1, 98.2, 113.9, 118.2, 120.4, 127.9, 128.8, 129.7, 132.9, 137.2, 137.4, 159.3, 168.8, 170.2. Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.99; H, 6.42; N, 4.03.

2c: 1.459 g, yield 87%, white solid; mp 117–118 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.20 (s, 3H), 3.51 (s, 3H), 5.36–5.41 (dd, $J_1 = 4.5$ Hz, $J_2 = 9.9$ Hz, 1H), 5.87 (d, $J = 3.0$ Hz, 1H), 6.28–6.31 (dd, $J_1 = 1.2$ Hz, $J_2 = 9.9$ Hz, 1H), 6.68 (d, $J = 8.4$ Hz, 1H), 6.84–6.92

(m, 3H), 6.99 (d, $J = 8.4$ Hz, 2H), 7.12–7.17 (m, 1H), 7.30 (d, $J = 7.2$ Hz, 1H), 14.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 21.0, 55.4, 60.5, 98.5, 110.9, 117.6, 120.5, 121.0, 127.5, 128.3, 129.0, 129.4, 136.9, 137.7, 156.1, 169.5, 169.7. Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.39; H, 6.36; N, 4.27.

2d: 1.421 g, yield 89%, white solid; mp 117–119 °C; 1H NMR (300 MHz, DMSO) δ 2.09 (s, 3H), 2.22 (s, 6H), 5.41 (q, $J = 6.0$ Hz, 1H), 5.56 (d, $J = 3.0$ Hz, 1H), 6.45 (d, $J = 11.2$ Hz, 1H), 6.92 (d, $J = 8.4$ Hz, 2H), 7.02 (d, $J = 8.4$ Hz, 2H), 7.04–7.08 (m, 3H), 14.82 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 18.0, 21.0, 21.1, 67.4, 98.2, 118.2, 120.4, 127.4, 127.8, 129.3, 129.7, 137.2, 137.5, 137.8, 168.9, 170.2; IR (KBr, cm^{-1}): 3128, 1666, 1624, 1609, 1595, 1580, 816, 768, 702. Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.64; H, 6.72; N, 4.17.

2e: 1.427 g, yield 84%, white solid; mp 207–208 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.71 (s, 6H), 6.36 (d, $J = 7.5$ Hz, 1H), 6.95 (d, $J = 8.1$ Hz, 2H), 7.06 (d, $J = 8.1$ Hz, 2H), 7.13 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 8.1$ Hz, 2H), 8.27 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 21.2, 31.1, 107.6, 126.5, 128.3, 128.4, 129.5, 129.8, 130.0, 133.3, 135.3, 138.7, 143.2, 154.0, 162.1, 197.6; IR (KBr, cm^{-1}): 3421, 3126, 1676, 1655, 1600, 1547, 1491, 810, 744. Anal. Calcd for $C_{20}H_{18}ClNO_2$: C, 70.69; H, 5.34; N, 4.12. Found: C, 71.02; H, 5.27; N, 3.99.

2f: 0.986 g, yield 86%, white solid; mp 228–231 °C; 1H NMR (300 MHz, DMSO) δ 1.07 (d, $J = 6.0$ Hz, 3H), 2.04 (s, 3H), 4.62 (t, $J = 5.1$ Hz, 1H), 5.45–5.50 (dd, $J_1 = 4.2$ Hz, $J_2 = 10.2$ Hz, 1H), 6.38–6.42 (dd, $J_1 = 1.2$ Hz, $J_2 = 10.2$ Hz, 1H), 7.28–7.31 (m, 2H), 7.34–7.37 (m, 1H), 7.45 (t, $J = 7.5$ Hz, 2H), 14.68 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 17.6, 22.2, 58.0, 98.1, 119.0, 120.5, 127.4, 128.0, 129.1, 139.8, 168.7, 169.3. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.69; H, 6.67; N, 6.25.

