

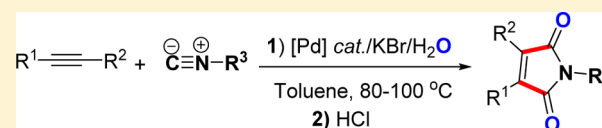
Assembly of Polysubstituted Maleimides via Palladium-Catalyzed Cyclization Reaction of Alkynes with Isocyanides

Weigao Hu, Jia Zheng, Jianxiao Li, Bifu Liu, Wanqing Wu, Haiyang Liu,* and Huanfeng Jiang*[✉]

Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510640, China

S Supporting Information

ABSTRACT: An efficient and convenient palladium-catalyzed cyclization reaction of alkynes with isocyanides is described herein. This protocol allows the practical synthesis of many valuable polysubstituted maleimide derivatives after hydrolysis with a broad scope of substrates and mild reaction conditions. C–C, C=O, and C–N bonds were constructed in this transformation with isocyanide serving as both C and N sources.



The maleimide skeleton is commonly embedded in various natural products which has demonstrated an important class of extraordinary biological and pharmaceutical properties.¹ For example, compound SB 216763 has shown inhibition to the R-isomer of GSK-3 in an ATP-competitive manner.^{1b} Himanimide A and C are used to inhibit the growth of bacteria and fungi. Granulatimide is commonly identified as a checkpoint inhibitor exhibiting good antitumor activity^{1c} (Figure 1). In particular, the arylmaleimide derivatives are also important building blocks in materials science.²

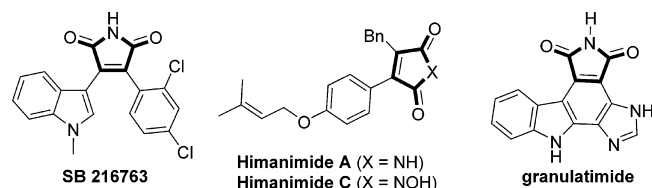


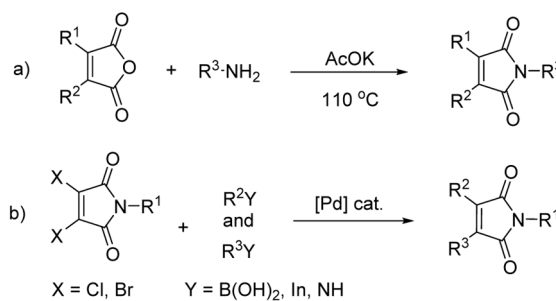
Figure 1. Selected examples containing maleimide motifs in medicine.

Therefore, considerable efforts have been devoted toward their synthesis in the past few decades. Generally, maleimides are prepared through an ammonolysis reaction of maleic anhydrides with ammonia or an ammonium source (Scheme 1a).³ However, this approach is unsuccessful for the synthesis of polysubstituted or unsymmetrical maleimides. To overcome these difficulties, the strategy of selective functionalization of 3,4-dihalomaleimide by Grignard addition⁴ and cross-coupling reaction⁵ has been developed (Scheme 1b). Furthermore, in 2004, Chen and co-workers developed a convenient procedure for preparing 3,4-diaryl-substituted maleimides from diaryl-substituted fumaronitrile.⁶

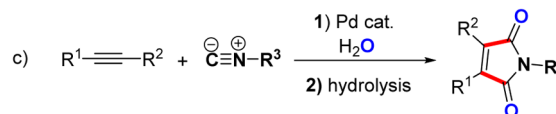
However, unavailable starting materials in these approaches significantly limited their library synthesis and applications. As far as we know, there are few reports on the direct synthesis of polysubstituted maleimides from alkynes under transition metal catalysis.⁷ In this regard, the development of a rapid and straightforward strategy to build small molecule libraries

Scheme 1. Synthesis of Maleimide Derivatives

Previous work



This work



containing diverse maleimide moieties is highly meaningful and desirable.

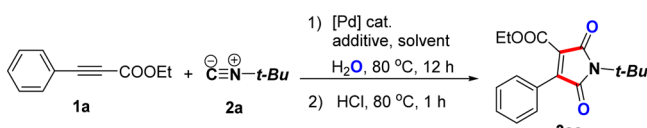
In addition, isocyanides have been recognized as valuable C1 building blocks in organic synthesis because of their structural and reactive properties.⁸ Over the past decade, transition-metal-catalyzed reactions involving isocyanides have drawn wide attention,⁹ especially for palladium catalysis.^{8f,10} To the best of our knowledge, isocyanides utilized as a source of amide have been achieved respectively by Cai,¹¹ Zhu¹², and our group.¹³ Inspired by our previous work on palladium-catalyzed isocyanide insertion reactions^{13,14} and synthesis of important heterocyclic compounds from alkynes,¹⁵ Herein, we would like to describe an efficient and practical palladium-catalyzed intermolecular cyclization reaction of alkynes and isocyanides for the synthesis of polysubstituted maleimides (Scheme 1c).

Received: September 10, 2016

Published: November 16, 2016

Our investigations were initiated with reaction of ethyl 3-phenylpropiolate (**1a**) and *tert*-butyl isocyanide (**2a**) for reaction condition optimization (Table 1). First, various

Table 1. Optimization of Reaction Conditions^a



entry	[Pd]	additive	solvent	yield (%) ^b
1	PdCl ₂	KBr	CH ₃ CN	10
2	Pd(OAc) ₂	KBr	CH ₃ CN	78
3	Pd(PPh ₃) ₄	KBr	CH ₃ CN	trace
4	–	KBr	CH ₃ CN	0
5	Pd(OAc) ₂	LiBr	CH ₃ CN	70
6	Pd(OAc) ₂	LiCl	CH ₃ CN	72
7	Pd(OAc) ₂	KI	CH ₃ CN	76
8	Pd(OAc) ₂	KBr	DCE	20
9	Pd(OAc) ₂	KBr	DMSO	30
10	Pd(OAc) ₂	KBr	Toluene	93 (86)
11	Pd(OAc) ₂	–	CH ₃ CN	46
12 ^c	Pd(OAc) ₂	KBr	Toluene	81
13 ^d	Pd(OAc) ₂	KBr	Toluene	96
14 ^e	Pd(OAc) ₂	KBr	Toluene	88
15 ^f	Pd(OAc) ₂	KBr	Toluene	80
16 ^g	Pd(OAc) ₂	KBr	Toluene	95

^aReaction conditions: **1a** (0.4 mmol), **2a** (1.0 mmol), H₂O (5 equiv, 2.0 mmol), [Pd] (5 mol %), additive (1 equiv, 0.4 mmol) in 2 mL of solvent at 80 °C for 12 h then cooled to room temperature, followed by the addition of HCl (4 M, 0.5 mL) and heating at 80 °C for 1 h. ^bYields were analyzed by GC/MS using *n*-dodecane as an internal standard. Yields of isolated products were given in parentheses. ^c0.2 mmol of KBr. ^d0.8 mmol of KBr. ^e1.6 mmol of KBr. ^f10 h. ^g14 h.

different palladium salts were examined in the presence of KBr (1.0 equiv) in CH₃CN at 80 °C for 12 h, and Pd(OAc)₂ provided the best result, affording the desired product in 78% yield (entries 1–3). As expected, no reaction occurred in the absence of a palladium catalyst (entry 4). Subsequently, a range of additives such as LiBr, LiCl, and KI were evaluated (entries 5–7) and gave similar results. Afterward, different solvents were screened, and toluene proved to be optimal (entries 8–10). However, a significantly lower yield was observed when the reaction proceeded without additives (entry 11). Reducing the loading of KBr led to a slightly lower yield of 81%, although increasing the amount of KBr did not give further enhancement of the yield (entries 12–14). These results revealed that KBr played a beneficial role in this process. Finally, when the reaction time was shortened or prolonged, the corresponding product was not increased (entries 15–16).

