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# C−C Bond Cleavage Initiated Cascade Reaction of β-Enaminones: One-Pot Synthesis of 5-Hydroxy-1*H*-pyrrol-2(5*H*)-ones

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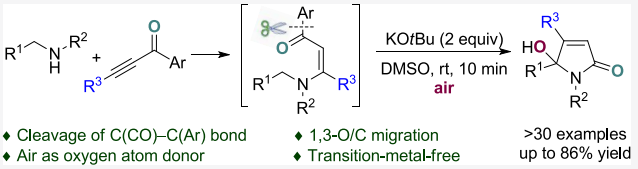
**ABSTRACT:** An unprecedented C(CO)−C(Ar) bond cleavage of β-enaminones has been realized under mild and transition-metal-free conditions. The cascade transformation based on this C−C bond cleavage involves 1,3-O/C migration and aerobic hydroxylation and leads to various 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones with broad functional group tolerance. The application of this methodology has been showcased by preparing 5-alkoxy-1*H*-pyrrol-2(5*H*)-one derivatives and a pyrrolo[2,1-*a*]isoquinolin-3-one derivative.




## INTRODUCTION

5-Hydroxy-1*H*-pyrrol-2(5*H*)-ones, also known as γ-hydroxy-γ-lactams, represent structural motifs that are widely present in many natural products and medicinally important agents.[1] As illustrated in Figure 1, notable examples possessing interesting

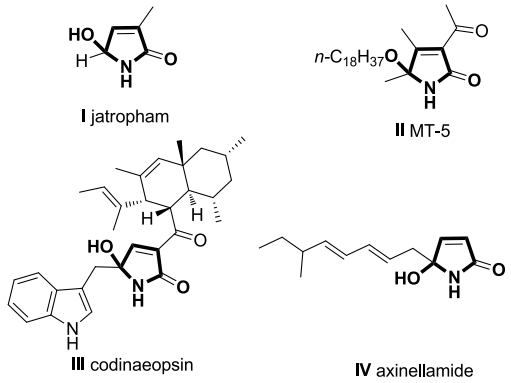



**Figure 1.** Biologically active compounds with a 5-hydroxy-1*H*-pyrrol-2(5*H*)-one skeleton.

structural and biological activities include jatropham[2] (**I**, antitumor), MT-5[3] (**II**, antitumor), codinaeopsin[4] (**III**, natural product), and axinellamide[5] (**IV**, antiplasmodium). In addition, they also have attracted a lot of interest as versatile building blocks in organic synthesis and medicinal chemistry.[6] As a consequence, a number of synthetic strategies have been developed to access these heterocycles, including intra- and intermolecular routes as well as oxidation reactions of heterocyclic compounds.[7] However, some of the reported methods suffer from one or more disadvantages such as long reaction time, use of transition-metal catalysts, unsatisfactory product yields, and harsh reaction conditions. Therefore, it is still in high demand to develop novel and efficient protocols for the synthesis of 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones.

The selective cleavage of unstrained C−C bonds has been a critical issue in modern organic synthesis because of its exceptionally high application potential associated with the ubiquitously available C−C bonds in nature.[8] Ketones are one of the most fundamental classes of compounds and have been extensively employed as main building blocks for the synthesis of a great variety of organic products.[9] In addition to considerable numbers of transformations of ketones via reduction, addition, and α-functionalization reactions, scissoring the corresponding C(CO)−C bond is gaining great attention and developing rapidly.[10,11] As typical ketone derivatives, β-enaminones have attracted a lot of interest because of their versatility in various organic and medicinal syntheses.[12] Predominantly, the functionalization of the vinyl C=C double bond cleavage has been identified as a highly beneficial strategy in the synthesis of many valuable chemical products.[13] In contrast, the reactions involving the cleavage of the C(CO)−C bond of β-enaminones have been barely described to date, which is probably due to its high energy.[14] Only Takai, Cui, and Cheng groups have reported such transformations of C(CO)−C(alkenyl) bond cleavage for the synthesis of pyridines, triazoles, and pyrroles. To the best of our knowledge, the process involving the C(CO)−C(Ar) bond cleavage and reformation of aryl-substituted β-enaminone ($R^4$ = Ar, Scheme 1a), which could deliver various valuable organic compounds, has not been described and remained a significant

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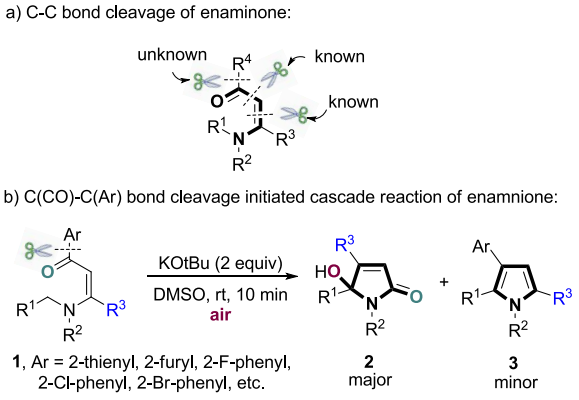
**Scheme 1. C−C Bond Cleavage of β-Enaminones**



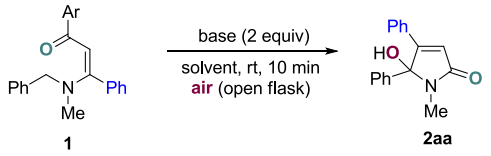

synthetic challenge. Recently, our group has reported the base-promoted *N*-α-sp$^3$C−H functionalization of *N*-benzyl β-enaminones **1** for the synthesis of substituted pyrroles **3** (Scheme 1b).[15] Interestingly, during our further endeavor in exploring the substrate scope, we have observed a tunable reaction pathway, affording 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones **2** by using steric hindrance aryl-group-substituted β-enaminones **1** as substrates (Scheme 1b). As our successive efforts in heterocyclic chemistry,[16] we report herein an unprecedented C(CO)−C(Ar) bond cleavage of *N*-benzyl β-enaminones, which could initiate an 1,3-O,C migration/aerobic hydroxylation cascade to offer substituted 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones.

## RESULTS AND DISCUSSION

Initially, thiophen-2-yl-substituted *N*-benzyl β-enaminone **1aa** was chosen as a model substrate to begin our exploration of the reaction conditions. Under the optimized conditions in our previous report,[15] 5-hydroxy-1*H*-pyrrol-2(5*H*)-one **2aa** was obtained in 84% yield as the major product, and only 9% of the expected pyrrole product, 1-methyl-2,5-diphenyl-3-(thiophen-2-yl)-1*H*-pyrrole **3aa**, was observed as a minor product (entry 1, Table 1). Based on this result, other bases, including inorganic bases and organic bases, were subsequently tested. Only NaO*t*Bu could also drive the reaction and give **2aa** in a lower yield (76%, entry 2). When other bases, such as KOH, NaOH, $Cs_2CO_3$, and DBU (1,8-diazabicyclo [5.4.0]undec-7-ene), were employed, **1aa** remained unreactive (entries 3−6). Further, a survey of different solvents, such as DMF, NMP, EtOH, THF, and toluene, indicated that DMSO was a better solvent than the other tested candidates. Two equiv of KO*t*Bu was crucial for a complete conversion. Reducing the amount of KO*t*Bu was found to be negative, and a considerably lower yield of **2aa** was afforded (55%, entry 12). Under the optimized reaction conditions (entry 1), other steric hindrance aryl-group-substituted β-enaminones **1b−1g** were then screened, and the desired 5-hydroxy-1*H*-pyrrol-2(5*H*)-one product **2aa** could also be successfully attained, albeit in decreased yields (entries 13−18). Finally, the standard reaction condition was identified as follows: 2 equiv of KO*t*Bu as the additive and DMSO as the solvent at rt for 10 min.