2g: 1.442 g, yield 86%, white solid; mp 127–130 °C; [dr = 61:39]; 1H NMR (major isomer) (300 MHz, $CDCl_3$) δ 2.16 (s, 3H), 2.33 (s, 3H), 3.80 (s, 3H), 5.01 (d, $J = 4.2$ Hz, 1H), 5.44 (t, $J = 4.2$ Hz, 1H), 6.45 (d, $J = 10.2$ Hz, 1H), 6.82 (d, $J = 8.7$ Hz, 2H), 7.01–7.07 (m, 3H), 7.26–7.31 (m, 3H), 14.77 (s, 1H); 1H NMR (minor isomer) (300 MHz, $CDCl_3$) δ 1.53 (s, 3H), 2.16 (s, 3H), 3.75 (s, 3H), 5.48 (d, $J = 6.6$ Hz, 2H), 6.29 (d, $J = 7.8$ Hz, 1H), 6.55 (d, $J = 8.7$ Hz, 1H), 6.72 (d, $J = 8.7$ Hz, 2H), 6.91–6.96 (m, 3H), 7.15–7.17 (m, 2H), 14.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.2, 17.6, 17.9, 55.1, 65.7, 67.1, 97.9, 98.1, 100.5, 113.4, 113.8, 117.3, 117.9, 120.5, 121.5, 126.0, 126.5, 126.9, 127.7, 127.9, 129.0, 129.8, 130.0, 130.5, 131.0, 132.8, 134.6, 138.0, 138.4, 138.9, 159.4, 167.2, 168.5, 170.0, 170.3. Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.92; H, 6.19; N, 4.35.

2h: 1.548 g, yield 87%, white solid; mp 201–204 °C; 1H NMR (300 MHz, $CDCl_3$) δ 2.15 (s, 3H), 3.78 (s, 3H), 5.40–5.45 (q, $J = 6.0$ Hz, 1H), 6.39–6.43 (dd, $J_1 = 12.0$ Hz, $J_2 = 3.0$ Hz, 1H), 6.77–6.81 (m, 2H), 6.84–6.88 (m, 2H), 7.02–7.04 (m, 2H), 7.23–7.26 (m, 2H), 14.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 55.2, 67.1, 98.1, 114.0, 118.0, 120.5, 128.8, 129.2, 129.6, 130.2, 132.4, 133.2, 138.7, 159.5, 168.7, 170.7. Anal. Calcd for $C_{20}H_{18}ClNO_3$: C, 67.51; H, 5.10; N, 3.94. Found: C, 67.22; H, 5.03; N, 4.11.

2i: 1.672 g, yield 94%, light blue solid; mp 123–126 °C; [dr = 86:14]; 1H NMR (major isomer) (300 MHz, $CDCl_3$) δ 2.16 (s, 3H), 3.78 (s, 3H), 5.26 (d, $J = 3.9$ Hz, 1H), 5.43–5.48 (dd, $J_1 = 9.9$ Hz, $J_2 = 3.9$ Hz, 1H), 6.43–6.45 (dd, $J_1 = 6.3$ Hz, $J_2 = 0.9$ Hz, 1H), 6.46–6.48 (dd, $J_1 = 7.2$ Hz, $J_2 = 1.2$ Hz, 1H), 6.80 (d, $J = 8.4$ Hz, 2H), 6.99–7.06 (m, 3H), 7.18–7.24 (m, 1H), 7.48–7.51 (dd, $J_1 = 7.8$ Hz, $J_2 = 0.9$ Hz, 1H), 14.46 (s, 1H); 1H NMR (minor isomer) (300 MHz, $CDCl_3$) δ 2.16 (s, 3H), 3.74 (s, 3H), 5.39 (d, $J = 3.9$ Hz, 1H), 5.48 (s, 1H), 6.51 (d, $J = 1.2$ Hz, 1H), 6.71 (d, $J = 8.4$ Hz, 2H), 6.99–7.06 (m, 2H), 7.18–7.24 (m, 2H), 7.30–7.36 (m, 1H), 7.39–7.41 (m, 1H), 14.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 55.2, 65.3, 67.2, 97.8, 113.3, 113.5, 113.9, 117.6, 117.9, 120.4, 121.1, 126.9, 127.7, 128.2, 128.8, 129.1, 129.9, 130.0, 130.2, 131.9, 132.2, 132.5, 136.9, 159.5, 168.6, 170.6. Anal. Calcd for $C_{20}H_{18}ClNO_3$: C, 67.51; H, 5.10; N, 3.94. Found: C, 67.33; H, 5.18; N, 3.82.