With the optimized reaction conditions in hand, we next explored the scope and limitation of the reaction between various alkynoates and isocyanides, and the results are summarized in Scheme 2. Gratifyingly, good yields were obtained when *tert*-butyl isocyanide **2a** was reacted with methyl or benzyl alkynoates under the optimal reaction conditions (**3ba** and **3ca**). The structure of **3ba** was unambiguously determined by X-ray crystallographic analysis (see the Supporting Information for details). Ethyl alkynoates bearing phenyl groups substituted at the *para* position with electron-donating groups (Me, MeO) and electron-withdrawing ones (F, Cl, Br, COOMe, CF₃) all displayed high reactivity, and the

corresponding products **3da**–**3ma** were obtained in good to excellent yields. Substitution at the 3- or 2-position of the aromatic ring also worked well in this catalytic cycle (**3ka**, **3la**, and **3ma**), which revealed that there was no obvious steric hindrance effect for this reaction. Gratifyingly, ethyl 3-(benzo[*d*][1,3]dioxol-5-yl)propiolate and ethyl 3-(3,5-dichlorophenyl)propiolate were successfully converted into the maleimide products **3na** and **3oa** in good yields. Notably, a vinyl group was tolerated under the standard reaction conditions, thus providing **3pa** in 80% yield. However, no desired product was detected when alkyl alkynoate was used in this catalyst system. Moreover, our system was widely applicable to alkynes activated by other electron-donating groups, resulting in the corresponding products **3qa** and **3ra** in 54% and 77% yields, respectively.

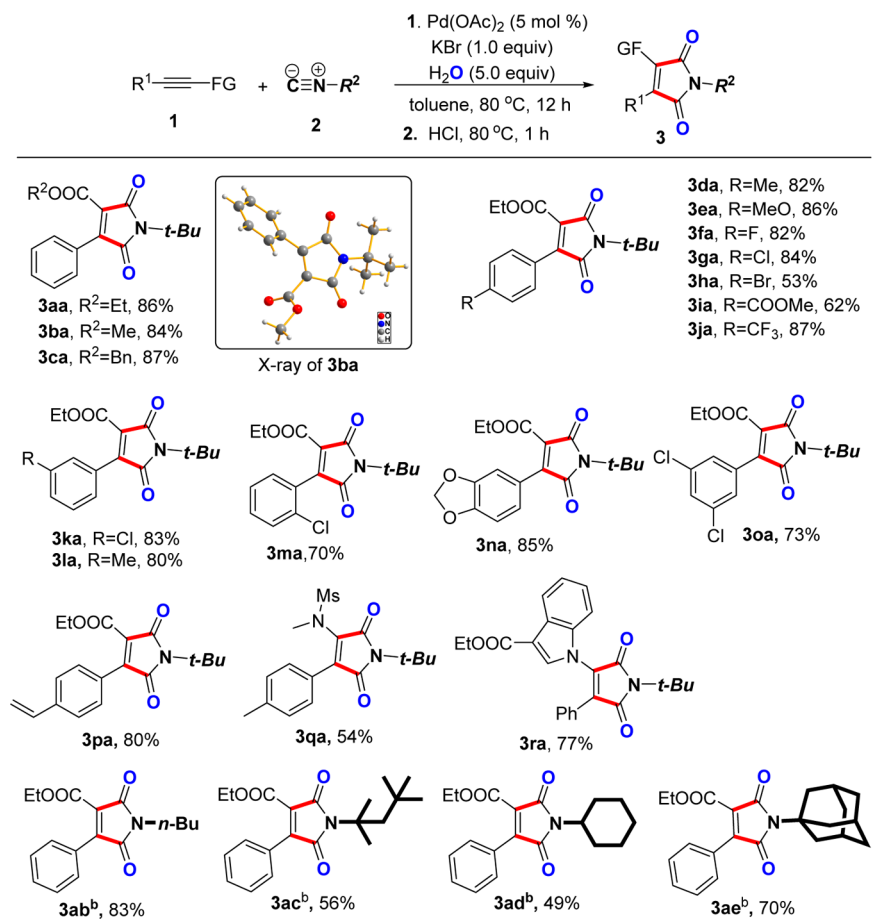
To further demonstrate the scope of the present reaction, various isocyanides were employed in this transformation. Fortunately, almost all alkyl isocyanides were found to be suitable for this transformation, affording the corresponding maleimides. For instance, *n*-butyl isocyanide and cyclohexyl isocyanide were converted into the desired products in 83% and 49% yields, respectively. Even sterically hindered 1,1,3,3-tetramethylbutyl isocyanide and adamantyl isocyanide were also found to be compatible with the present cycloaddition protocol. Unfortunately, 2,6-dimethylphenyl isocyanide and 4-methoxyphenyl isocyanide failed to afford the desired products. It is proposed that the cyclopalladium intermediate is nonproductive during the reaction.

Subsequently, the scope of the reaction was further expanded to a variety of unactivated alkynes despite the more harsh reaction conditions that were required, and the results are summarized in Scheme 3. Symmetrical substituted diaryl acetylenes bearing halogen or methyl groups at the *para* position delivered the desired products **5a**–**5c** in 69–86% yields. Moreover, dithiophenylacetylene could also react smoothly under the optimal conditions and afford the target molecule **5d** in excellent 86% yield. For unsymmetrical alkynes, the reactions also showed a remarkably wide scope. Only a trace amount of the cycloadducts was detected for 1-bromo-2-(phenylethynyl)benzene (**4i**) and a 46% yield was obtained when 1-(phenylethynyl)naphthalene (**4j**) was employed as substrate, which revealed that the steric hindrance of substituents on the phenyls did have a strong influence in this process. In addition, aryl alkyl alkynes displayed good to high reactivity and gave the corresponding products **5l** and **5m** in 74% and 80% yields, respectively. Importantly, this catalytic system could be expanded to terminal alkynes even though a lower yield was obtained (**5n**). It is worth noting that 1,4-diphenylbuta-1,3-diyne (**1o**) was also a good substrate for this reaction and converted to the desired products in 82% yield.

Furthermore, the diyne **4p** was transferred to the corresponding product **5p** containing two maleimide rings in 43% yield, and **5p'** bearing one maleimide ring was also detected at the same time (Scheme 4).

The practicality of this method was demonstrated by the gram-scale reaction. Under the standard reaction conditions, 1.42 g of 1,2-diphenylethyne (**4a**, 8 mmol) was readily converted into **5a** in 69% yield (Scheme 5).

In order to obtain more information on the reaction mechanism of the present catalytic process, a control experiment was conducted as shown in Scheme 6. **5a**-¹⁸O was observed nearly as the sole product when 1,2-diphenylethyne **4a** and *tert*-butyl isocyanide **2a** were treated

Scheme 2. Substrate Scope of Various Activated Alkynes and Isocyanides^{a,b}

^aReaction conditions: **1** (0.4 mmol), **2** (1 mmol), Pd(OAc)₂ (5 mol %), KBr (0.4 mmol), H₂O (2.0 mmol), and toluene (3 mL) were stirred 80 °C for 12 h and then cooled to room temperature, followed by the addition of HCl (4 M, 0.5 mL) and heating at 80 °C for 1 h. Yields of the isolated products are given. ^bIn DMSO.

in anhydrous toluene in the presence of H₂¹⁸O, which indicated that the oxygen atom of the amide was grabbed from water.

It is noteworthy that the newly formed *N-tert*-butyl maleimide products could be further transformed to the unprotected maleimides according to the literature.¹⁶ For example, when 1-(*tert*-butyl)-3,4-diphenyl-1*H*-pyrrole-2,5-dione **5a** was heated to reflux in trifluoroacetic acid for 24 h, the desired 3,4-diphenyl-1*H*-pyrrole-2,5-dione **6a** was obtained in more than 80% yield (Scheme 7).