Since the *N*-benzyl β-enaminones **1** could be readily prepared from benzylamines and ynones via a Michael reaction,[12] a "one-pot" strategy to 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones **2** direct from benzylamines **4** and ynones **5** was adopted to further make this reaction more attractive. To our

**Table 1. Optimization of Reaction Conditions**[a]




| entry | base | solvent | Ar (**1**) | yield (%)[b] |
|---|---|---|---|---|
| 1 | KO*t*Bu | DMSO | 2-thienyl (**1aa**) | 84 |
| 2 | NaO*t*Bu | DMSO | 2-thienyl (**1aa**) | 76 |
| 3[c] | NaOH | DMSO | 2-thienyl (**1aa**) | NR |
| 4[c] | KOH | DMSO | 2-thienyl (**1aa**) | NR |
| 5[c] | $Cs_2CO_3$ | DMSO | 2-thienyl (**1aa**) | NR |
| 6[c] | DBU | DMSO | 2-thienyl (**1aa**) | NR |
| 7 | KO*t*Bu | DMF | 2-thienyl (**1aa**) | 58 |
| 8 | KO*t*Bu | NMP | 2-thienyl (**1aa**) | 65 |
| 9[c] | KO*t*Bu | EtOH | 2-thienyl (**1aa**) | NR |
| 10[c] | KO*t*Bu | THF | 2-thienyl (**1aa**) | NR |
| 11[c] | KO*t*Bu | toluene | 2-thienyl (**1aa**) | NR |
| 12[d] | KO*t*Bu | DMSO | 2-thienyl (**1aa**) | 55 |
| 13 | KO*t*Bu | DMSO | 2-furanyl (**1b**) | 26 |
| 14 | KO*t*Bu | DMSO | 2-$OMeC_6H_4$ (**1c**) | 48 |
| 15 | KO*t*Bu | DMSO | 2-$FC_6H_4$ (**1d**) | 59 |
| 16 | KO*t*Bu | DMSO | 2-$ClC_6H_4$(**1e**) | 69 |
| 17 | KO*t*Bu | DMSO | 2-$BrC_6H_4$ (**1f**) | 21 |
| 18 | KO*t*Bu | DMSO | 2-$MeC_6H_4$ (**1g**) | trace |

[a]Reaction conditions: **1** (0.2 mmol), base (0.4 mmol), in 1 mL of solvent under an air atmosphere for 10 min. [b]Isolated yields. NR = no reaction. [c]The reaction was performed for 2 h. [d]0.2 mmol base was used. DMF = *N*,*N*-dimethylformamide. DMSO = dimethylsulfoxide. NMP = *N*-methyl-2-pyrrolidone. THF = tetrahydrofuran.

delight, from the one-pot strategy, 5-hydroxy-1*H*-pyrrol-2(5*H*)-one **2aa** was afforded in a comparable yield to that from β-enaminones **1aa** (82% vs 84%). Then, the scope of benzylamines **4** was explored. As illustrated in Scheme 2, when $R^1$ was an aryl substituent, the reaction proved to be tolerant of different substituents on the aromatic core. Aryl substituents bearing either electron-rich or electron-deficient groups were all tolerated and afforded the desired products in good yields (**2ba−2ia**, 76−84%). The steric hindrance did not significantly affect this reaction either. Substrates with *ortho*- or *para*-methyl, methoxyl, and F- substituents did not diminish the efficiency of this transformation (**2ba−2ga**). β-Enaminones equipped with halogens (F, Cl, and Br) on $R^1$ afforded the corresponding halogenated 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones in satisfactory yields (**2fa−2ia**, 76−82%). The fused aryl and heteroaryl groups, including naphthyl, furanyl, thienyl, and pyridyl, were also suitable, and the desired 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones were offered smoothly (**2ja−2ma**, 59−75%). When $R^1$ was an aryl group (phenyl, for example), $R^2$ could be various alkyl groups, such as methyl, ethyl, *i*-propyl, *n*-butyl, benzyl, and phenethyl, and the 1-alkyl-5-hydroxy-1*H*-pyrrol-2(5*H*)-ones were provided in 63−88% yields (**2na−2ra**). An aryl group, such as phenyl, was also suitable, and the reaction processed smoothly (**2sa**, 81% yield). When $R^2$ was H, the secondary β-enaminone substrate failed to give the targeted product, and only a trace amount of 1,3-diketone from the hydrolyzation of the substrate was detected.

The scope of 2-thienyl-substituted ynones **5** was investigated as well. Similarly, $R^3$ could also be various aryl substituents; the electric effect and steric hindrance effect did not significantly affect this reaction, and the corresponding products **2ab−2ai**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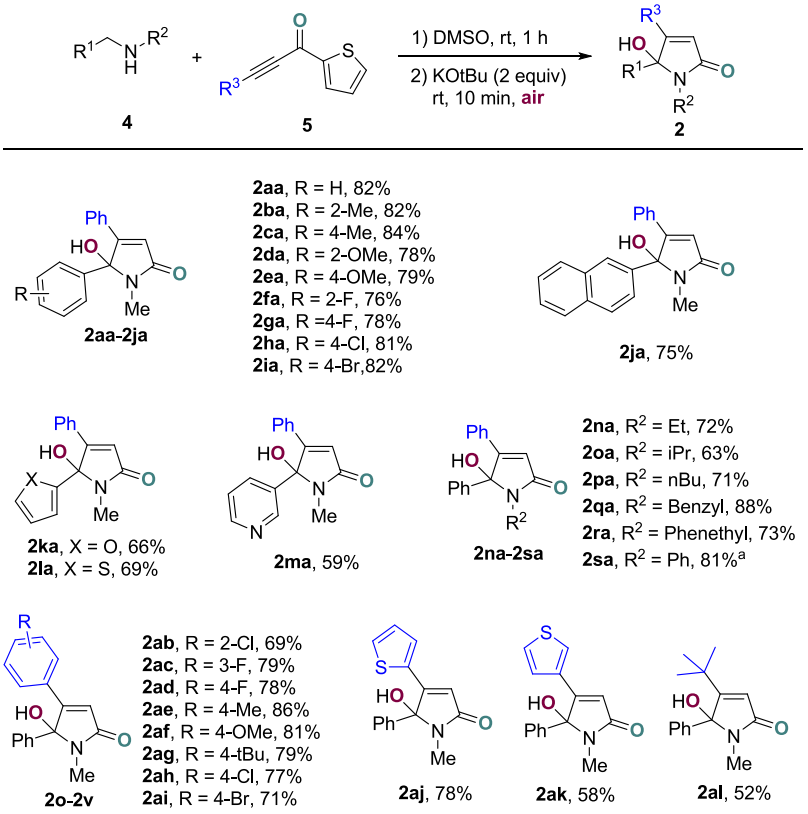
**Scheme 2. Substrate Scope**[a]



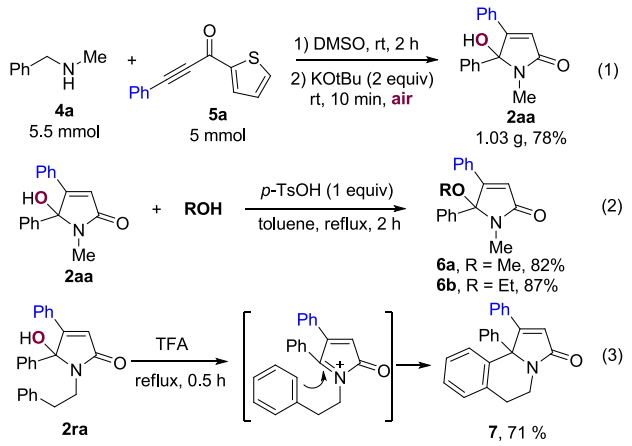

[a]Direct from the corresponding *β*-enaminone substrate **1sa**.

were obtained efficiently (69−86%). The structure of **2ab** was confirmed by single-crystal X-ray diffraction (see Supporting Information for details), and the substituent at C-4 was proven to undergo a 1,3-migration to provide **2ab**. Furthermore, the heteroaryl groups, such as 2-thienyl and 3-thienyl, were also suitable, and the desired products **2aj** and **2ak** were obtained in 78% and 58% yields, respectively. It is worth noting that the aliphatic group (such as *tertiary*-butyl) could also be tolerated; the C-4-alkyl-substituted 5-hydroxy-1*H*-pyrrol-2(5*H*)-one product **2al** was achieved in a good yield (52%).

To prove the practicality of this base-promoted cascade transformation, a gram-scale synthesis of 5-hydroxy-1*H*-pyrrol-2(5*H*)-one **2aa** was conducted. When 0.67 g of **4a** (5.5 mmol) and 1.06 g of **5a** (5 mmol) were loaded, 1.03 g of product could be obtained in 78% yield (eq 1). In order to show the synthetic applicability of prepared compounds, we examined the syntheses of 5-alkoxy-1*H*-pyrrol-2(5*H*)-one derivatives **6a** and **6b** and lactam-fused isoquinoline derivative **7**. As shown in Scheme 3, the reaction of **2aa** with MeOH and EtOH in the presence of *p*-TsOH in refluxing toluene afforded **6a** and **6b** in good yields (82% and 87%, respectively, eq 2). The cyclization reaction of **2ra** in refluxing $CF_3COOH$ was conducted to offer pyrrolo[2,1-*a*]isoquinolin-3-one **7** in a good yield via the *N*-acyliminium ion cyclization mechanism (eq 3).