Crystal data for **2i**: $C_{20}H_{18}ClNO_3$, light blue crystal, $M = 355.80$, Monoclinic, $P2_1/c$, $a = 12.269$ (4) Å, $b = 12.814$ (4) Å, $c = 11.380$ (3) Å, $\alpha = 90.00^\circ$, $\beta = 98.462$ (5)°, $\gamma = 90.00^\circ$, $V = 1769.7$ (9) Å³, $Z = 4$, $T = 293$ K, $F(000) = 744$, $T_{min} = 0.9667$, $T_{max} = 0.9893$, $R = 0.0797$,

$wR_2 = 0.3123$. CCDC deposition number: 910106. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, U.K. (fax (+44)1223-336-033 or deposit@ccdc.cam.ac.uk).

2j: 1.493 g, yield 85%, white solid; mp 110–112 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 2.16 (s, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 5.29 (d, $J = 3.9$ Hz, 1H), 5.41–5.46 (dd, $J_1 = 10.2$ Hz, $J_2 = 3.9$ Hz, 1H), 6.41–6.44 (dd, $J_1 = 10.2$ Hz, $J_2 = 0.9$ Hz, 1H), 6.79–6.85 (m, 6H), 7.05 (d, $J = 8.4$ Hz, 2H), 14.76 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 17.9, 55.1, 55.2, 67.2, 98.2, 113.8, 114.3, 118.1, 120.4, 128.8, 129.1, 132.7, 132.8, 158.5, 159.3, 168.9, 170.2. Anal. Calcd for $\text{C}_{21}\text{H}_{21}\text{NO}_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 72.09; H, 6.11; N, 3.80.

2k: 1.298 g, yield 85%, white solid; mp 112–116 °C; [dr = 65:35]; $^1\text{H NMR}$ (major isomer) (300 MHz, CDCl_3): 2.17 (s, 3H), 2.33 (s, 3H), 5.05 (d, $J = 3.9$ Hz, 1H), 5.44–5.46 (m, 1H), 6.28 (d, $J = 7.8$ Hz, 1H), 6.46 (d, $J = 10.2$ Hz, 1H), 6.90 (t, $J = 7.5$ Hz, 1H), 7.01 (t, $J = 7.5$ Hz, 2H), 7.13–7.30 (m, 5H), 14.73 (s, 1H); $^1\text{H NMR}$ (minor isomer) (300 MHz, CDCl_3): 1.48 (s, 3H), 2.17 (s, 3H), 5.47–5.50 (m, 2H), 6.57 (d, $J = 10.2$ Hz, 1H), 7.13–7.30 (m, 9H), 14.77 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 19.1, 19.4, 19.7, 68.3, 69.6, 99.8, 99.9, 118.9, 119.6, 122.6, 123.6, 127.9, 128.3, 128.8, 129.6, 129.8, 130.0(1), 130.0(2), 130.1, 130.4, 130.5, 131.7, 132.3, 132.9, 136.5, 140.3, 142.6, 169.2, 170.5, 172.1, 172.3. Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.50; H, 6.18; N, 4.44.