CONCLUSION

In summary, we have developed an efficient and practical protocol for the synthesis of various polysubstituted maleimide derivatives through the palladium-catalyzed intermolecular cyclization reaction of alkynes with isocyanides. In this process, isocyanides serve as both C and N sources and C–C, C=O, and C–N bonds were constructed in one pot. Furthermore, this reaction also demonstrated many advantages such as good functional group compatibility, easily available starting materials, and operational simplicity.

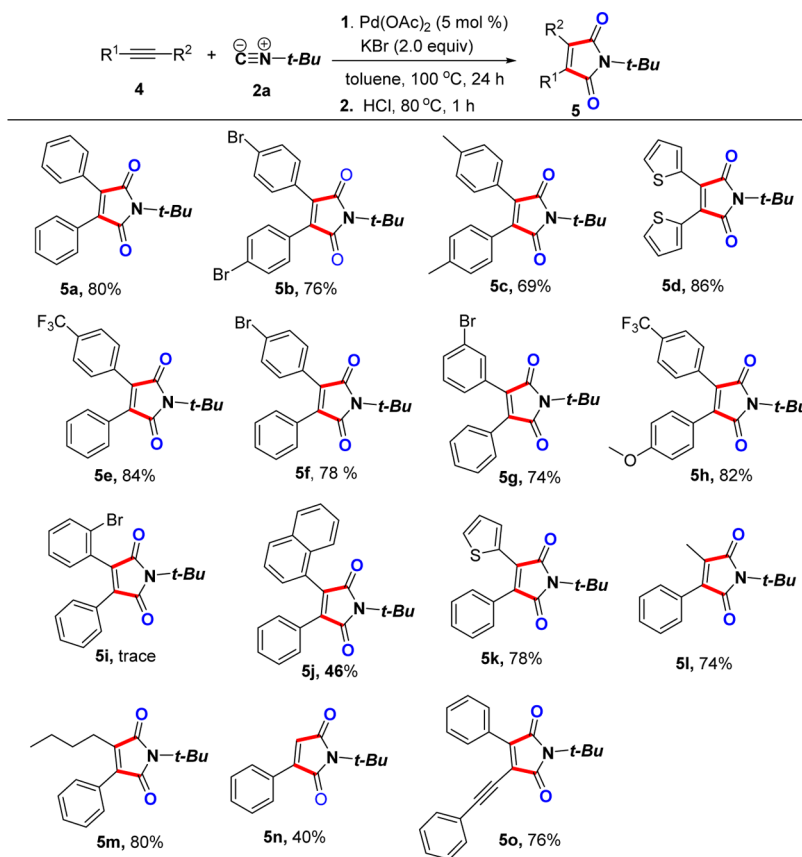
EXPERIMENTAL SECTION

General Methods. All reactions were carried out in 10 mL tubes under an air atmosphere. ¹H and ¹³C NMR spectra were recorded using a 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively, and

chloroform is the solvent with TMS as the internal standard. Reagents and solvents were purchased commercially and used without further purification. Mass spectra were recorded on a gas chromatograph–mass spectrometer. Melting points were measured with a melting point apparatus. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a spectrometer. The data of HRMS were carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). TLC was performed by using commercially prepared 100–400 mesh silica gel plates. X-ray structural analyses were conducted on an X-ray analysis instrument.

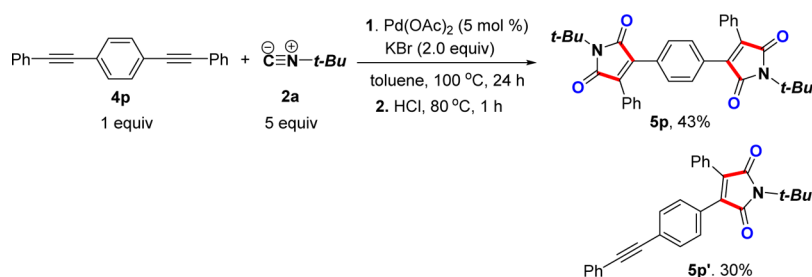
General Procedure for the Synthesis of Polymaleimides. A mixture of alkynes **1** or **4** (0.4 mmol), isocyanides **2** (1.0 mmol), H₂O (2.0 mmol), Pd(OAc)₂ (5 mol %), and KBr (0.4 mmol) was stirred in toluene (2 mL) at 80 °C (oil bath temperature) for 12–24 h. After the resulting solution was cooled to room temperature, HCl (4 M, 0.5 mL) was added and the mixture was heated to 80 °C for 1 h. The reaction mixture was cooled to room temperature, quenched with water, and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. Purification using flash chromatography on silica gel provided product **3** or **5** with petroleum ether/ethyl acetate as the eluent.

Ethyl 1-(*tert*-Butyl)-2,5-dioxo-4-phenyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate (3aa**).** Yellow solid (104 mg, 86%). Mp 74–75 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.63 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.44 (m, 3H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.64 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 168.2, 161.9, 141.1, 131.0, 123.0, 128.4, 128.3, 127.4, 62.2, 58.4, 28.8, 13.9. IR (KBr): 2992, 2358,

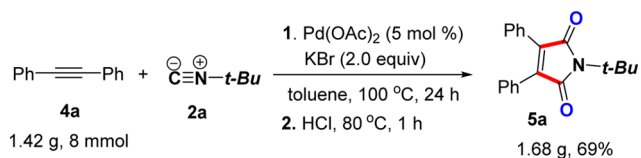
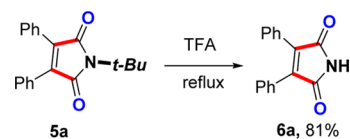
Scheme 3. Substrate Scope of Unactivated Alkynes^a

^aReaction conditions: **4** (0.4 mmol), **2a** (1 mmol), Pd(OAc)₂ (5 mol %), KBr (0.8 mmol), H₂O (2.0 mmol), and toluene (3 mL) were stirred at 100 °C for 24 h then cooled to room temperature, followed by the addition of HCl (4 M, 0.5 mL) and heating at 80 °C for 1 h. Yields of the isolated products are given.

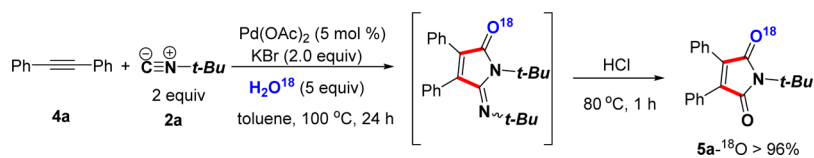
Scheme 4. Substrate of 1,4-Bis(phenylethynyl)benzene



Scheme 5. Gram Scale Diphenylmaleimide Synthesis

Scheme 7. Deprotection of *N*-tert-Butylmaleimide **5a**

Scheme 6. Control Experiment



1833, 1633, 1497, 1378, 1243, 1055, 750 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{19}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 324.1206, found: 324.1214.

Methyl 1-(tert-Butyl)-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (3ba). Yellow solid (96 mg, 84%). Mp 66–67 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.63 (dd, $J = 7.9, 1.5$ Hz, 2H), 7.46 (m, 3H), 3.86 (s, 3H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 168.2, 162.4, 141.8, 131.1, 130.0, 128.5, 127.8, 127.3, 58.5, 52.8, 28.8. IR (KBr): 2991, 2357, 1784, 1377, 1243, 1056 cm^{-1} . ESI-HRMS calcd for $\text{C}_{16}\text{H}_{17}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 310.1050, found: 310.1046.