In order to gain insight into the mechanism, some control experiments were carried out (Scheme 4). At first, the radical scavengers, such as TEMPO (2,2,6,6-tetramethylpiperidinooxy) and 1,1-diphenylethylene, did not inhibit this transformation (eq 4), which indicated that a radical pathway might not be involved in this reaction. Then, the optimized reaction conditions failed to generate **2aa** from pyrrole **3aa** (eq 1),

**Scheme 3. Gram-Scale Reaction and Synthetic Application**




which suggested that it is unlikely for **3aa** to serve as an intermediate in the reaction. On the other hand, when the reaction of *β*-enaminones **1aa** with KO*t*Bu under an atmosphere of $N_2$ was quenched with water after 1 min, only 1*H*-pyrrol-2(3*H*)-one **8aa** and 1*H*-pyrrol-2(5*H*)-one **9aa** were isolated in 12% and 66% yields, respectively. Under the same conditions, **8aa** could be quickly transformed into **9aa** in a nearly quantitative yield. Under an air atmosphere, the reaction of **9aa** gave the desired 5-hydroxy-1*H*-pyrrol-2(5*H*)-one product **2aa** in 95% yield, suggesting that the final 5-hydroxy-1*H*-pyrrol-2(5*H*)-one products **2** were formed by the aerobic oxidation of 1,5-dihydro-2*H*-pyrrol-2-one intermediates.



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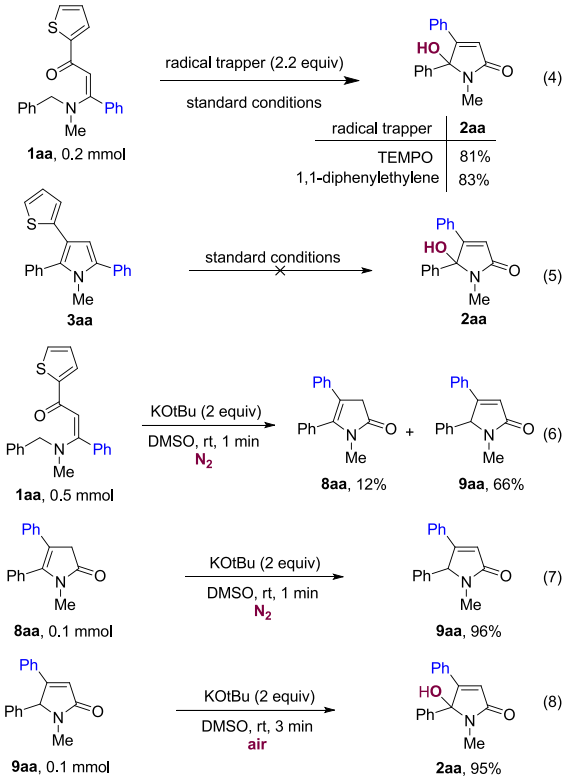
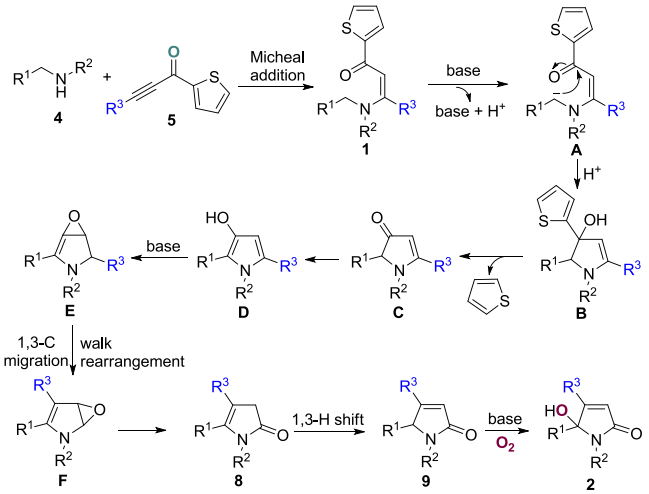
**Scheme 4. Control Experiments**




On the basis of the aforementioned observations, a tentative reaction mechanism was proposed, as depicted in Scheme 5.

**Scheme 5. Proposed Reaction Mechanism**




Initially, the Michael addition of benzylamines **4** and ynones **5** provides *N*-benzyl *β*-enaminones **1**. Then, the superbase-promoted abstraction of the benzylic proton from **1** generates the anions **A**.[15] Anions **A** attacked the electrophilic carbonyl carbon and produced the unstable species **B**. Due to the steric hindrance, 1*H*-pyrrol-3(2*H*)-one intermediates **C** are formed via the elimination of thiophene instead of 1,2,3,5-tetrasubstituted pyrroles **3** via dehydration. The tautomerization of **C** followed with a base-promoted addition leads to epoxy intermediates **E**. The walk rearrangement[17] and 1,3-C migration of **E** give epoxides **F**, which subsequently isomerize to give 1*H*-pyrrol-2(3*H*)-ones **8**. The base-promoted 1,3-H shift of **8** results in the formation of 1*H*-pyrrol-2(5*H*)-one intermediates **9**.[18] Finally, in basic conditions and in the presence of atmospheric oxygen, 1*H*-pyrrol-2(5*H*)-ones **9** are easily converted into 5-hydroxy-1*H*-pyrrol-2(5*H*)-one **2**.[19]

## CONCLUSION

In conclusion, we have achieved the synthesis of substituted 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones via the unprecedented cleavage of the C(CO)−C(Ar) bond in aryl-substituted enaminones under transition-metal-free conditions. This protocol only required 2 equiv of KO*t*Bu as an additive and used environmentally benign $O_2$ (in the air) as an oxygen source, which made this process environmentally friendly. In view of the readily available starting materials, the broad range of substrates, and good reaction efficiencies, this base-mediated cascade reaction can be expected to find wide synthetic applications.

## EXPERIMENTAL SECTION

**General Information.** Unless otherwise stated, all commercial materials and solvents were used directly without further purification. $^1$H NMR spectra were recorded on 400 MHz spectrometers, and $^{13}$C NMR spectra were recorded on a 100 MHz spectrometer. Chemical shifts (in ppm) were referenced to tetramethylsilane ($\delta$ = 0 ppm) in $CDCl_3$ and DMSO-$d_6$ as an internal standard at room temperature. $^{13}$C NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ ($\delta$ = 77.00 ppm) and DMSO-$d_6$ ($\delta$ = 40.00 ppm). High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. Column chromatography was performed on silica gel (70−230 mesh ASTM) using the reported eluents. Thin-layer chromatography (TLC) was carried out on 4 × 15 cm plates with a layer thickness of 0.2 mm (silica gel 60 F254). The heat source is an oil bath. The benzylamines **4** were obtained from commercial suppliers, and most of them were purchased from Adamas and Innochem.

**General Procedure for the Preparation of Ynones 5.** The ynones **5** were prepared according to the reported literature.[20] To a solution of the acid chloride (2 mmol) and alkyne (2.2 mmol) in anhydrous THF (4 mL), under a $N_2$ atmosphere, were added $PdCl_2(PPh_3)_2$ (12.6 mg, 18 $\mu$mol, 0.9 mol %) and then CuI (11.4 mg, 60 $\mu$mol, 3 mol %). After 1 min of stirring, $Et_3N$ (2.5 mmol) was added, and the reaction was left to stir for 2 h at rt. During this time, $Et_3NHCl$ precipitated out of solution, and the solution became dark orange/brown in color. The reaction was then diluted with $Et_2O$ (30 mL) and washed with $H_2O$ (30 mL). The aqueous layer was then extracted with $CH_2Cl_2$ (3 × 30 mL), and all organics were combined and dried ($Na_2SO_4$). The suspension was then filtered, concentrated, and purified by flash chromatography (EtOAc/PE, 1:30). Ynones **5a**,[21] **5d**,[22] **5e**,[23] and **5j**[24] are known compounds.

**General Procedure for the Preparation of *β*-Enaminone 1aa.** A mixture of 3-phenyl-1-(thiophen-2-yl)prop-2-yn-1-one (**5a**, 10 mmol) and *N*-methyl-1-phenylmethanamine (**4a**, 11 mmol) in MeOH (30 mL) was stirred at rt for 12 h. After completion of the Micheal reaction (monitored by TLC), the solvent was evaporated, and the residue was purified by recrystallization using DCM and petroleum to give **1aa** in 91% yield.

**General Procedure for the Preparation of *β*-Enaminone 1sa.** A mixture of 3-phenyl-1-(thiophen-2-yl)prop-2-yn-1-one (**5a**, 2 mmol) and *N*-benzylaniline (**4s**, 2.2 mmol) in MeOH (5 mL) was stirred in a sealed tube at 120 °C (in an oil bath) for 24 h. After completion of the Micheal reaction (monitored by TLC), the solvent was evaporated, and the residue was purified by chromatography (silica gel, EtOAc/PE, 1:10) to give **1sa** in 31% yield.

**General Procedure for the Synthesis of 5-Hydroxy-1*H*-pyrrol-2(5*H*)-ones 2.** A mixture of ynones **5** (0.2 mmol) and benzylamines **4** (0.22 mmol, 1.1 equiv) in DMSO (1 mL) was stirred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at rt for 1 h. After completion of the Micheal reaction (monitored by TLC), KO*t*Bu (0.4 mmol, 2 equiv) was added, and the mixture was stirred under an air atmosphere for 10 min. Then $H_2O$ was added, and the resultant was extracted with EtOAc (3 × 10 mL). The combined EtOAc extracts were dried over $Na_2SO_4$ and concentrated. Then solvent was evaporated, and the residue was purified by chromatography (silica gel, EtOAc/PE 1:2) to give **2**.