2l: 1.336 g, yield 82%, white solid; mp 139–141 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 2.15 (s, 3H), 5.35 (d, $J = 3.0$ Hz, 1H), 5.42–5.46 (m, 1H), 6.40–6.43 (m, 1H), 6.86–6.89 (m, 2H), 7.11–7.14 (m, 2H), 7.21–7.24 (m, 3H), 7.28–7.30 (m, 2H), 14.53 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 17.9, 67.6, 98.0, 117.7, 120.5, 127.4, 128.2, 128.7, 129.1, 129.4, 133.1, 138.6, 140.2, 168.7, 170.7; IR (KBr, cm^{-1}): 3446, 1664, 1614, 1585, 1494, 1443, 1281, 833, 702. Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{ClNO}_2$: C, 70.05; H, 4.95; N, 4.30. Found: C, 70.31; H, 5.02; N, 4.39.

2m: 1.417 g, yield 87%, white solid; mp 152–156 °C; [dr = 86:14]; $^1\text{H NMR}$ (major isomer) (300 MHz, CDCl_3) δ 2.17 (s, 3H), 5.31 (d, $J = 3.9$ Hz, 1H), 5.45–5.50 (dd, $J_1 = 10.2$ Hz, $J_2 = 4.2$ Hz, 1H), 6.44–6.46 (dd, $J_1 = 4.5$ Hz, $J_2 = 0.9$ Hz, 1H), 6.48 (s, 1H), 6.96–7.02 (m, 1H), 7.10–7.23 (m, 4H), 7.28 (t, $J = 2.7$ Hz, 2H), 7.48–7.51 (m, 1H), 14.46 (s, 1H); $^1\text{H NMR}$ (minor isomer) (300 MHz, CDCl_3): 2.17 (s, 3H), 5.42 (d, $J = 3.9$ Hz, 1H), 5.54 (s, 1H), 6.50 (s, 1H), 6.54 (d, $J = 1.2$ Hz, 1H), 7.10–7.29 (m, 4H), 7.33–7.36 (m, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 14.50 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 17.9, 65.9, 67.8, 97.8, 117.2, 117.6, 120.6, 121.3, 126.8, 127.7, 127.8, 128.0, 128.1, 128.3, 128.6, 128.8, 129.1, 130.0, 130.2, 131.9, 132.0, 136.8, 140.3, 167.4, 168.6, 170.6. Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{ClNO}_2$: C, 70.05; H, 4.95; N, 4.30. Found: C, 69.89; H, 5.05; N, 4.42.

2n: 1.446 g, yield 90%, white solid; mp 88–89 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 2.14 (s, 3H), 3.74 (s, 3H), 5.33 (d, $J = 3.0$ Hz, 1H), 5.41–5.46 (m, 1H), 6.39–6.43 (m, 1H), 6.75–6.84 (m, 4H), (m, 1H), 7.12–7.15 (m, 2H), 7.25–7.28 (m, 4H), 14.72 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 17.5, 54.8, 67.5, 97.8, 113.9, 117.5, 120.2, 127.2, 127.7, 128.2, 128.7, 132.3, 140.3, 158.1, 168.6, 169.9; IR (KBr, cm^{-1}): 3447, 2968, 1659, 1607, 1587, 1491, 1454, 1283, 768. Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.66; H, 5.81; N, 4.28.

2o: 1.326 g, yield 91%, white solid; mp 116–119 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 2.15 (s, 3H), 5.38 (d, $J = 3.6$ Hz, 1H), 5.42–5.47 (dd, $J_1 = 1.8$ Hz, $J_2 = 10.2$ Hz, 1H), 6.42 (d, $J = 10.2$ Hz, 1H), 6.93 (d, $J = 7.2$ Hz, 2H), 7.12–7.14 (m, 2H), 7.21–7.26 (m, 6H), 14.67 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 17.9, 67.7, 98.1, 117.9, 120.6, 127.5, 128.0, 128.6, 128.7, 129.0, 140.1, 140.6, 168.7, 170.5; IR (KBr, cm^{-1}): 3142, 1655, 1647, 1607, 1587, 1491, 168, 696. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 77.95; H, 5.75; N, 5.03.