Benzyl 1-(tert-Butyl)-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (3ca). Yellow solid (126 mg, 87%). Mp 91–92 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.52 (m, 2H), 7.43 (d, $J = 7.5$ Hz, 1H), 7.33 (m, 7H), 5.31 (s, 2H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 168.1, 161.7, 141.6, 134.5, 131.0, 130.0, 128.7, 128.6, 128.4, 127.2, 67.8, 58.5, 28.8. IR (KBr): 2990, 2357, 1763, 1705, 1243, 1056 cm^{-1} . ESI-HRMS calcd for $\text{C}_{22}\text{H}_{21}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 386.1363, found: 386.1369.

Ethyl 1-(tert-Butyl)-2,5-dioxo-4-(p-tolyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (3da). Yellow solid (103 mg, 82%). Mp 65–66 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.58 (d, $J = 8.1$ Hz, 2H), 7.28 (d, $J = 2.8$ Hz, 2H), 4.37 (q, $J = 7.1$ Hz, 2H), 2.42 (s, 3H), 1.66 (s, 9H), 1.32 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.6, 168.4, 162.2, 141.8, 141.2, 130.1, 129.2, 127.3, 124.6, 62.1, 58.3, 28.9, 21.6, 14.0. IR (KBr): 2989, 2358, 1764, 1707, 1374, 1242, 1055 cm^{-1} . ESI-HRMS calcd for $\text{C}_{18}\text{H}_{21}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 338.1363, found: 338.1367.

Ethyl 1-(tert-Butyl)-4-(4-methoxyphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3ea). Yellow solid (114 mg, 86%). Mp 48–49 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, $J = 8.7$ Hz, 2H), 6.94 (d, $J = 8.7$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 3.85 (s, 3H), 1.63 (s, 9H), 1.31 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 168.6, 162.4, 162.1, 140.7, 132.1, 125.7, 119.9, 114.0, 62.1, 58.3, 55.4, 28.9, 14.0. IR (KBr): 2988, 2358, 1764, 1705, 1375, 1244, 1053 cm^{-1} . ESI-HRMS calcd for $\text{C}_{18}\text{H}_{21}\text{NNaO}_5$ $[\text{M} + \text{Na}]^+$: 354.1312, found: 354.1314.

Ethyl 1-(tert-Butyl)-4-(4-fluorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3fa). Yellow solid (105 mg, 82%). Mp 62–63 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.68 (dd, $J = 8.6, 5.4$ Hz, 2H), 7.13 (t, $J = 8.6$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.64 (s, 9H), 1.30 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 168.1, 164.4 (d, $J = 252.3$ Hz), 161.9, 140.2, 132.5, 132.4 (d, $J = 8.7$ Hz), 127.8, 123.5 (d, $J = 3.2$ Hz), 123.5, 115.8 (d, $J = 21.8$ Hz), 62.3, 58.5, 28.8, 14.0. IR (KBr): 2987, 2357, 1763, 1708, 1341, 1241, 1053 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{FNNaO}_4$ $[\text{M} + \text{Na}]^+$: 342.1112, found: 342.1107.

Ethyl 1-(tert-Butyl)-4-(4-chlorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3ga). White solid (113 mg, 84%). Mp 68–69 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, $J = 8.5$ Hz, 2H), 7.42 (d, $J = 8.5$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.63 (s, 9H), 1.30 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.1, 168.0, 161.7, 140.4, 137.8, 131.4, 128.8, 128.3, 125.8, 62.4, 58.6, 28.8, 14.0. IR (KBr): 2987, 2357, 1763, 1708, 1344, 1242, 1102, 1054 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{ClNNaO}_4$ $[\text{M} + \text{Na}]^+$: 358.0817, found: 358.0824.

Ethyl 4-(4-Bromophenyl)-1-(tert-butyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3ha). Yellow solid (80 mg, 53%). Mp 75–76 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.58 (d, $J = 8.5$ Hz, 2H), 7.52 (d, $J = 8.4$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.63 (s, 9H), 1.30 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.1, 168.0, 161.7, 140.2, 131.8, 131.6, 128.4, 126.2, 126.1, 62.4, 58.6, 28.8, 14.0. IR (KBr): 2989, 2357, 1764, 1707, 1376, 1243, 1056 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{BrNNaO}_4$ $[\text{M} + \text{Na}]^+$: 402.0311, found: 402.0310.

Ethyl 1-(tert-Butyl)-4-(4-(methoxycarbonyl)phenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3ia). Yellow oil (89 mg, 62%). ^1H NMR (400 MHz, CDCl_3) δ 8.09 (d, $J = 8.3$ Hz, 2H), 7.70 (d, $J = 8.3$ Hz, 2H), 4.34 (q, $J = 7.1$ Hz, 2H), 3.94 (s, 3H), 1.64 (s, 9H), 1.29 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.0, 167.8, 166.3, 161.5, 140.2, 132.1, 131.5, 130.0, 129.5, 129.4, 62.4, 58.7, 52.4, 28.8, 13.9. IR (KBr): 2989, 2357, 1763, 1715, 1373, 1242, 1055 cm^{-1} . ESI-HRMS calcd for $\text{C}_{19}\text{H}_{21}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$: 382.1261, found: 382.1263.

Ethyl 1-(tert-Butyl)-2,5-dioxo-4-(4-(trifluoromethyl)phenyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (3ja). White solid (128 mg,

87%). Mp 103–104 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.75 (d, $J = 8.3$ Hz, 2H), 7.70 (d, $J = 8.5$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.64 (s, 9H), 1.29 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 167.7, 161.4, 140.0, 132.6 (q, $J = 32.6$ Hz), 130.8, 130.4, 129.7, 125.3 (q, $J = 3.7$ Hz), 123.6 (q, $J = 270.9$ Hz), 62.5, 58.7, 28.8, 14.0. IR (KBr): 2987, 2357, 1710, 1337, 1168, 1113, 851 cm^{-1} . ESI-HRMS calcd for $\text{C}_{18}\text{H}_{18}\text{F}_3\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 392.1080, found: 392.1079.

Ethyl 1-(tert-Butyl)-4-(3-chlorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3ka). White solid (111 mg, 83%). Mp 64–65 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.65 (s, 1H), 7.52 (d, $J = 7.7$ Hz, 1H), 7.45 (d, $J = 8.1$ Hz, 1H), 7.38 (t, $J = 7.9$ Hz, 1H), 4.36 (q, $J = 7.1$ Hz, 2H), 1.64 (s, 9H), 1.30 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.0, 167.9, 161.5, 139.7, 134.5, 131.0, 129.9, 129.7, 129.1, 128.9, 128.1, 62.4, 58.6, 28.8, 14.0. IR (KBr): 2988, 2359, 1764, 1708, 1337, 1241, 1054 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{ClNNaO}_4$ $[\text{M} + \text{Na}]^+$: 358.0817, found: 358.0824.

Ethyl 1-(tert-Butyl)-2,5-dioxo-4-(m-tolyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (3la). Yellow solid (101 mg, 80%). Mp 40–41 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.47–7.39 (m, 2H), 7.35–7.27 (m, 2H), 4.34 (q, $J = 7.1$ Hz, 2H), 2.38 (s, 3H), 1.64 (s, 9H), 1.29 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 168.3, 162.0, 141.3, 138.1, 131.9, 130.5, 128.3, 128.1, 127.3, 127.1, 62.1, 58.4, 28.8, 21.4, 14.0. IR (KBr): 2989, 2359, 1765, 1706, 1375, 1339, 1243, 1055 cm^{-1} . ESI-HRMS calcd for $\text{C}_{18}\text{H}_{21}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 338.1363, found: 338.1370.

Ethyl 1-(tert-Butyl)-4-(2-chlorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3ma). Yellow liquid (94 mg, 70%). ^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 7.7$ Hz, 1H), 7.42–7.37 (m, 1H), 7.35 (d, $J = 4.2$ Hz, 2H), 4.23 (q, $J = 7.1$ Hz, 2H), 1.64 (s, 9H), 1.16 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.3, 167.6, 160.4, 143.2, 133.5, 131.3, 131.1, 130.0, 129.7, 127.1, 126.4, 61.9, 58.6, 28.8, 13.8. IR (KBr): 2990, 2358, 1713, 1489, 1340, 1239, 1105, 1028 cm^{-1} ; ESI-HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{ClNNaO}_4$ $[\text{M} + \text{Na}]^+$: 358.0817, found: 358.0819.