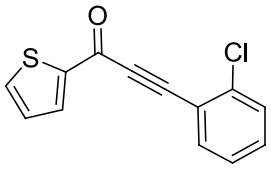
For **2aa** (gram-scale), a mixture of 3-phenyl-1-(thiophen-2-yl)prop-2-yn-1-one **5a** (5 mmol) and *N*-methyl-1-phenylmethanamine **4a** (5.5 mmol, 1.1 equiv) in DMSO (10 mL) was stirred at rt for 2 h. After completion of the Micheal reaction (monitored by TLC), KO*t*Bu (10 mmol, 2 equiv) was added, and the mixture was stirred under an air atmosphere for 10 min. Then $H_2O$ was added, and the resultant was extracted with EtOAc (3 × 20 mL). The combined EtOAc extracts were dried over $Na_2SO_4$ and concentrated. Then solvent was evaporated, and the residue was purified by chromatography (silica gel, EtOAc/PE, 1:2) to give **2aa** in 78% yield (1.03 g).

**Procedure for the Preparation of 6.** A stirred mixture of **2aa** (53 mg, 0.2 mmol), alcohols (MeOH and EtOH, 40 mmol, 20 equiv), and *p*-toluenesulfonic acid (0.2 mmol, 1 equiv) in toluene (2.0 mL) was heated to reflux for 2 h. After the usual aqueous extractive workup and column chromatographic purification process (EtOAc/PE, 1:4), products **6a** and **6b** were obtained as white solids in 82% and 87% yields, respectively.

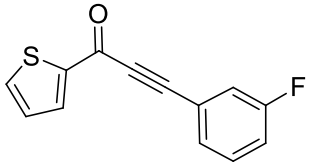
**Procedure for the Preparation of 7.** A stirred mixture of **2ra** (71 mg, 0.2 mmol) in trifluoroacetic acid (2.0 mL) was heated to reflux for 0.5 h. After completion of the reaction (monitored by TLC), the resulting solution was poured into ice water (20 mL), neutralized by NaOH, and extracted with EtOAc (3 × 10 mL). The combined EtOAc extracts were dried over $Na_2SO_4$ and concentrated. Then the solvent was evaporated, and the residue was purified by chromatography (silica gel, EtOAc/PE, 1:4) to give **7** in 71% yield.

**Crystal Growth Procedure.** Approximately 15 mg of the sample (**2ab**) was dissolved in DCM (10 mL) and filtered. A small piece of cotton was used to ensure no solid particles would be present in the solubilized sample. This solution was transferred to a 25 mL vial. This vial was completed with hexanes (10 mL) and then closed. The crystal was formed within 7 days. The crystal was then analyzed.

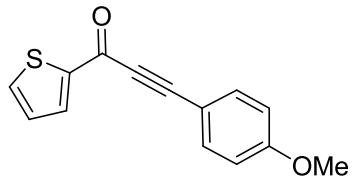
**Analytical Data of Compounds.**



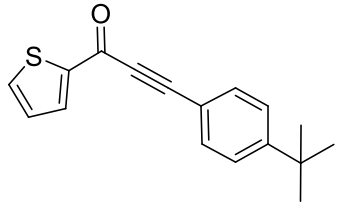

*3-(2-Chlorophenyl)-1-(thiophen-2-yl)prop-2-yn-1-one* ***5b.*** The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 403 mg, 82% yield; brown solid, mp 66−68 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.14 (d, $J$ = 1.1 Hz, 1H), 7.75 (d, $J$ = 4.4 Hz, 1H), 7.70 (d, $J$ = 7.6 Hz, 1H), 7.49 (d, $J$ = 8.0 Hz, 1H), 7.42 (t, $J$ = 7.7 Hz, 1H), 7.32 (t, $J$ = 7.5 Hz, 1H), 7.21 (s, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.6, 144.9, 137.5, 135.9, 135.5, 135.0, 131.8, 129.7, 128.4, 126.9, 120.3, 90.5, 87.6; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{13}H_8ClOS$ 246.9979, found 246.9982.



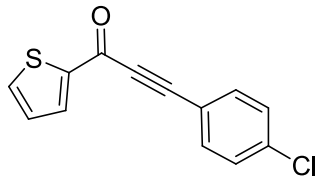

*3-(3-Fluorophenyl)-1-(thiophen-2-yl)prop-2-yn-1-one* ***5c.*** The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 386 mg, 84% yield; pale yellow solid, mp 64−66 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 2.1 Hz, 1H), 7.75 (d, $J$ = 4.7 Hz, 1H), 7.47−7.31 (m, 3H), 7.20 (s, 2H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.4, 162.3 (C−F, $^1J_{C-F}$ = 248.3 Hz), 144.7, 135.5, 135.2, 130.4 (C−F, $^3J_{C-F}$ = 8.5 Hz), 128.9 (C−F, $^4J_{C-F}$ = 3.2 Hz), 128.4, 121.7 (C−F, $^3J_{C-F}$ = 9.3 Hz), 119.6 (C−F, $^2J_{C-F}$ = 23.2 Hz), 118.3 (C−F, $^2J_{C-F}$ = 21.2 Hz), 89.7, 86.7; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{13}H_8FOS$ 231.0274, found 231.0276.



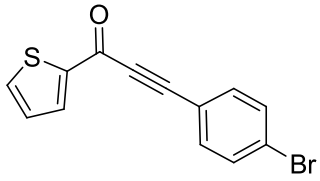

*3-(4-Methoxyphenyl)-1-(thiophen-2-yl)prop-2-yn-1-one* ***5f.*** The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 431 mg, 89% yield; pale yellow solid, mp 71−73 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.99 (s, 1H), 7.71 (d, $J$ = 3.5 Hz, 1H), 7.62 (d, $J$ = 7.9 Hz, 2H), 7.18 (s, 1H), 6.93 (d, $J$ = 8.1 Hz, 2H), 3.86 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.9, 161.7, 145.1, 135.1, 134.9, 134.7, 128.2, 114.4, 111.7, 93.0, 86.4, 55.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{14}H_{11}O_2S^+$ 243.0474, found 243.0477.




*3-(4-(tert-Butyl)phenyl)-1-(thiophen-2-yl)prop-2-yn-1-one* ***5g.*** The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 445 mg, 83% yield: pale yellow solid, mp 59−61 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.01 (s, 1H), 7.72 (d, $J$ = 4.3 Hz, 1H), 7.61 (d, $J$ = 7.3 Hz, 2H), 7.44 (d, $J$ = 7.3 Hz, 2H), 7.19 (s, 1H), 1.34 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.9, 154.6, 145.1, 135.0, 134.9, 132.9, 128.3, 125.8, 116.8, 92.4, 86.3, 35.1, 31.0; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{17}OS$ 269.0995, found 269.0999.




*3-(4-Chlorophenyl)-1-(thiophen-2-yl)prop-2-yn-1-one* ***5h.*** The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 369 mg, 75% yield; brown solid, mp 81−83 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.99 (d, $J$ = 1.6 Hz, 1H), 7.74 (d, $J$ = 4.5 Hz, 1H), 7.59 (d, $J$ = 7.8 Hz, 2H), 7.40 (d, $J$ = 7.9 Hz, 2H), 7.19 (s, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.5, 144.7, 137.2, 135.4, 135.1, 134.2, 129.2, 128.4, 118.4, 90.2, 87.1; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{13}H_8ClOS$ 246.9979, found 246.9984.




*3-(4-Bromophenyl)-1-(thiophen-2-yl)prop-2-yn-1-one* ***5i.*** The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 452 mg, 78% yield; gray solid, mp 122−123 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 2.7 Hz, 1H), 7.75 (d, $J$ = 4.7 Hz, 1H), 7.55 (dd, $J$ = 21.0, 8.1 Hz, 4H), 7.20 (d, $J$ = 4.2 Hz, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.5, 144.7, 135.5, 135.2, 134.3, 132.1, 128.4, 125.7, 118.9, 90.2, 87.3; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{13}H_8BrOS$ 290.9474, found 290.9478.


https://dx.doi.org/10.1021/acs.joc.0c02832
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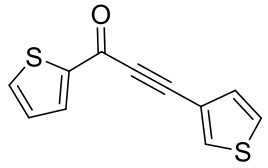
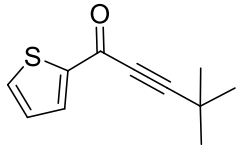
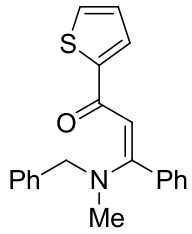


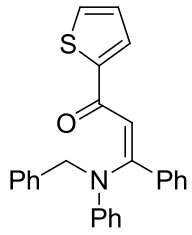
*1-(Thiophen-2-yl)-3-(thiophen-3-yl)prop-2-yn-1-one* ***5k***. The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 314 mg, 72% yield; brown solid, mp 55−56 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.99 (d, $J$ = 2.7 Hz, 1H), 7.83 (s, 1H), 7.72 (d, $J$ = 4.6 Hz, 1H), 7.37 (s, 1H), 7.30 (d, $J$ = 4.3 Hz, 1H), 7.19 (d, $J$ = 3.4 Hz, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.7, 144.9, 135.2, 135.0, 133.9, 130.2, 128.3, 126.3, 119.2, 87.1, 86.7; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{11}H_7OS_2$ 218.9933, found 218.9937.