2p: 1.206 g, yield 79%, white solid; mp 105–107 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.11 (s, 3H), 3.47 (d, $J = 16.0$ Hz, 1H), 4.98 (s, 3H), 5.24–5.27 (m, 1H), 5.52 (d, $J = 16.0$ Hz, 1H), 6.26 (d, $J = 8.0$ Hz, 1H), 7.23–7.29 (m, 4H), 7.31–7.40 (m, 6H), 14.91 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 17.9, 45.9, 62.6, 97.9, 117.8, 120.1, 127.0, 127.5, 128.1, 128.2, 128.7, 129.1, 136.5, 140.8, 169.0, 169.7; IR (KBr, cm^{-1}): 3443, 1677, 1600, 1583, 1493, 1454, 1258, 719, 696. Anal. Calcd for

$\text{C}_{20}\text{H}_{19}\text{NO}_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.47; H, 6.35; N, 4.71.

2q: 1.405 g, yield 88%, white solid; mp 196–198 °C; $^1\text{H NMR}$ (300 MHz, DMSO) δ 0.92 (t, $J = 9.0$ Hz, 3H), 1.54–1.64 (m, 2H), 3.07 (t, $J = 4.0$ Hz, 2H), 7.20–7.25 (m, 1H), 7.36 (d, $J = 9.0$ Hz, 1H), 7.59–7.65 (m, 1H), 7.86 (d, $J = 4.0$ Hz, 1H), 8.43 (s, 1H), 12.11 (s, 1H); $^{13}\text{C NMR}$ (150 MHz, DMSO) δ 13.7, 17.0, 44.0, 115.0, 118.1, 122.3, 129.6, 129.9, 132.7, 140.3, 142.7, 160.3, 200.1; IR (KBr, cm^{-1}): 3447, 2968, 1659, 1607, 1587, 1491, 1454, 1283, 768. Anal. Calcd for $\text{C}_{21}\text{H}_{21}\text{NO}_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 79.31; H, 6.57; N, 4.56.

2r: 1.525 g, yield 83%, white solid; mp 112–114 °C; $^1\text{H NMR}$ (300 MHz, DMSO) δ 2.24 (s, 3H), 5.52–5.56 (m, 1H), 5.67 (d, $J = 3.0$ Hz, 1H), 6.33–6.37 (m, 1H), 6.98 (d, $J = 9.0$ Hz, 2H), 7.09 (d, $J = 6.0$ Hz, 2H), 7.23 (t, $J = 6.0$ Hz, 3H), 7.30 (t, $J = 9.0$ Hz, 2H), 7.52 (t, $J = 3.0$ Hz, 3H), 7.55–7.60 (m, 2H), 15.16 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, DMSO) δ 20.5, 66.5, 98.4, 120.1, 120.3, 127.2, 127.6, 127.8, 128.46, 128.6, 129.2, 130.2, 133.9, 136.5, 137.2, 140.4, 168.0, 168.8; IR (KBr, cm^{-1}): 3447, 1659, 1591, 1570, 1512, 1458, 1283, 816. Anal. Calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_2$: C, 81.72; H, 5.76; N, 3.81. Found: C, 81.41; H, 5.87; N, 3.94.

Typical Procedure for the Synthesis of Substituted Pyridin-2(1H)-ones 3 (3a as an example). To a 50 mL round bottomed flask was added **2a** (0.710 g, 2.0 mmol), SeO_2 (0.266g, 2.4 mmol), and toluene (10.0 mL). The mixture was heated to reflux for 1.5 h. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL) and extracted with dichloromethane (3×20 mL). The combined organic phase was washed with water and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 9:1) to give 86% yield of **3a** (0.522 g): white solid, mp 187–189 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 2.29 (s, 3H), 2.72 (s, 3H), 6.39 (d, $J = 7.5$ Hz, 1H), 6.97 (d, $J = 8.4$ Hz, 2H), 7.09–7.13 (m, 4H), 7.18–7.26 (m, 3H), 8.29 (d, $J = 7.5$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 21.1, 31.2, 107.6, 126.1, 128.1, 128.5, 128.7, 129.0, 129.6, 135.0, 135.6, 138.4, 143.3, 155.4, 162.2, 197.8; IR (KBr, cm^{-1}): 3394, 1672, 1653, 1544, 1404, 764. Anal. Calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 78.89; H, 5.60; N, 4.83.