Ethyl 4-(Benzo[d][1,3]dioxol-5-yl)-1-(tert-butyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3na). Yellow liquid (117 mg, 85%). ^1H NMR (400 MHz, CDCl_3) δ 7.20 (d, $J = 6.6$ Hz, 1H), 7.11 (d, $J = 1.3$ Hz, 1H), 6.80 (d, $J = 8.2$ Hz, 1H), 5.96 (s, 2H), 4.29 (q, $J = 7.1$ Hz, 2H), 1.56 (s, 9H), 1.25 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 168.4, 162.3, 150.3, 147.9, 140.3, 126.5, 125.8, 121.2, 110.0, 108.5, 101.7, 62.2, 59.5, 28.9, 14.0. IR (KBr): 2989, 2359, 1764, 1704, 1337, 1244, 1050 cm^{-1} . ESI-HRMS calcd for $\text{C}_{18}\text{H}_{19}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$: 368.1105, found: 368.1106.

Ethyl 1-(tert-Butyl)-4-(3,5-dichlorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrole-3-carboxylate (3oa). Brown liquid (128 mg, 87%). ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, $J = 1.8$ Hz, 2H), 7.46 (t, $J = 1.8$ Hz, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 1.63 (s, 9H), 1.32 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.5, 167.5, 161.0, 138.4, 135.2, 130.8, 129.9, 129.8, 128.3, 62.6, 58.8, 28.8, 14.0. IR (KBr): 2991, 2358, 1764, 1708, 1377, 1243, 1056 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{17}\text{Cl}_2\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 392.0427, found: 392.0440.

Ethyl 1-(tert-Butyl)-2,5-dioxo-4-(4-vinylphenyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (3pa). Yellow solid (105 mg, 80%). Mp 67–68 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 7.7$ Hz, 2H), 7.46 (d, $J = 7.7$ Hz, 2H), 6.73 (dd, $J = 17.5, 10.9$ Hz, 1H), 5.85 (d, $J = 17.6$ Hz, 1H), 5.37 (d, $J = 10.8$ Hz, 1H), 4.35 (q, $J = 6.6$ Hz, 2H), 1.64 (s, 9H), 1.30 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 168.3, 162.1, 140.6, 140.3, 135.9, 130.4, 127.6, 126.7, 126.2, 116.3, 62.2, 58.4, 28.8, 14.0. IR (KBr): 2987, 2358, 1764, 1705, 1377, 1240, 1242, 1106, 1054 cm^{-1} . ESI-HRMS calcd for $\text{C}_{19}\text{H}_{21}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$: 350.1363, found: 350.1366.

N-(1-(tert-Butyl)-2,5-dioxo-4-(p-tolyl)-2,5-dihydro-1H-pyrrol-3-yl)-N-methylmethanesulfonamide (3qa). Yellow solid (76 mg, 54%). Mp 120–121 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.69 (d, $J = 7.5$ Hz, 2H), 7.29 (d, $J = 7.6$ Hz, 2H), 3.36 (s, 3H), 3.02 (s, 3H), 2.41 (s, 3H), 1.65 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 168.8, 141.1, 135.5, 132.1, 129.7, 129.4, 124.2, 58.2, 40.0, 36.3, 29.0, 21.5. IR (KBr): 2985, 2928, 2358, 1764, 1706, 1348, 1243, 1054 cm^{-1} . ESI-HRMS calcd for $\text{C}_{17}\text{H}_{22}\text{N}_2\text{NaO}_4\text{S}$ $[\text{M} + \text{Na}]^+$: 373.1192, found: 373.1190.

Ethyl 1-(1-(tert-Butyl)-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-indole-3-carboxylate (3ra). Yellow solid (128 mg, 77%). Mp

185–186 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.20 (d, *J* = 7.8 Hz, 1H), 8.12 (s, 1H), 7.31 (s, 1H), 7.30 (s, 2H), 7.27–7.19 (m, 3H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.59 (d, *J* = 8.2 Hz, 1H), 4.45–4.38 (m, 2H), 1.72 (s, 9H), 1.43 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.1, 167.7, 164.2, 134.4, 133.6, 130.8, 130.4, 129.6, 128.6, 127.2, 127.1, 127.0, 123.5, 123.2, 121.8, 112.8, 112.4, 60.1, 58.7, 29.0, 14.5. IR (KBr): 2985, 2357, 1764, 1707, 1548, 1456, 1355, 1245, 1200, 1053 cm⁻¹. ESI-HRMS calcd for C₂₅H₂₅N₂O₄ [M + H]⁺: 417.1809, found: 417.1815.

Ethyl 1-Butyl-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (3ab). Brown oil (93 mg, 77%). ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 6.8 Hz, 2H), 7.50–7.43 (m, 3H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.60 (t, *J* = 7.2 Hz, 2H), 1.65–1.59 (m, 2H), 1.39–1.33 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 169.4, 167.3, 161.7, 142.2, 131.4, 130.1, 128.5, 127.7, 127.3, 62.2, 38.4, 30.4, 19.9, 13.9, 13.5. IR (KBr): 2961, 1733, 1710, 1635, 1444, 1404, 1347, 1288, 1053 cm⁻¹. ESI-HRMS calcd for C₁₇H₁₉NNaO₄ [M + Na]⁺: 324.1206, found: 324.1204.

Ethyl 2,5-Dioxo-4-phenyl-1-(2,4,4-trimethylpentan-2-yl)-2,5-dihydro-1H-pyrrole-3-carboxylate (3ac). Yellow oil (80 mg, 56%). ¹H NMR (400 MHz, CDCl₃) δ 7.66–7.60 (m, 2H), 7.49–7.41 (m, 3H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.95 (s, 2H), 1.72 (s, 6H), 1.29 (t, *J* = 7.1 Hz, 4H), 0.97 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 168.7, 161.9, 141.3, 131.1, 130.0, 128.4, 128.3, 127.4, 62.2, 61.9, 50.8, 31.6, 31.0, 29.8, 14.0. IR (KBr): 2986, 2358, 1764, 1704, 1371, 1242, 1055 cm⁻¹. ESI-HRMS calcd for C₂₁H₂₇NNaO₄ [M + Na]⁺: 380.1832, found: 380.1829.

Ethyl 1-Cyclohexyl-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (3ad). Yellow oil (73 mg, 56%). ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, *J* = 7.2 Hz, 2H), 7.47 (dd, *J* = 10.7, 7.4 Hz, 3H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.00 (ddd, *J* = 12.2, 8.0, 3.8 Hz, 1H), 2.10 (qd, *J* = 12.4, 3.0 Hz, 2H), 1.85 (d, *J* = 13.3 Hz, 2H), 1.72 (d, *J* = 14.1 Hz, 3H), 1.33–1.24 (m, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 169.3, 167.2, 161.8, 141.7, 131.3, 130.1, 128.5, 127.8, 127.4, 62.2, 51.6, 29.8, 25.9, 25.0, 13.9. IR (KBr): 2934, 1769, 1734, 1707, 1452, 1343, 1238, 1055 cm⁻¹. ESI-HRMS calcd for C₁₉H₂₁NNaO₄ [M + Na]⁺: 350.1363, found: 350.1359.