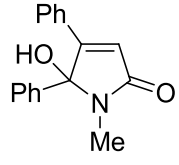
*4,4-Dimethyl-1-(thiophen-2-yl)pent-2-yn-1-one* ***5l***. The compound was purified by column chromatography (EtOAc/Pe, 1:30 v/v): 311 mg, 81% yield: yellow oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.87 (s, 1H), 7.71−7.63 (m, 1H), 7.14 (s, 1H), 1.37 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 170.1, 145.1, 134.7, 128.1, 102.5, 77.8, 30.0, 27.9; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{11}H_{13}OS$ 193.0682, found 193.0685.



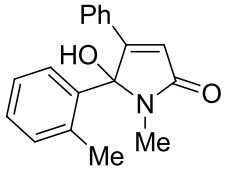
*(Z)-3-(benzyl(methyl)amino)-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-one* ***1aa***. The compound was purified by recrystallization (DCM and PE): 3.03 g, 91% yield; pale yellow solid, mp 95−97 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.56 (s, 1H), 7.35 (dd, $J$ = 23.7, 14.2 Hz, 9H), 7.16 (s, 2H), 7.02 (s, 1H), 5.96 (s, 1H), 4.32 (s, 2H), 2.98 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 179.4, 164.1, 149.0, 136.3, 130.0, 128.7, 128.5, 128.5, 128.1, 127.9, 127.5, 127.3, 127.3, 126.9, 93.6, 55.6, 38.0; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{21}H_{20}NOS$ 334.1260, found 334.1263.



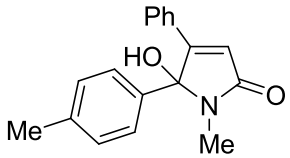
*(Z)-3-(benzyl(phenyl)amino)-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-one* ***1sa***. The compound was purified by column chromatography (EtOAc/Pe, 1:10 v/v): 91.5 mg, 31% yield; pale yellow solid, mp 111−113 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.37−7.21 (m, 14H), 7.15 (d, $J$ = 6.5 Hz, 3H), 6.94 (s, 1H), 6.03 (s, 1H), 4.84 (s, 2H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 180.1, 163.0, 148.8, 144.8, 137.2, 135.8, 130.6, 129.3, 129.1, 128.6, 128.6, 128.2, 127.5, 127.4, 127.4, 127.3, 126.4, 98.8, 57.0; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{26}H_{22}NOS$ 396.1417, found 396.1420.



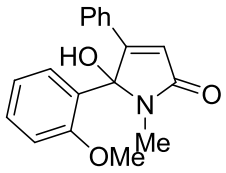
*5-Hydroxy-1-methyl-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***2aa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 43.5 mg, 82% yield (one-pot operation); white solid, mp 198−200 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.77−7.63 (m, 2H), 7.46−7.33 (m, 4H), 7.29 (dd, $J$ = 9.4, 6.2 Hz, 4H), 7.14 (s, 1H), 6.81 (s, 1H), 2.48 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.6, 159.6, 139.2, 131.1, 130.0, 129.1, 128.8, 128.5, 128.1, 125.9, 120.6, 92.0, 23.5; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{17}H_{16}NO_2$ 266.1176, found 266.1173.



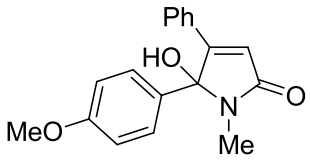
*5-Hydroxy-1-methyl-4-phenyl-5-(o-tolyl)-1H-pyrrol-2(5H)-one* ***2ba***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 45.8 mg, 82% yield; white solid, mp 166−168 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 8.12 (d, $J$ = 7.8 Hz, 1H), 7.73−7.56 (m, 2H), 7.46−7.24 (m, 4H), 7.20 (t, $J$ = 7.2 Hz, 1H), 7.04 (d, $J$ = 7.2 Hz, 1H), 6.97 (s, 1H), 6.77 (s, 1H), 2.46 (s, 3H), 1.93 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 169.4, 158.9, 136.3, 135.3, 132.4, 131.5, 130.1, 128.9, 128.9, 128.7, 127.8, 126.8, 121.7, 91.3, 23.6, 19.5; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{18}H_{18}NO_2$ 280.1332, found 280.1322.



*5-Hydroxy-1-methyl-4-phenyl-5-(p-tolyl)-1H-pyrrol-2(5H)-one* ***2ca***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 46.9 mg, 84% yield; white solid, mp 202−204 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.71−7.64 (m, 2H), 7.28 (dd, $J$ = 7.4, 4.8 Hz, 5H), 7.15 (d, $J$ = 8.0 Hz, 2H), 7.04 (s, 1H), 6.75 (s, 1H), 2.47 (s, 3H), 2.25 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.5, 159.6, 137.7, 136.2, 131.1, 129.9, 129.6, 128.8, 128.1, 125.8, 120.4, 92.0, 23.4, 21.1; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{18}H_{18}NO_2$ 280.1332, found 280.1333.



*5-Hydroxy-5-(2-methoxyphenyl)-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2da***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 46.0 mg, 78% yield; white solid, mp 171−173 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.97 (dd, $J$ = 7.7, 1.3 Hz, 1H), 7.63 (dd, $J$ = 6.5, 3.0 Hz, 2H), 7.34−7.19 (m, 4H), 7.05 (t, $J$ = 7.4 Hz, 1H), 6.88 (d, $J$ = 8.1 Hz, 1H), 6.84 (s, 1H), 6.64 (s, 1H), 3.49 (s, 3H), 2.42 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 169.6, 158.7, 156.9, 131.9, 130.3, 129.6, 129.4, 128.7, 127.6, 126.4, 120.9, 120.7, 112.5, 90.2, 56.1, 23.8; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{18}H_{18}NO_3$ 296.1281, found 296.1282.



*5-Hydroxy-5-(4-methoxyphenyl)-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2ea***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 46.6 mg, 79% yield; white solid, mp 223−224 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.72−7.65 (m, 2H), 7.29 (dd, $J$ = 7.4, 2.6 Hz, 5H), 7.02 (s, 1H), 6.89 (d, $J$ = 8.9 Hz, 2H), 6.74 (s, 1H), 3.71 (s, 3H), 2.47 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz,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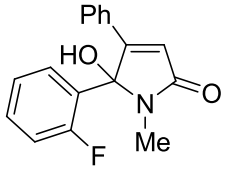
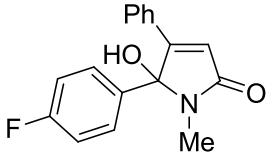
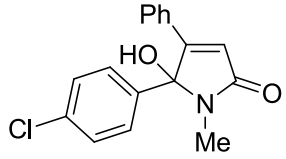
DMSO) $\delta$ 168.4, 159.6, 159.3, 131.2, 130.9, 129.9, 128.8, 128.1, 127.2, 120.3, 114.3, 91.9, 55.4, 23.4; HRMS (ESI) $m/z$ [M + H]+ calcd for $C_{18}H_{18}NO_3$ 296.1281, found 296.1278.



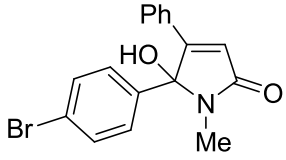

*5-(2-Fluorophenyl)-5-hydroxy-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2fa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 43.0 mg, 76% yield; white solid, mp 165−167 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 8.02 (t, $J$ = 7.0 Hz, 1H), 7.67 (s, 2H), 7.30 (t, $J$ = 25.8 Hz, 6H), 7.10−7.00 (m, 1H), 6.76 (s, 1H), 2.50 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.9, 159.33 (C−F, $^1J_{C-F}$ = 249.0 Hz), 158.4, 131.3, 131.2, 130.1, 130.0 (C−F, $^4J_{C-F}$ = 1.7 Hz), 128.9, 127.7, 126.3 (C−F, $^2J_{C-F}$ = 9.2 Hz), 125.1 (C−F, $^3J_{C-F}$ = 3.4 Hz), 120.9 (C−F, $^3J_{C-F}$ = 2.7 Hz), 116.6 (C−F, $^2J_{C-F}$ = 21.9 Hz), 89.5, 23.6; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}FNO_2$ 284.1081, found 284.1078.