3i: 0.644 g, yield 91%, white solid; mp 160–161 °C; $^1\text{H NMR}$ (300 MHz, DMSO) δ 2.54 (s, 3H), 3.69 (s, 3H), 6.50 (d, $J = 9.0$ Hz, 1H), 6.81 (d, $J = 9.0$ Hz, 1H), 7.18 (d, $J = 9.0$ Hz, 2H), 7.33–7.37 (m, 2H), 7.48–7.52 (m, 2H), 8.19 (d, $J = 6.0$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 30.4, 54.5, 106.9, 112.8, 125.0, 125.7, 126.9, 129.2, 129.4, 129.5, 130.0, 131.7, 135.9, 143.2, 154.7, 159.7, 160.7, 129.6; IR (KBr, cm^{-1}): 1678, 1664, 1609, 1545, 1508, 1477, 825, 762, 737. Anal. Calcd for $\text{C}_{20}\text{H}_{16}\text{ClNO}_3$: C, 67.90; H, 4.56; N, 3.96. Found: C, 67.63; H, 4.49; N, 4.11.

■ ASSOCIATED CONTENT

📄 Supporting Information

ORTEP drawing and crystal data (CIF) of **2i**, copies of $^1\text{H NMR}$ and $^{13}\text{C NMR}$ spectra for new compounds **1**, **2**, and **3**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

✉ Corresponding Author

*E-mail: ning.zhang@ciac.jl.cn; dwdong@ciac.jl.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support of this research by the National Natural Science Foundation of China (51073150 and 21172211), the Department of Science and Technology of Jilin Province (20111802), and “Hundred Talents Program” of the Chinese Academy of Sciences is greatly acknowledged.

