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Synthesis of Unsymmetrical 3,4-Diaryl-3-pyrrolin-2-ones Utilizing Pyrrole Weinreb Amides

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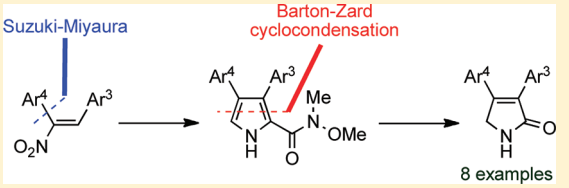
Supporting Information

ABSTRACT: A regiocontrolled synthesis of unsymmetrical 3,4-diaryl-3-pyrrolin-2-ones has been achieved in three steps from 1,2-diaryl-1-nitroethenes with pyrrole-2-carboxamides (pyrrole Weinreb amides) serving as the key linchpin intermediates. Two different methods for the preparation of the requisite nitroalkenes were investigated: (1) modified Henry reaction between arylnitromethanes and arylimines; and (2) Suzuki−Miyaura cross-coupling reaction of 2-aryl-1-bromo-1-nitroethenes with arylboronic acids. Some difficulty was encountered in the preparation of arylnitromethanes, thus leading to the exploration of a cross-coupling strategy that proved more useful. A Barton−Zard pyrrole cyclocondensation reaction between 1,2-diaryl-1-nitroethenes and *N*-methoxy-*N*-methyl-2-isocyanoacetamide gave the corresponding pyrrole Weinreb amides, which were then converted into the desired 3-pyrrolin-2-ones in two steps. Overall, this method allowed for the construction of 3,4-diaryl-3-pyrrolin-2-ones with complete regiocontrol of the substituents with respect to the lactam carbonyl. The utility of this synthetic methodology was demonstrated by the preparation of eight unsymmetrical and symmetrical 3,4-diaryl-3-pyrrolin-2-ones including the *N*-H lactam analogue of the selective COX-II inhibitor, rofecoxib.



INTRODUCTION

3-Pyrrolin-2-ones (1*H*-pyrrol-2(5*H*)-ones) are an important class of nitrogen heterocycles that are the central components of natural products (e.g., plant pigments[1] and heme metabolites[2]), biologically active drug candidates, and molecular probes. 3-Pyrrolin-2-ones also serve as building blocks for the preparation of 5-arylidene-3-pyrrolin-2-ones,[3] pyrroles,[4] azacarbohydrates,[5] and γ-amino acid derivatives.[6] We are particularly interested in 3,4-diaryl-3-pyrrolin-2-ones because of their diverse biological activity. Examples of biologically active 3,4-diaryl-3-pyrrolin-2-ones include the following (Figure 1): imrecoxib (**1**)[7] and structurally related sulfone **2**,[8] selective cyclooxygenase-II (COX-II) inhibitors; **3**,[9] a vascular endothelial growth factor receptor (VEGF-R) inhibitor; staurosporinone (**4**),[10] a potent inhibitor of protein kinase C (PKC); Gö6976 (**5**),[11] an isozyme selective inhibitor of PKC. The latter two compounds are examples of indolocarbazoles, a class of molecules that has demonstrated a wide range of biological activity[12] and has drawn a significant level of synthetic interest.[13] Winterfeldt[14] and others[15] have developed syntheses of differentially protected 3,4-bis(indol-2′-yl)-3-pyrrolin-2-ones as precursors to indolocarbazoles. Additional examples of biologically active 3,4-diaryl-3-pyrrolin-2-ones have recently appeared in the patent literature including corticoid receptor antagonists (e.g., **6**),[16] phosphodiesterase inhibitors (e.g., **7**),[17] and cytokine inhibitors.[18] Because of the wide array of biological activity demonstrated by 3,4-diaryl-3-pyrrolin-2-ones, these molecules make attractive synthetic targets.