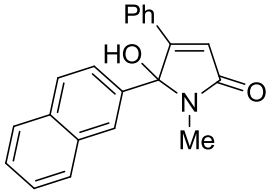

*5-(4-Fluorophenyl)-5-hydroxy-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2ga***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 44.1 mg, 78% yield; white solid, mp 169−171 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.71−7.63 (m, 2H), 7.42 (dd, $J$ = 8.7, 5.5 Hz, 2H), 7.34−7.26 (m, 3H), 7.23−7.13 (m, 3H), 6.79 (s, 1H), 2.48 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.4, 162.1 (C−F, $^1J_{C-F}$ = 244.4 Hz), 159.4, 135.4 (C−F, $^4J_{C-F}$ = 2.9 Hz), 131.0, 130.0, 128.8, 128.2 (C−F, $^3J_{C-F}$ = 8.5 Hz), 128.1, 120.7, 115.9 (C−F, $^2J_{C-F}$ = 21.6 Hz), 91.6, 23.3; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}FNO_2$ 284.1081, found 284.1078.



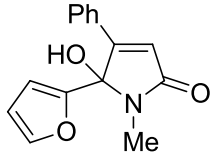

*5-(4-Chlorophenyl)-5-hydroxy-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2ha***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 48.4 mg, 81% yield; white solid, mp 165−167 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.67 (s, 2H), 7.41 (s, 4H), 7.31 (s, 3H), 7.25 (s, 1H), 6.81 (s, 1H), 2.49 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.5, 159.2, 138.3, 133.2, 130.9, 130.1, 129.1, 128.9, 128.0, 127.9, 120.8, 91.6, 23.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}ClNO_2$ 300.0786, found 300.0782.



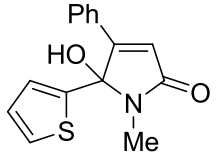

*5-(4-Bromophenyl)-5-hydroxy-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2ia***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 56.3 mg, 82% yield; white solid, mp 176−177 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.67 (dd, $J$ = 6.5, 3.0 Hz, 2H), 7.55 (d, $J$ = 8.6 Hz, 2H), 7.37−7.28 (m, 5H), 7.25 (s, 1H), 6.81 (s, 1H), 2.49 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.5, 159.2, 138.8, 132.0, 130.9, 130.1, 128.9, 128.3, 128.0, 121.8, 120.8, 91.6, 23.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}BrNO_2$ 344.0281, found 344.0282.



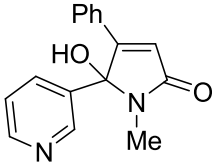

*5-Hydroxy-1-methyl-5-(naphthalen-2-yl)-4-phenyl-1H-pyrrol-2(5H)-one* ***2ja***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 47.3 mg, 75% yield; white solid, mp 229−231 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 8.22 (s, 1H), 8.05−7.96 (m, 1H), 7.85 (t, $J$ = 8.9 Hz, 2H), 7.73 (dd, $J$ = 6.6, 3.1 Hz, 2H), 7.58−7.45 (m, 2H), 7.40−7.02 (m, 5H), 6.88 (s, 1H), 2.49 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.7, 159.4, 136.7, 133.2, 133.0, 131.1, 130.1, 128.9, 128.9, 128.8, 128.1, 128.0, 127.0, 126.9, 125.5, 123.4, 120.9, 92.1, 23.5; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{21}H_{18}NO_2$ 316.1332, found 316.1335.




*5-(Furan-2-yl)-5-hydroxy-1-methyl-4-phenyl-1H-pyrrol-2(5H)-one* ***2ka***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 33.7 mg, 66% yield; white solid, mp 154−156 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.79−7.72 (m, 2H), 7.53 (d, $J$ = 0.7 Hz, 1H), 7.38−7.32 (m, 3H), 7.25 (s, 1H), 6.75 (s, 1H), 6.69 (d, $J$ = 2.8 Hz, 1H), 6.45 (dd, $J$ = 3.2, 1.8 Hz, 1H), 2.56 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.4, 157.3, 151.7, 143.5, 131.1, 130.2, 128.9, 127.8, 120.7, 111.0, 109.6, 89.3, 23.7; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{15}H_{14}NO_3$ (MH+) 256.0968, found 256.0971.




*5-Hydroxy-1-methyl-4-phenyl-5-(thiophen-2-yl)-1H-pyrrol-2(5H)-one* ***2la***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 37.4 mg, 69% yield; white solid, mp 198−200 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.83−7.70 (m, 2H), 7.45 (dd, $J$ = 4.0, 2.3 Hz, 1H), 7.33 (dd, $J$ = 6.3, 3.0 Hz, 4H), 6.99−6.91 (m, 2H), 6.74 (s, 1H), 2.59 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 167.9, 159.3, 143.9, 131.0, 130.1, 128.8, 128.1, 127.7, 126.7, 125.5, 120.1, 90.9, 23.5; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{15}H_{14}NO_2S$ 272.0740, found 272.0735.




*5-Hydroxy-1-methyl-4-phenyl-5-(pyridin-3-yl)-1H-pyrrol-2(5H)-one* ***2ma***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 31.4 mg, 59% yield; white solid, mp 202−204 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 8.64 (d, $J$ = 1.8 Hz, 1H), 8.50 (dd, $J$ = 4.6, 1.2 Hz, 1H), 7.75−7.68 (m, 3H), 7.41 (s, 1H), 7.37 (dd, $J$ = 7.9, 4.8 Hz, 1H), 7.34−7.29 (m, 3H), 6.86 (s, 1H), 2.52 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.5, 158.9, 149.9, 147.7, 134.9, 134.0, 130.8, 130.3, 129.0, 128.1, 124.2, 121.1, 91.1, 23.5; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{16}H_{15}N_2O_2$ 267.1128, found 267.1125.



https://dx.doi.org/10.1021/acs.joc.0c02832
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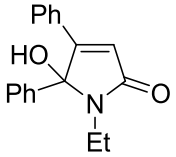
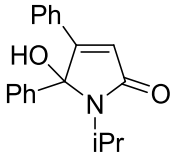
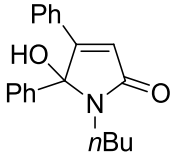


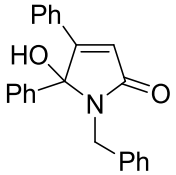
*1-Ethyl-5-hydroxy-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***2na***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 40.2 mg 72% yield; white solid, mp 170−172 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.69−7.63 (m, 2H), 7.44 (d, $J$ = 7.4 Hz, 2H), 7.34 (t, $J$ = 7.5 Hz, 2H), 7.31−7.23 (m, 4H), 7.10 (s, 1H), 6.78 (s, 1H), 3.17 (dq, $J$ = 14.3, 7.1 Hz, 1H), 2.92 (dq, $J$ = 14.2, 7.1 Hz, 1H), 0.80 (t, $J$ = 7.2 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.6, 159.2, 139.8, 131.0, 129.9, 128.9, 128.8, 128.5, 128.1, 125.9, 120.7, 92.2, 33.2, 14.5; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{18}H_{18}NO_2$ 280.1332, found 280.1332.



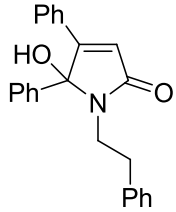
*5-Hydroxy-1-isopropyl-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***2oa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 36.9 mg, 63% yield; white solid, mp 187−189 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.65−7.59 (m, 2H), 7.47 (d, $J$ = 7.3 Hz, 2H), 7.34 (t, $J$ = 7.5 Hz, 2H), 7.30−7.21 (m, 4H), 7.07 (s, 1H), 6.70 (s, 1H), 3.36 (dd, $J$ = 13.6, 6.8 Hz, 1H), 1.29 (d, $J$ = 6.8 Hz, 3H), 0.90 (d, $J$ = 6.8 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.4, 158.2, 139.6, 131.0, 129.8, 128.7, 128.4, 128.0, 126.0, 121.7, 92.5, 43.4, 21.2, 19.9; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{19}H_{20}NO_2$ 294.1489, found 294.1484.



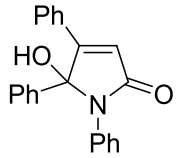
*1-Butyl-5-hydroxy-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***2pa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 43.6 mg, 71% yield; white solid, mp 172−174 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.66 (s, 2H), 7.43 (d, $J$ = 6.8 Hz, 2H), 7.38−7.22 (m, 6H), 7.09 (s, 1H), 6.78 (s, 1H), 3.12 (d, $J$ = 9.0 Hz, 1H), 2.83 (dd, $J$ = 13.2, 7.8 Hz, 1H), 1.24 (s, 1H), 1.08 (s, 3H), 0.71 (t, $J$ = 6.7 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.9, 159.1, 139.8, 131.0, 129.9, 128.9, 128.7, 128.4, 128.1, 125.8, 120.7, 92.2, 38.2, 30.9, 20.1, 14.0; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{20}H_{22}NO_2$ 308.1645, found 308.1641.