Ethyl 1-((3*S*,5*S*,7*S*)-Adamantan-1-yl)-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (3ae). Yellow solid (106 mg, 70%). Mp 132–133 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.44 (qd, *J* = 6.6, 3.3 Hz, 3H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.44 (d, *J* = 2.7 Hz, 6H), 2.15 (s, 3H), 1.77–1.67 (m, 6H), 1.28 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 168.3, 162.0, 140.8, 131.0, 130.0, 128.4, 128.1, 127.4, 62.2, 60.9, 40.0, 36.1, 29.7, 13.9. IR (KBr): 2918, 2860, 1710, 1455, 1234, 1055 cm⁻¹. ESI-HRMS calcd for C₂₃H₂₅NNaO₄ [M + Na]⁺: 402.1676, found: 402.1685.

1-(tert-Butyl)-3,4-diphenyl-1H-pyrrole-2,5-dione (5a). Yellow solid (98 mg, 80%). Mp 136–137 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.43 (dd, *J* = 7.5, 1.8 Hz, 4H), 7.35 (t, *J* = 6.3 Hz, 6H), 1.70 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.7, 136.0, 130.0, 129.5, 128.8, 128.4, 57.8, 29.0. IR (KBr): 2987, 2358, 1762, 1701, 1348, 1243, 1054 cm⁻¹. ESI-HRMS calcd for C₂₀H₁₉NNaO₂ [M + Na]⁺: 328.1308, found: 328.1311.

3,4-Bis(4-bromophenyl)-1-(tert-butyl)-1H-pyrrole-2,5-dione (5b). Yellow solid (140 mg, 76%). Mp 166–167 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (d, *J* = 8.4 Hz, 4H), 7.29 (d, *J* = 8.4 Hz, 4H), 1.67 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.1, 135.1, 131.9, 131.5, 127.4, 124.5, 58.1, 29.0. IR (KBr): 2924, 2357, 1764, 1700, 1646, 1348, 1243, 1065 cm⁻¹. ESI-HRMS calcd for C₂₀H₁₇Br₂NNaO₂ [M + Na]⁺: 483.9518, found: 483.9522.

1-(tert-Butyl)-3,4-di-*p*-tolyl-1H-pyrrole-2,5-dione (5c). Yellow solid (92 mg, 69%). Mp 147–148 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.33 (d, *J* = 8.1 Hz, 4H), 7.14 (d, *J* = 8.0 Hz, 4H), 2.35 (s, 6H), 1.67 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 172.1, 139.6, 135.4, 129.9, 129.1, 126.1, 57.7, 29.1, 21.4. IR (KBr): 2983, 2357, 1759, 1701, 1347, 1237, 1019 cm⁻¹. ESI-HRMS calcd for C₂₂H₂₃NNaO₂ [M + Na]⁺: 356.1621, found: 356.1627.

1-(tert-Butyl)-3,4-di(thiophen-2-yl)-1H-pyrrole-2,5-dione (5d). Dark green solid (109 mg, 86%). Mp 77–78 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 0.9 Hz, 1H), 7.73 (d, *J* = 0.9 Hz, 1H),

7.57 (d, *J* = 0.9 Hz, 1H), 7.56 (d, *J* = 0.9 Hz, 1H), 7.11 (dd, *J* = 5.0, 3.8 Hz, 2H), 1.67 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.2, 130.8, 129.6, 127.5, 127.3, 58.1, 29.0. IR (KBr): 2986, 2358, 1763, 1698, 1351, 1243, 1058 cm⁻¹. ESI-HRMS calcd for C₁₆H₁₅NNaO₂S₂ [M + Na]⁺: 340.0436, found: 340.0433.

1-(tert-Butyl)-3-phenyl-4-(4-(trifluoromethyl)phenyl)-1H-pyrrole-2,5-dione (5e). Yellow solid (125 mg, 84%). Mp 138–139 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.41 (s, 1H), 7.39 (s, 2H), 7.37 (d, *J* = 5.6 Hz, 2H), 1.69 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.3, 171.2, 137.6, 134.4, 132.5, 131.2 (q, *J* = 32.5 Hz), 130.4, 130.0, 129.9, 128.6, 128.2, 125.3 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 270.7 Hz), 58.1, 29.0. IR (KBr): 2985, 2358, 1764, 1703, 1644, 1354, 1243, 1062 cm⁻¹. ESI-HRMS calcd for C₂₁H₁₈F₃NNaO₂ [M + Na]⁺: 396.1182, found: 396.1179.

3-(4-Bromophenyl)-1-(tert-butyl)-4-phenyl-1H-pyrrole-2,5-dione (5f). Yellow solid (119 mg, 78%). Mp 131–132 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.43–7.39 (m, 2H), 7.37 (d, *J* = 6.7 Hz, 2H), 7.35 (s, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 1.68 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.5, 171.4, 136.4, 134.8, 131.7, 131.6, 129.9, 129.8, 128.6, 128.5, 127.7, 124.2, 58.0, 29.0. IR (KBr): 2990, 2359, 1764, 1700, 1642, 1376, 1243, 1057 cm⁻¹. ESI-HRMS calcd for C₂₀H₁₈BrNNaO₂ [M + Na]⁺: 406.0413, found: 406.0408.

3-(3-Bromophenyl)-1-(tert-butyl)-4-phenyl-1H-pyrrole-2,5-dione (5g). Yellow solid (113 mg, 74%). Mp 106–107 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.63 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.44–7.40 (m, 2H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.35 (s, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.9 Hz, 1H), 1.68 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.4, 171.3, 137.00, 134.4, 132.8, 132.5, 130.8, 129.9, 129.9, 129.9, 128.5, 128.3, 122.4, 58.0, 29.0. IR (KBr): 2983, 2358, 1764, 1702, 1643, 1346, 1243, 1057 cm⁻¹. ESI-HRMS calcd for C₂₀H₁₈BrNNaO₂ [M + Na]⁺: 406.0413, found: 406.0418.

1-(tert-Butyl)-3-(4-methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)-1H-pyrrole-2,5-dione (5h). Yellow solid (132 mg, 82%). Mp 112–113 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 1.68 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.6, 171.5, 161.1, 137.1, 133.0, 132.5, 131.7, 131.0 (q, *J* = 32.4 Hz), 130.3, 125.3 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 270.6 Hz), 120.4, 114.1, 57.9, 55.3, 29.0. IR (KBr): 2969, 1765, 1702, 1462, 1350, 1257, 1067 cm⁻¹. ESI-HRMS calcd for C₂₂H₂₀F₃NNaO₃ [M + Na]⁺: 426.1287, found: 426.1289.

1-(tert-Butyl)-3-(naphthalen-1-yl)-4-phenyl-1H-pyrrole-2,5-dione (5j). Yellow solid (65 mg, 46%). Mp 115–116 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.44–7.39 (m, 1H), 7.34 (ddd, *J* = 7.4, 5.0, 4.0 Hz, 2H), 7.31–7.24 (m, 3H), 7.14–7.10 (m, 1H), 7.05 (dd, *J* = 10.2, 4.6 Hz, 2H), 1.65 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.8, 171.8, 137.9, 136.5, 133.7, 130.6, 129.9, 129.8, 129.6, 128.8, 128.6, 128.3, 128.2, 127.1, 126.5, 126.1, 125.3, 125.2, 58.0, 29.1. IR (KBr): 2970, 1764, 1702, 1460, 1345, 1260 cm⁻¹. ESI-HRMS calcd for C₂₄H₂₁NNaO₂ [M + Na]⁺: 378.1464, found: 378.1466.

1-(tert-Butyl)-3-phenyl-4-(thiophen-2-yl)-1H-pyrrole-2,5-dione (5k). Dark green solid (97 mg, 78%). Mp 53–54 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 3.8 Hz, 1H), 7.49–7.44 (m, 6H), 7.02–6.98 (m, 1H), 1.68 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 171.9, 171.4, 132.3, 131.4, 131.2, 130.2, 130.0, 129.6, 129.2, 128.7, 127.3, 57.9, 29.0. IR (KBr): 2970, 2357, 1762, 1700, 1645, 1349, 1244, 1058 cm⁻¹. ESI-HRMS calcd for C₁₈H₁₇NNaO₂S [M + Na]⁺: 334.0872, found: 334.0875.