Prior to our work in this field,[19,20] all of the reported[21] synthetic approaches to 3,4-diaryl-3-pyrrolin-2-ones **I** employed intramolecular aldol-like condensation reactions of completely functionalized amidoketones **II** (Scheme 1). Given their significant biological activity and the lack of different synthetic approaches available for their preparation, we aimed to develop a common synthetic strategy that could target a diverse array of 3,4-diaryl-3-pyrrolin-2-ones **I** (e.g., **1**−**7**) employing simple

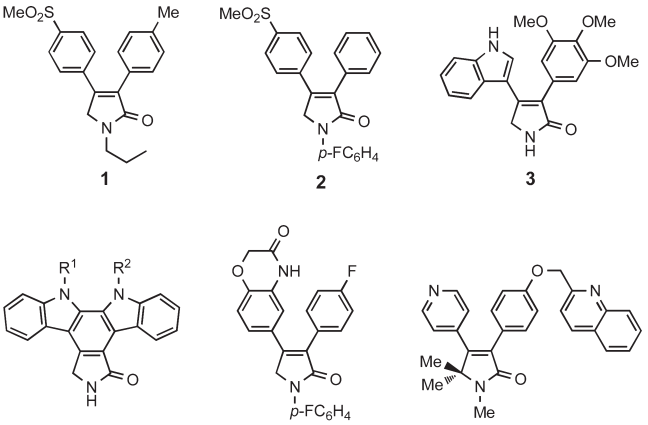


Figure 1. Selected 3,4-diaryl-3-pyrrolin-2-ones.

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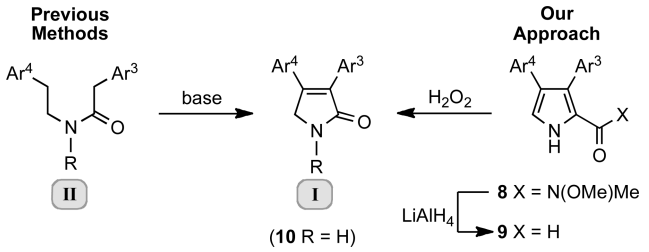
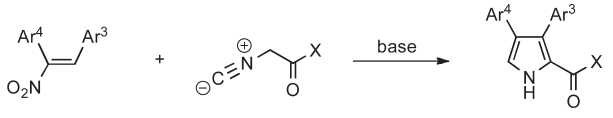
Scheme 1. Synthesis of 3,4-Diaryl-3-pyrrolin-2-ones



Scheme 2. Barton−Zard Pyrrole Cyclocondensation



starting materials. Thus, we developed a novel synthetic approach to pyrrole-2-carboxamides **8** and found these compounds to be competent precursors to 3,4-diaryl-3-pyrrolin-2-ones through a two-step sequence (Scheme 1):[19] (1) reduction of *N*-methoxy-*N*-methylamide (Weinreb amide)[22] **8** to aldehyde **9** utilizing lithium aluminum hydride; (2) conversion of **9** to 3,4-diaryl-3-pyrrolin-2-ones **10** by oxidation with hydrogen peroxide.[23] One advantage of the present method compared to previous methods to 3,4-diaryl-3-pyrrolin-2-ones is the wide range of aryl groups that are possible because of the large pool of commercially available benzaldehydes and arylboronic acids.

Our synthesis of 3,4-diaryl-3-pyrrolin-2-ones **10** is predicated on the ease of synthesizing pyrrole-2-carboxamides **8**. A versatile approach to 2,3,4-trisubstituted pyrroles involves a reaction first reported by Schöllkopf and his students[24] and later by Barton and Zard.[25] The transformation, often referred to as the Barton−Zard pyrrole reaction,[26] involves a cyclocondensation between nitroalkenes (e.g., **11**) and activated isocyanides (e.g., **12**) (Scheme 2). This strategy and close variants have been utilized to prepare a number of 2,3,4-trisubstituted pyrroles including 3,4-diarylpyrroles.[27] We previously adapted the Barton−Zard reaction to prepare pyrrole-2-carboxamides **8** including one example of a 3,4-diarylpyrrole.[19] We synthesized **8a** (Ar^3 = Ph; Ar^4 = Ph) by the cyclocondensation of the corresponding nitroalkene **11a** with 2-isocyano-*N*-methoxy-*N*-methylacetamide (**12**).[19] We herein report a significant extension of our methodology to the synthesis of unsymmetrical 3,4-diarylpyrrole-2-carboxamides **8** and to their subsequent conversion to the corresponding 3,4-diaryl-3-pyrrolin-2-ones **10** ($Ar^3 \neq Ar^4$). This work describes an entirely new approach that varies greatly from previously reported methods to this class of molecules. The key to the utility of our strategy is the simplicity of the starting materials: arylboronic acids (source of Ar^4), arylaldehydes (source of Ar^3), and Boc-protected glycine (precursor to isocyanide **12**).