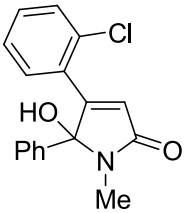
*1-Benzyl-5-hydroxy-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***2qa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 60.0 mg, 88% yield; white solid, mp 215−217 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.68 (s, 2H), 7.40 (s, 2H), 7.32−7.16 (m, 7H), 7.16−6.98 (m, 5H), 6.91−6.83 (m, 1H), 4.28 (d, $J$ = 15.6 Hz, 1H), 4.08 (d, $J$ = 14.8 Hz, 1H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 169.3, 159.6, 139.4, 138.8, 131.1, 130.0, 128.8, 128.8, 128.4, 128.2, 128.1, 128.1, 126.7, 126.0, 120.5, 92.4, 42.3; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{23}H_{20}NO_2$ 342.1489, found 342.1492.



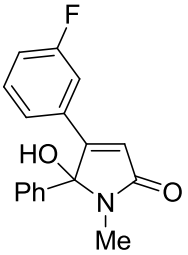
*5-Hydroxy-1-phenethyl-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***2ra***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 51.8 mg, 73% yield; white solid, mp 155−157 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.69 (s, 2H), 7.49 (d, $J$ = 6.9 Hz, 2H), 7.38 (t, $J$ = 7.4 Hz, 2H), 7.30 (s, 4H), 7.26−7.21 (m, 3H), 7.16 (d, $J$ = 7.0 Hz, 1H), 6.99 (d, $J$ = 7.2 Hz, 2H), 6.86 (s, 1H), 3.32−3.24 (m, 1H), 3.09−2.99 (m, 1H), 2.68 (td, $J$ = 12.1, 5.0 Hz, 1H), 2.19 (td, $J$ = 12.2, 5.0 Hz, 1H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.8, 159.2, 139.7, 139.6, 131.0, 130.1, 129.1, 128.9, 128.9, 128.7, 128.3, 126.6, 125.9, 120.7, 92.2, 35.1; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{24}H_{22}NO_2$ 356.1645, found 356.1642.



*5-Hydroxy-1,4,5-triphenyl-1H-pyrrol-2(5H)-one* ***2sa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 53.0 mg, 81% yield; white solid, mp 188−190 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.82 (s, 1H), 7.74 (dd, $J$ = 6.4, 2.8 Hz, 2H), 7.42 (d, $J$ = 7.7 Hz, 2H), 7.32 (dd, $J$ = 8.8, 5.9 Hz, 4H), 7.26−7.14 (m, 5H), 7.07 (t, $J$ = 7.3 Hz, 2H), 6.95 (s, 1H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.7, 159.8, 139.3, 136.7, 130.9, 130.3, 128.9, 128.8, 128.6, 128.4, 126.1, 125.9, 125.7, 125.7, 120.4, 94.2; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{22}H_{18}NO_2$ 328.1332, found 328.1329.



*4-(2-Chlorophenyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2ab***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 41.3 mg, 69% yield; white solid, mp 180−182 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.70 (dt, $J$ = 7.0, 3.4 Hz, 1H), 7.42−7.38 (m, 1H), 7.32−7.23 (m, 7H), 7.20−7.18 (m, 1H), 6.53 (d, $J$ = 2.1 Hz, 1H), 2.58 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.6, 156.7, 137.8, 133.0, 130.7, 130.7, 130.5, 130.2, 128.9, 128.7, 127.1, 126.2, 125.9, 93.5, 24.0; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}ClNO_2$ 300.0786, found 300.0782.



*4-(3-Fluorophenyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2ac***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 44.7 mg, 79% yield; white solid, mp 163−165 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.50 (dd, $J$ = 15.3, 4.8 Hz, 2H), 7.43−7.33 (m, 5H), 7.32−7.27 (m, 1H), 7.21 (s, 1H), 7.15 (td, $J$ = 8.6, 2.3 Hz, 1H), 6.92 (s, 1H), 2.47 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.3, 162.3 (C−F, $^1J_{C-F}$ = 242.9 Hz), 158.2, 138.8, 133.4 (C−F, $^3J_{C-F}$ = 8.3 Hz), 130.9 (C−F, $^3J_{C-F}$ = 8.4 Hz),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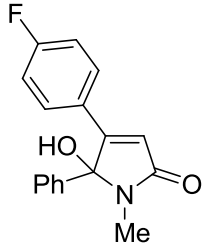
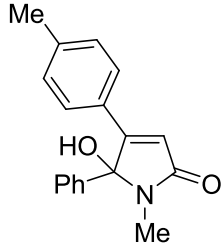
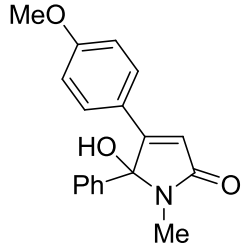
129.2, 128.7, 125.9, 124.3 (C−F, $^4J_{C-F}$ = 2.7 Hz), 122.1, 116.8 (C−F, $^2J_{C-F}$ = 21.1 Hz), 114.6 (C−F, $^2J_{C-F}$ = 22.8 Hz), 91.9, 23.5; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}FNO_2$ 284.1081, found 284.1081.



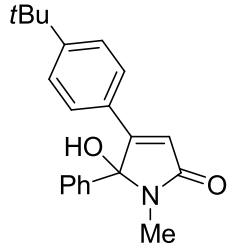

*4-(4-Fluorophenyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2ad***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 44.1 mg, 78% yield; white solid, mp 169−171 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.80−7.69 (m, 2H), 7.37 (dt, $J$ = 15.3, 7.5 Hz, 4H), 7.28 (dd, $J$ = 9.4, 4.3 Hz, 1H), 7.20−7.06 (m, 3H), 6.78 (s, 1H), 2.47 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.5, 163.0 (C−F, $^1J_{C-F}$ = 248.2 Hz), 158.5, 139.0, 130.4 (C−F, $^3J_{C-F}$ = 8.4 Hz), 129.1, 128.6, 127.7 (C−F, $^4J_{C-F}$ = 3.3 Hz), 125.8, 120.5, 115.8 (C−F, $^2J_{C-F}$ = 21.6 Hz), 91.9, 23.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}FNO_2$ 284.1081, found 284.1078.



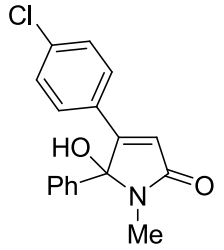

*5-Hydroxy-1-methyl-5-phenyl-4-(p-tolyl)-1H-pyrrol-2(5H)-one* ***2ae***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 48.0 mg, 86% yield; white solid, mp 204−205 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.58 (d, $J$ = 8.0 Hz, 2H), 7.44−7.31 (m, 4H), 7.26 (t, $J$ = 6.8 Hz, 1H), 7.14−7.05 (m, 3H), 6.73 (s, 1H), 2.47 (s, 3H), 2.23 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.7, 159.7, 139.8, 139.3, 129.4, 129.0, 128.5, 128.3, 128.1, 125.9, 119.5, 91.9, 23.4, 21.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{18}H_{18}NO_2$ 280.1332, found 280.1332.



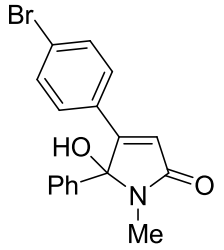

*5-Hydroxy-4-(4-methoxyphenyl)-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2af***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 47.8 mg, 81% yield; white solid, mp 185−187 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.64 (d, $J$ = 8.9 Hz, 2H), 7.36 (dt, $J$ = 15.2, 7.5 Hz, 4H), 7.27 (t, $J$ = 6.9 Hz, 1H), 7.08 (s, 1H), 6.85 (d, $J$ = 8.9 Hz, 2H), 6.65 (s, 1H), 3.71 (s, 3H), 2.45 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.9, 160.7, 159.4, 139.5, 129.8, 129.0, 128.5, 125.8, 123.5, 118.2, 114.3, 91.9, 55.7, 23.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{18}H_{18}NO_3$ 296.1281, found 296.1282.



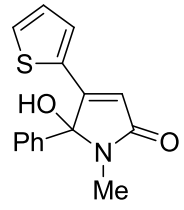

*4-(4-(tert-Butyl)phenyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2ag***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 50.7 mg, 79% yield; white solid, mp 199−201 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.60 (d, $J$ = 8.4 Hz, 2H), 7.34 (ddd, $J$ = 24.1, 14.2, 6.9 Hz, 7H), 7.05 (s, 1H), 6.72 (s, 1H), 2.46 (s, 3H), 1.21 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.6, 159.5, 152.8, 139.3, 129.0, 128.5, 128.2, 127.9, 125.8, 125.6, 119.7, 91.9, 34.9, 31.2, 23.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{21}H_{24}NO_2$ 322.1802, found 322.1799.