1-(tert-Butyl)-3-methyl-4-phenyl-1H-pyrrole-2,5-dione (5l). Yellow solid (72 mg, 74%). Mp 110–111 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.53 (m, 2H), 7.44 (m, 3H), 2.12 (s, 3H), 1.63 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 172.1, 136.7, 136.4, 129.6, 129.3, 129.2, 128.4, 57.4, 29.0, 9.6. IR (KBr): 2991, 1766, 1707, 1462, 1376, 1243, 1056 cm⁻¹. ESI-HRMS calcd for C₁₅H₁₇NNaO₂ [M + Na]⁺: 266.1151, found: 266.1148.

1-(tert-Butyl)-3-butyl-4-phenyl-1H-pyrrole-2,5-dione (5m). Light yellow oil (91 mg, 80%). ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 6.6 Hz, 2H), 7.44 (s, 2H), 7.42–7.39 (m, 1H), 2.54–2.47 (m, 2H), 1.63 (s, 9H), 1.56 (dd, *J* = 9.8, 5.8 Hz, 2H), 1.36 (dd, *J* = 14.8, 7.4 Hz, 2H), 0.90 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 172.9,

172.2, 140.7, 136.7, 129.4, 129.2, 128.4, 57.3, 30.8, 29.0, 23.8, 22.9, 13.7. IR (KBr): 2963, 1766, 1701, 1461, 1351, 1243, 1055 cm^{-1} . ESI-HRMS calcd for $\text{C}_{18}\text{H}_{23}\text{NNaO}_2$ $[\text{M} + \text{Na}]^+$: 308.1621, found: 308.1618.

1-(tert-Butyl)-3-phenyl-1H-pyrrole-2,5-dione (5n). Light yellow oil (37 mg, 40%). ^1H NMR (400 MHz, CDCl_3) δ 7.85 (dd, $J = 6.3, 2.7$ Hz, 2H), 7.47–7.42 (m, 3H), 6.58 (s, 1H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 171.8, 171.7, 143.0, 130.7, 128.9, 128.8, 128.6, 124.7, 57.6, 29.0. IR (KBr): 2991, 2358, 1764, 1702, 1377, 1243, 1056 cm^{-1} . ESI-HRMS calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_2$ $[\text{M} + \text{H}]^+$: 230.1176, found: 230.1172.

1-(tert-Butyl)-3-phenyl-4-(phenylethynyl)-1H-pyrrole-2,5-dione (5o). Yellow solid (108 mg, 82%). Mp 120–121 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 8.19 (d, $J = 6.1$ Hz, 2H), 7.58 (d, $J = 6.5$ Hz, 2H), 7.50 (s, 1H), 7.48 (s, 2H), 7.41 (d, $J = 6.6$ Hz, 2H), 7.38 (d, $J = 5.9$ Hz, 1H), 1.68 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 171.4, 168.6, 139.0, 132.2, 130.7, 129.9, 129.6, 129.1, 128.5, 128.5, 121.8, 120.8, 106.3, 80.9, 58.2, 28.9. IR (KBr): 2978, 2358, 1764, 1703, 1346, 1244, 1057 cm^{-1} . ESI-HRMS calcd for $\text{C}_{22}\text{H}_{19}\text{NNaO}_2$ $[\text{M} + \text{Na}]^+$: 352.1308, found: 352.1307.

4,4'-(1,4-Phenylene)bis(1-(tert-butyl)-3-phenyl-1H-pyrrole-2,5-dione) (5p). Yellow solid (92 mg, 43%). Mp 242–243 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.41 (s, 4H), 7.38 (dd, $J = 7.6, 1.6$ Hz, 4H), 7.33 (t, $J = 7.1$ Hz, 5H), 1.68 (s, 18H). ^{13}C NMR (100 MHz, CDCl_3) δ 171.6, 171.5, 136.8, 135.0, 130.0, 129.9, 129.7, 128.5, 128.5, 58.0, 29.0. IR (KBr): 2963, 1764, 1703, 1461, 1344, 1250, 1059 cm^{-1} . ESI-HRMS calcd for $\text{C}_{34}\text{H}_{32}\text{N}_2\text{NaO}_4$ $[\text{M} + \text{Na}]^+$: 555.2254, found: 555.2256.

1-(tert-Butyl)-3-phenyl-4-(4-(phenylethynyl)phenyl)-1H-pyrrole-2,5-dione (5p'). Yellow solid (49 mg, 30%). Mp 143–144 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.51 (dd, $J = 14.7, 6.1$ Hz, 4H), 7.46–7.40 (m, 4H), 7.39–7.32 (m, 6H), 1.69 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 171.6, 136.3, 135.2, 131.7, 131.6, 130.0, 130.0, 129.7, 128.7, 128.6, 128.6, 128.5, 128.4, 124.6, 122.9, 91.3, 89.0, 58.0, 29.0. IR (KBr): 2971, 2926, 2358, 1763, 1700, 1345, 1242, 1016 cm^{-1} . ESI-HRMS calcd for $\text{C}_{28}\text{H}_{23}\text{NNaO}_2$ $[\text{M} + \text{Na}]^+$: 428.1621, found: 428.1621.

3,4-Diphenyl-1H-pyrrole-2,5-dione (6a).¹ Yellow solid (81 mg, 81%). Mp 213–214 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (s, 1H), 7.47 (d, $J = 7.6$ Hz, 4H), 7.38 (p, $J = 6.5$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 137.1, 130.0, 129.9, 128.6, 128.3. IR (KBr): 2925, 1715, 1451, 1389, 1266, 1062 cm^{-1} . MS (EI) m/z 89, 152, 178, 205, 220, 230, 249.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02227.

Spectral data for all compounds (PDF)

Crystallographic data for 3ba (CIF)

AUTHOR INFORMATION

Corresponding Authors

*E-mail: chhyliu@scut.edu.cn.

*E-mail: jianghf@scut.edu.cn.

ORCID

Huanfeng Jiang: 0000-0002-4355-0294

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank the National Key Research and Development Program of China (2016YFA0602900), the National Natural Science Foundation of China (21420102003 and 21490572), and the Fundamental Research Funds for the Central Universities (2015ZYY001) for financial support.