REFERENCES

- (1) (a) Elbein, A. D.; Molyneux, R. J. *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1981; Vol. 5, pp 1–54. (b) Jones, G. *Pyridines and Their Benzo Derivatives: Synthesis in Comprehensive Heterocyclic Chemistry II*; McKillop, A., Ed.; Pergamon Press: Oxford, U.K., 1996; Vol. 5, p 167. (c) Li, Q.; Mitscher, L. A.; Shen, L. L. *Med. Res. Rev.* **2000**, *20*, 231. (d) Nagarajan, M.; Xiao, X. S.; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M. *J. Med. Chem.* **2003**, *46*, 5712.
- (2) Fischer, C. B.; Steininger, H.; Stephenson, D. S.; Zipse, H. *J. Phys. Org. Chem.* **2005**, *18*, 901.
- (3) Rawson, J. M.; Winpenny, R. E. P. *Coord. Chem. Rev.* **1995**, *139*, 313.
- (4) Grundon, M. F. *Nat. Prod. Rep.* **1989**, *6*, 523.
- (5) Fujita, R.; Watanabe, K.; Ikeura, W.; Ohtake, Y. H. *Heterocycles* **2000**, *53*, 2607.
- (6) Casamitjana, N.; López, V.; Jorge, A.; Bosch, J.; Molins, E.; Roig, A. *Tetrahedron* **2000**, *56*, 4027.
- (7) (a) Jones, T. H.; Blum, M. S. *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1983; Vol. 1, pp 33–84. (b) Fodor, G. B.; Colasanti, B. *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1985; Vol. 3, pp 1–90. (c) Strunz, G. M.; Findlay, J. A. *The Alkaloids*; Brossi, A., Ed.; Academic Press: Orlando, FL, 1985; Vol. 26, p 89.
- (8) (a) Paulvannan, K.; Chen, T. *J. Org. Chem.* **2000**, *65*, 6160. (b) Tasker, S. Z.; Bosscher, M. A.; Shandro, C. A.; Lanni, E. L.; Ryu, K. A.; Snapper, G. S.; Utter, J. M.; Ellsworth, B. A.; Anderson, C. E. *J. Org. Chem.* **2012**, *77*, 8220.
- (9) (a) Adibatti, N. A.; Thirugnanasambantham, P.; Kulothungan, C.; Viswanathan, S.; Kameswaran, L.; Balakrishna, K.; Sukumar, E. *Phytochemistry* **1991**, *30*, 2449. (b) Kelly, T. R.; Walsh, J. J. *J. Org. Chem.* **1992**, *57*, 6657. (c) Hong, H.; Comins, D. L. *J. Org. Chem.* **1996**, *61*, 391.
- (10) (a) Josien, H.; Ko, S. B.; Bom, D.; Curran, D. P. *Chem.—Eur. J.* **1998**, *4*, 67. (b) Comins, D. L.; Nolan, J. M. *Org. Lett.* **2001**, *3*, 4255. (c) Yabu, K.; Masumoto, S.; Yamasaki, S.; Hamashima, Y.; Kanai, M.; Du, W.; Curran, D. P.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 9908.
- (11) (a) Decker, H. *Chem. Ber.* **1892**, *25*, 443. (b) Comins, D. L.; Saha, J. K. *J. Org. Chem.* **1996**, *61*, 9623. (c) Du, W. *Tetrahedron* **2003**, *59*, 8649.
- (12) (a) Comins, D. L.; Gao, J. L. *Tetrahedron Lett.* **1994**, *35*, 2819. (b) Hu, T.; Li, C. *Org. Lett.* **2005**, *7*, 2035. (c) Cristau, H. J.; Cellier, P.; Spindler, J. F.; Taillefer, M. *Chem.—Eur. J.* **2004**, *10*, 5607.
- (13) (a) Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14058. (b) Inamoto, K.; Saito, T.; Hiroya, K.; Doi, T. *J. Org. Chem.* **2010**, *75*, 3900.
- (14) (a) Fiorelli, C.; Savoia, D. *J. Org. Chem.* **2007**, *72*, 6022. (b) Lee, J. H.; Shin, S.; Kang, J.; Lee, S. G. *J. Org. Chem.* **2007**, *72*, 7443.
- (15) (a) Chen, Z.; Lin, L.; Chen, D.; Li, J.; Liu, X.; Feng, X. *Tetrahedron Lett.* **2010**, *51*, 3088. (b) Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4796.