RESULTS AND DISCUSSION[28]

Our initial approach to 1,2-diaryl-1-nitroethenes **11** utilized the method first reported by Robertson[29] that involved a modified Henry reaction between arylnitromethanes **14**−**18**[30] and benzylideneimines **19**[31] (Table 1, method #1). The latter were prepared by condensation of the corresponding aldehydes with *n*-butylamine in benzene utilizing a Dean−Stark apparatus. Phenylnitromethane (**14**)[30,32] was prepared in up to 53% yield by treatment of benzyl bromide **13** (R^1 = H) with sodium nitrite and urea in DMF at −10 °C. Condensation of **14** with different benzylideneimines **19** in acetic acid gave nitroethenes **11a**−**c** in moderate yields. This strategy worked well for preparing **11** with different "B" rings. In order to prepare **11** with different "A" rings, we explored the synthesis of functionalized arylnitromethanes **15**−**18**.

Unfortunately, the synthesis of arylnitromethanes **15** and **16** from the corresponding para-substituted benzyl bromides **13** proved to be problematic. Utilizing the conditions that were successful for the synthesis of unsubstituted **14**, we only obtained thioether **15** in low yields while sulfone **16** was seemingly never obtained. Different reaction conditions including silver nitrite/ether[33] or silver nitrite/H_2O[34] did not improve matters for preparing these substrates. These low yields are likely due to the ambident nature[35] of nitrite as a nucleophile and/or the relative instability of the nitroalkane products (e.g., Nef reactions[36]). Byproducts observed in these reactions include the corresponding benzyl alcohols, benzyl nitrites, and benzaldehydes. The compounds are distinguishable by ^{1}H NMR analysis of the benzylic protons (see Supporting Information). We briefly explored other options for the synthesis of arylnitromethanes **15** and **16**[32] such as converting benzaldoximes into the corresponding arylnitromethanes via oxidation, but this transformation also proved to be elusive.[32c] Interestingly, the preparation of nitro-substituted arylnitromethanes **17** and **18** using silver nitrite in ether did not present the same problem as sulfone **16**, as moderate yields were obtained.[33,37]

Given the difficulties encountered in preparing arylnitromethanes **15** and **16**, we decided to investigate alternate methods for obtaining nitroethenes **11**. We were inspired to explore a cross-coupling strategy (Table 1, method #2) after reading the work of Namboothiri and Ganesh.[38] They prepared **11** by employing a Suzuki−Miyaura cross-coupling reaction between 2-aryl-1-bromo-1-nitroethenes **22** and arylboronic acids. Thus, our synthesis began with β-nitrostyrenes **21** which were prepared by a Henry reaction of the corresponding benzaldehyde **20** with nitromethane.[39,40] Following the procedure utilized by Namboothiri[38] (and Parham[41]), we brominated **21** by treatment with bromine in the presence of pyridine, which gave **22** in relatively good yields. The cross-coupling of **22** with commercially available arylboronic acids and palladium tetrakis(triphenylphosphine) in the presence of sodium carbonate afforded **11** in moderate yields. This method proved to be highly versatile, allowing for the easy integration of different aryl substituents, including different "A" rings containing electron-donating groups, electron-withdrawing groups, and halogens. Overall, we found method #2 to be the superior approach to making nitroethenes **11** because of the availability of arylboronic acids compared to the corresponding arylnitromethanes.[42]

We prepared sulfone-substituted nitroethene **11k** by treatment of thioether-substituted nitroethene **11c** with 2 equiv of *m*-CPBA (Supporting Information: method #3).[43] This also served as an alternative synthesis of nitroethene **11j** (from **11e**).