REFERENCES

- (1) (a) Coghlan, M.; Culbert, A.; Cross, D.; Corcoran, S.; Yates, J.; Pearce, N.; Rausch, O.; Murphy, G.; Carter, P.; Cox, L.; Mills, D.; Brown, M.; Haigh, D.; Ward, R.; Smith, D.; Murray, K.; Reith, A.; Holder, J. *Chem. Biol.* **2000**, *7*, 793. (b) Cheng, C.-F.; Lai, Z.-C.; Lee, Y.-J. *Tetrahedron* **2008**, *64*, 4347. (c) Sortino, M.; Garibotto, F.; Filho, V. C.; Gupta, M.; Enriz, R.; Zacchino, S. *Bioorg. Med. Chem.* **2011**, *19*, 2823. (d) Nirogi, R.; Dwarampudi, A.; Kambhampati, R.; Bhatta, V.; Kota, L.; Shinde, A.; Badange, R.; Jayarajan, P.; Bhyrapuneni, G.; Dubey, P. K. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4577.
- (2) (a) Yeh, H.-C.; Wu, W.-C.; Chen, C.-T. *Chem. Commun.* **2003**, 404. (b) Kaletas, B. K.; Mandl, C.; van der Zwan, G.; Fanti, M.; Zerbetto, F.; De Cola, L.; König, B.; Williams, R. M. *J. Phys. Chem. A* **2005**, *109*, 6440. (c) El Yahyaoui, A.; Félix, G.; Heynderickx, A.; Moustrou, C.; Samat, A. *Tetrahedron* **2007**, *63*, 9482. (d) Hugon, B.; Anizon, F.; Bailly, C.; Golsteyn, R. M.; Pierré, A.; Léonce, S.; Hickman, J.; Pfeiffer, B.; Prudhomme, M. *Bioorg. Med. Chem.* **2007**, *15*, 5965. (e) Nourmohammadian, F.; Wu, T.; Branda, N. R. *Chem. Commun.* **2011**, 47, 10954. (f) Ambrogio, M.; Ciogli, A.; Mancinelli, M.; Ranieri, S.; Mazzanti, A. *J. Org. Chem.* **2013**, *78*, 3709.
- (3) (a) Shih, H.; Shih, R. J.; Carson, D. A. *J. Heterocyclic Chem.* **2011**, *48*, 1243. (b) Sati, G. C.; Crich, D. *Org. Lett.* **2015**, *17*, 4122. (c) Thale, P. B.; Borase, P. N.; Shankarling, G. S. *Dalton Trans.* **2015**, *44*, 13947. (d) Zhu, C.; Xu, G.; Ding, D.; Qiu, L.; Sun, J. *Org. Lett.* **2015**, *17*, 4244.
- (4) Brenner, M.; Rexhausen, H.; Steffan, B.; Steglich, W. *Tetrahedron* **1988**, *44*, 2887.
- (5) (a) Brenner, M.; Mayer, G.; Terpin, A.; Steglich, W. *Chem. - Eur. J.* **1997**, *3*, 70. (b) El Yahyaoui, A. E.; Félix, G.; Heynderickx, A.; Moustrou, C.; Samat, A. *Tetrahedron* **2007**, *63*, 9482. (c) Stewart, S. G.; Polomska, M. E.; Lim, R. W. *Tetrahedron Lett.* **2007**, *48*, 2241. (d) Bouissane, L.; Sestelo, J. P.; Sarandeses, L. A. *Org. Lett.* **2009**, *11*, 1285. (e) Awuah, E.; Capretta, A. *J. Org. Chem.* **2011**, *76*, 3122.
- (6) Yeh, H.-C.; Wu, W.-C.; Wen, Y.-S.; Dai, D.-C.; Wang, J.-K.; Chen, C.-T. *J. Org. Chem.* **2004**, *69*, 6455.
- (7) (a) Kondo, T.; Nomura, M.; Ura, Y.; Wada, K.; Mitsudo, T.-A. *J. Am. Chem. Soc.* **2006**, *128*, 14816. (b) Inoue, S.; Fukumoto, Y.; Chatani, N. *J. Org. Chem.* **2007**, *72*, 6588.
- (8) For selected reviews, see: (a) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168. (b) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003**, *36*, 899. (c) Dömling, A. *Chem. Rev.* **2006**, *106*, 17. (d) Gulevich, A. V.; Zhdanko, A. G.; Orru, R. V. A.; Nenajdenko, V. G. *Chem. Rev.* **2010**, *110*, 5235. (e) Lygin, A. V.; de Meijere, A. D. *Angew. Chem., Int. Ed.* **2010**, *49*, 9094. (f) Vlaar, T.; Ruijter, E.; Maes, B. U. W.; Orru, R. V. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 7084. (g) Qiu, G.; Ding, Q.; Wu, J. *Chem. Soc. Rev.* **2013**, *42*, 5257.
- (9) For selected references: (a) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 9260. (b) Zhu, C.; Xie, W.; Falck, J. R. *Chem. - Eur. J.* **2011**, *17*, 12591. (c) Zhu, T.-H.; Wang, S.-Y.; Tao, Y. Q.; Wei, T. Q.; Ji, S.-J. *Org. Lett.* **2014**, *16*, 1260. (d) Wang, J.; Li, J.; Zhu, Q. *Org. Lett.* **2015**, *17*, 5336. (e) Liu, J.; Liu, Z.; Liao, P.; Zhang, L.; Tu, T.; Bi, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 1. (f) Liao, J.-Y.; Shao, P.-L.; Zhao, Y. *J. Am. Chem. Soc.* **2015**, *137*, 628.
- (10) For recent selected examples, see: (a) Jiang, X.; Tang, T.; Wang, J.-M.; Chen, Z.; Zhu, Y.-M.; Ji, S.-J. *J. Org. Chem.* **2014**, *79*, 5082. (b) Chen, Z.; Duan, H.-Q.; Jiang, X.; Zhu, Y.-M.; Ji, S.-J.; Yang, S.-L. *J. Org. Chem.* **2015**, *80*, 8183. (c) Gu, J.-W.; Zhang, X. *Org. Lett.* **2015**, *17*, 5384. (d) Dang, Y.; Deng, X.; Guo, J.; Song, C.; Hu, W.; Wang, Z.-X. *J. Am. Chem. Soc.* **2016**, *138*, 2712. (e) Kong, W.-J.; Liu, Y.-J.; Xu, H.; Chen, Y.-Q.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2016**, *138*, 2146. (f) Chen, Z.-B.; Zhang, Y.; Yuan, Q.; Zhang, F.-L.; Zhu, Y.-M.; Shen, J.-K. *J. Org. Chem.* **2016**, *81*, 1610.
- (11) Zhou, F.; Ding, K.; Cai, Q. *Chem. - Eur. J.* **2011**, *17*, 12268.
- (12) (a) Peng, J.; Liu, L.; Hu, Z.; Huang, J.; Zhu, Q. *Chem. Commun.* **2012**, *48*, 3772. (b) Hu, Z.; Liang, D.; Zhao, J.; Huang, J.; Zhu, Q. *Chem. Commun.* **2012**, *48*, 7371.
- (13) (a) Jiang, H.; Liu, B.; Li, Y.; Wang, A.; Huang, H. *Org. Lett.* **2011**, *13*, 1028. (b) Li, Y.; Zhao, J.; Chen, H.; Liu, B.; Jiang, H. *Chem.*

Commun. **2012**, *48*, 3545. (c) Jiang, H.; Yin, M.; Li, Y.; Liu, B.; Zhao, J.; Wu, W. *Chem. Commun.* **2014**, *50*, 2037.

(14) (a) Liu, B.; Li, Y.; Jiang, H.; Yin, M.; Huang, H. *Adv. Synth. Catal.* **2012**, *354*, 2288. (b) Liu, B.; Li, Y.; Yin, M.; Wu, W.; Jiang, H. *Chem. Commun.* **2012**, *48*, 11446. (c) Liu, B.; Yin, M.; Gao, H.; Wu, W.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 3009. (d) Liu, B.; Gao, H.; Yu, Y.; Wu, W.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 10319. (e) Jiang, H.; Gao, H.; Liu, B.; Wu, W. *RSC Adv.* **2014**, *4*, 17222. (f) Jiang, H.; Gao, H.; Liu, B.; Wu, W. *Chem. Commun.* **2014**, *50*, 15348.

(15) (a) Huang, L.; Wang, Q.; Liu, X.; Jiang, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 5696. (b) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2014**, *47*, 2483. (c) Huang, L.; Wang, Q.; Wu, W.; Jiang, H. *J. Org. Chem.* **2014**, *79*, 7734. (d) Yu, Y.; Huang, L.; Wu, W.; Jiang, H. *Org. Lett.* **2014**, *16*, 2146. (e) Li, J.; Yang, W.; Yang, S.; Huang, L.; Wu, W.; Sun, Y.; Jiang, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 7219. (f) Li, J.; Zhu, Z.; Yang, S.; Zhang, Z.; Wu, W.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 3870.

(16) (a) Watson, D. J.; Dowdy, E. D.; Li, W.-S.; Wang, J.; Polniaszek, R. *Tetrahedron Lett.* **2001**, *42*, 1827. (b) Schleicher, K. D.; Jamison, T. F. *Org. Lett.* **2007**, *9*, 875.