*4-(4-Chlorophenyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2ah***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 46.0 mg, 77% yield; white solid, mp 196−198 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.70 (d, $J$ = 8.6 Hz, 2H), 7.38 (t, $J$ = 8.2 Hz, 6H), 7.29 (d, $J$ = 6.3 Hz, 1H), 7.18 (s, 1H), 6.84 (s, 1H), 2.48 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.3, 158.3, 138.8, 134.7, 129.9, 129.8, 129.1, 128.9, 128.6, 125.8, 121.3, 91.8, 23.4; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}ClNO_2$ 300.0786, found 300.0782.




*4-(4-Bromophenyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2ai***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 48.7 mg, 71% yield; white solid, mp 212−214 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.63 (d, $J$ = 8.6 Hz, 2H), 7.51 (d, $J$ = 8.6 Hz, 2H), 7.45−7.31 (m, 4H), 7.31−7.25 (m, 1H), 7.20 (s, 1H), 6.86 (s, 1H), 2.47 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 168.4, 158.4, 138.8, 131.9, 130.3, 130.1, 129.1, 128.7, 125.9, 123.6, 121.4, 91.8, 23.5; HRMS (ESI) $m/z$ [M + H]$^+$ calcd for $C_{17}H_{15}BrNO_2$ 344.0281, found 344.0282.




*5-Hydroxy-1-methyl-5-phenyl-4-(thiophen-2-yl)-1H-pyrrol-2(5H)-one* ***2aj***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 42.3 mg, 78% yield; white solid, mp 202−204 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.65−7.57 (m, 1H), 7.38 (dt, $J$ = 15.1, 7.4 Hz, 5H), 7.32−7.27 (m, 1H), 7.15 (s, 1H), 7.02 (dd, $J$ = 4.9, 3.8 Hz, 1H), 6.51 (s, 1H), 2.47 (s, 3H); $^{13}$C{$^1$H} NMR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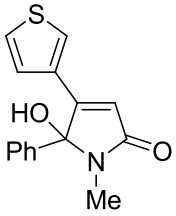
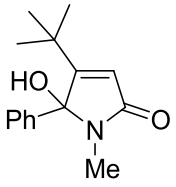
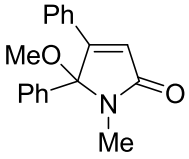
(100 MHz, DMSO) $\delta$ 168.6, 155.0, 138.8, 133.7, 130.0, 129.6, 129.0, 128.7, 128.2, 126.1, 117.8, 91.8, 23.7; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{15}H_{14}NO_2S$ 272.0740, found 272.0750.



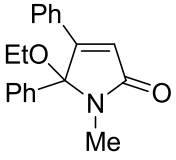

*5-Hydroxy-1-methyl-5-phenyl-4-(thiophen-3-yl)-1H-pyrrol-2(5H)-one* ***2ak***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 31.4 mg, 58% yield; white solid, mp 192−193 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.64 (d, $J$ = 1.9 Hz, 1H), 7.51 (dd, $J$ = 5.1, 2.9 Hz, 1H), 7.45−7.33 (m, 5H), 7.31−7.26 (m, 1H), 7.05 (s, 1H), 6.60 (s, 1H), 2.46 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 169.1, 155.8, 139.2, 132.6, 129.1, 128.5, 127.5, 127.0, 127.0, 126.0, 119.0, 91.7, 23.5; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{15}H_{14}NO_2S$ 272.0740, found 272.0742.



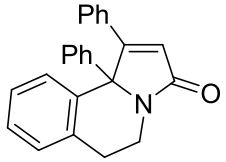

*4-(tert-Butyl)-5-hydroxy-1-methyl-5-phenyl-1H-pyrrol-2(5H)-one* ***2al***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 25.5 mg, 52% yield; white solid, mp 158−160 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.80 (s, 1H), 7.33 (dd, $J$ = 20.0, 13.3 Hz, 3H), 6.87 (t, $J$ = 85.9 Hz, 1H), 6.64 (s, 1H), 6.02 (s, 1H), 2.35 (s, 3H), 0.94 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 172.8, 168.9, 139.0, 128.8, 128.4, 126.4, 121.1, 93.0, 34.3, 30.7, 23.3; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{15}H_{20}NO_2$ 246.1489, found 246.1490.



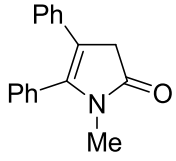

*5-Methoxy-1-methyl-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***6a***. The compound was purified by column chromatography (EtOAc/Pe, 1:4 v/v): 45.8 mg, 82% yield; white solid, mp 147−149 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.58−7.51 (m, 2H), 7.46 (d, $J$ = 7.4 Hz, 2H), 7.34−7.24 (m, 6H), 6.69 (s, 1H), 3.18 (s, 3H), 2.58 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.4, 156.6, 137.1, 130.2, 130.1, 128.7, 128.6, 128.5, 127.1, 125.8, 122.2, 96.7, 50.1, 23.6; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{18}H_{18}NO_2$ 280.1332, found 280.1328.



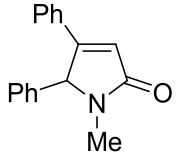

*5-Ethoxy-1-methyl-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***6b***. The compound was purified by column chromatography (EtOAc/Pe, 1:4 v/v): 51.0 mg, 87% yield; white solid, mp 158−160 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.57 (d, $J$ = 7.7 Hz, 2H), 7.49 (d, $J$ = 7.6 Hz, 2H), 7.34−7.22 (m, 6H), 6.67 (s, 1H), 3.32 (dp, $J$ = 45.4, 7.5 Hz, 2H), 2.58 (s, 3H), 1.26 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.3, 157.0, 137.3, 130.3, 130.0, 128.6, 128.6, 128.4, 127.1, 125.8, 121.8, 96.2, 58.1, 23.6, 15.0; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{19}H_{20}NO_2$ 294.1489, found 294.1486.




*1,10b-Diphenyl-5,6-dihydropyrrolo[2,1-a]isoquinolin-3(10bH)-one* ***7***. The compound was purified by column chromatography (EtOAc/Pe, 1:4 v/v): 47.9 mg, 71% yield; pale yellow solid, mp 203−205 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34 (d, $J$ = 5.6 Hz, 4H), 7.27−7.22 (m, 4H), 7.14 (d, $J$ = 5.3 Hz, 2H), 7.07−6.90 (m, 4H), 6.43 (s, 1H), 4.25−4.11 (m, 1H), 3.15−3.00 (m, 2H), 2.78−2.67 (m, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.5, 163.7, 139.2, 135.4, 134.7, 134.7, 129.8, 129.4, 128.8, 128.6, 128.4, 127.9, 127.8, 127.7, 127.7, 125.6, 124.3, 72.8, 35.0, 28.8; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{24}H_{20}NO$ 338.1539, found 338.1535.




*1-Methyl-4,5-diphenyl-1H-pyrrol-2(3H)-one* ***8aa***. The compound was purified by column chromatography (EtOAc/Pe, 1:8 v/v): 15.0 mg, 12% yield; pale yellow semisolid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.51−7.44 (m, 3H), 7.33 (dd, $J$ = 6.5, 3.0 Hz, 2H), 7.15−7.05 (m, 3H), 6.98−6.91 (m, 2H), 3.55 (s, 2H), 2.86 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 176.0, 140.1, 134.0, 131.4, 129.7, 129.3, 129.3, 128.3, 126.4, 126.1, 113.8, 39.3, 27.7; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1226, found 250.1223.




*1-Methyl-4,5-diphenyl-1H-pyrrol-2(5H)-one* ***9aa***. The compound was purified by column chromatography (EtOAc/Pe, 1:2 v/v): 90.1 mg, 73% yield (from **1aa**, eq 5); white solid, mp 128−130 °C; $^1$H NMR (400 MHz, DMSO) $\delta$ 7.59−7.51 (m, 2H), 7.30 (dt, $J$ = 15.0, 7.0 Hz, 8H), 6.73 (s, 1H), 5.80 (s, 1H), 2.64 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, DMSO) $\delta$ 170.2, 158.7, 136.8, 131.9, 130.1, 129.5, 129.1, 128.9, 128.2, 127.5, 121.3, 67.1, 27.0; HRMS (ESI) $m/z$ $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1226, found 250.1223.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02832.

Single-crystal structure and crystallographic data for **2ab** and copies of $^1$H and $^{13}$C NMR spectra for all products (PDF)

### Accession Codes

CCDC 2034572 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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### Notes

The authors declare no competing financial interest.

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