- (16) (a) Torres, M.; Gil, S.; Parra, M. *Curr. Org. Chem.* **2005**, *9*, 1757. (b) Angibaud, P. R.; Venet, M. G.; Filliers, W.; Broeckx, R.; Ligny, Y. A.; Muller, P.; Poncelet, V. S.; End, D. W. *Eur. J. Org. Chem.* **2004**, 479. (c) Litvinov, V. P. *Russ. Chem. Rev.* **2003**, *72*, 69.
- (17) Beaudry, C. M.; Malerich, J. P.; Trauner, D. *Chem. Rev.* **2005**, *105*, 4757.
- (18) (a) Marvell, E. N.; Caple, G.; Schatz, B.; Pippin, W. *Tetrahedron* **1973**, *29*, 3781. (b) Marvell, E. N.; Caple, G.; Delphey, C.; Platt, J.; Polston, N.; Tashiro, J. *Tetrahedron* **1973**, *29*, 3797. (c) Spangler, C. W.; Jondahl, T. P.; Spangler, B. *J. Org. Chem.* **1973**, *38*, 2478. (d) Palenzuela, J. A.; Elnagar, H. Y.; Okamura, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 1770. (e) Beaudry, C. M.; Malerich, J. P.; Trauner, D. *Chem. Rev.* **2005**, *105*, 4757. (f) Okamura, W. H.; de Lera, A. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Paquette, L. A., Vol. Ed.; Pergamon Press: London, 1991; Vol. 5, Chapter 6.2, pp 699–750.
- (19) Marvell, E. N. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980.
- (20) Parker, K. A.; Mindt, T. L. *Org. Lett.* **2001**, *3*, 3875.
- (21) Colabroy, K. L.; Begley, T. P. *J. Am. Chem. Soc.* **2005**, *127*, 840.
- (22) Parish, C. A.; Hashimoto, M.; Nakanishi, K.; Dillon, J.; Sparrow, J. *Proc. Natl. Acad. Sci. U. S. A.* **1998**, *95*, 14609.
- (23) Tsuchikawa, H.; Maekawa, Y.; Katsumura, S. *Org. Lett.* **2012**, *14*, 2326.
- (24) (a) Liu, X.; Xin, X.; Xiang, D.; Zhang, R.; Kumar, S.; Zhou, F.; Dong, D. *Org. Biomol. Chem.* **2012**, *10*, S643. (b) Liu, X.; Xin, X.; Xiang, D.; Liang, Y.; Xin, X.; Li, W.; Dong, D. *RSC Adv.* **2013**, *3*, 1456.
- (25) Raman, N. *J. Indian Chem. Soc.* **2007**, *84*, 29.
- (26) Maekawa, Y.; Sakaguchi, T.; Tsuchikawa, H.; Katsumura, S. *Tetrahedron Lett.* **2012**, *53*, 837.
- (27) Hatano, B.; Hashimoto, K.; Katagiri, H.; Kijima, T.; Murakami, S.; Matsuba, S.; Kusakari, M. *J. Org. Chem.* **2012**, *77*, 3595.
- (28) (a) Tanaka, K.; Mori, H.; Fujii, S.; Itagaki, Y.; Katsumura, S. *Tetrahedron Lett.* **1998**, *39*, 1185. (b) Tanaka, K.; Katsumura, S. *Org. Lett.* **2000**, *2*, 373. (c) Yu, T.; Fu, Y.; Liu, L.; Guo, Q. *J. Org. Chem.* **2006**, *71*, 6157.
- (29) Bishop, L. M.; Barbarow, J. E.; Bergman, R. G.; Trauner, D. *Angew. Chem., Int. Ed.* **2008**, *47*, 8100.
- (30) (a) Malamidou-Xenikaki, E.; Spyroudis, S.; Tsanakopoulou, M.; Krautscheid, H. *J. Org. Chem.* **2007**, *72*, S02. (b) Malamidou-Xenikaki, E.; Spyroudis, S.; Tsanakopoulou, M.; Hadjipavlou-Litina, D. *J. Org. Chem.* **2009**, *74*, 7315.
- (31) (a) Wang, Z.; Bi, X.; Liao, P.; Zhang, R.; Liang, Y.; Dong, D. *Chem. Commun.* **2012**, *48*, 7076. (b) Vicente, V.; Martin, J.; Jiménez-Barbero, J.; Chiara, J. L.; Vicent, C. *Chem.—Eur. J.* **2004**, *10*, 4240. (c) Zhang, Y.; Zimmerman, S. C. *Beilstein J. Org. Chem.* **2012**, *8*, 486. (d) Zhang, Y.; Lavin, J. M.; Shimizu, K. D. *J. Am. Chem. Soc.* **2009**, *131*, 12062.
- (32) Bickelhaupt, F.; De Graaf, W. L.; Klumpp, G. W. *Chem. Commun.* **1968**, 53.
- (33) Sengupta, T.; Gayen, K. S.; Pandit, P.; Maiti, D. K. *Chem.—Eur. J.* **2012**, *18*, 1905.