From **11**, we finished our synthesis of 3-pyrrolin-2-ones in three subsequent steps (Table 2):[19] (1) treatment of **11** with 1.5 equiv of isocyanide **12**[44,45] in the presence of DBU and inhibitor-free THF[46] gave pyrrole-2-carboxamides **8** (Barton−Zard reaction[26]); (2) reduction of Weinreb amide functional group by treatment of **8** with $LiAlH_4$ gave pyrrole-2-carboxaldehydes **9**;[47] (3) Baeyer−Villiger

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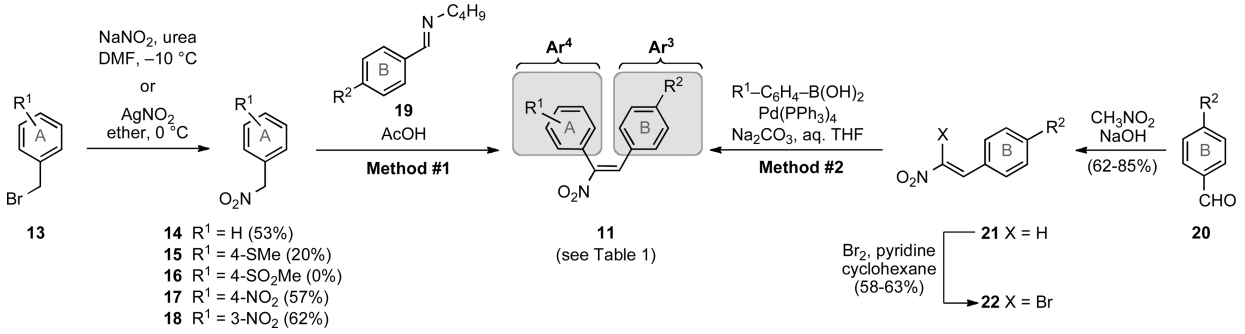
Table 1. Synthesis of 1,2-Diaryl-1-nitroethenes



substrate	nitroalkene **11** Ar^3	Ar^4	method #1, yield (%)	method #2, yield (%)
a	Ph	Ph	42	77
b	4-MeOPh	Ph	62	77
c	4-MeSPh	Ph	70	83
d	Ph	4-MeOPh	—[a]	84
e	Ph	4-MeSPh	25	81
f	Ph	4-FPh	—[a]	76
g	Ph	4-ClPh	—[a]	75
h	4-MeOPh	4-MeOPh	—[a]	70
i	4-MeSPh	4-MeSPh	—[a]	68
j[b]	Ph	4-MeSO$_2$Ph	—[a]	48
k[b]	4-MeSO$_2$Ph	Ph	—[a]	—[a]
m	Ph	4-NO$_2$Ph	36	0
n	Ph	3-NO$_2$Ph	12	52

[a] Not attempted. [b] Method #3: Oxidation of corresponding thioether-substituted nitroalkene with 2 equiv of *m*-CPBA (84% for **11j** from **11e**; 95% for **11k** from **11c**).

type oxidation[23] via treatment of **9** with excess hydrogen peroxide in the presence of sodium bicarbonate gave 3-pyrrolin-2-ones **10**.[48] In most cases, this strategy worked well for the synthesis of pyrrole-2-carboxamides **8**,[49] pyrrole-2-carboxaldehydes **9**,[50] and 3-pyrrolin-2-ones **10**.[51,52] These results demonstrate the flexibility of our methodology for preparing 3,4-diaryl-3-pyrrolin-2-ones including regioisomers (e.g., **10b** and **10d**) and halogen-substituted analogues (**10f** and **10g**). It is important to note that the oxidation of **9** operates with complete regioselectivity; we have never observed the presence of regioisomers in ^{1}H NMR analyses of the crude reaction mixtures.

A few substrates proved to be problematic. This strategy did not work for the synthesis of thioether-substituted 3-pyrrolin-2-ones **10c** and **10e**. Oxidation of neither **9c** or **9e** gave known 3-pyrrolin-2-one **10c**[20a] or the unknown **10e**, respectively. Instead, it appears that the H_2O_2 partially oxidized the thioether and left the aldehyde unchanged. Another shortfall was the pyrrole cyclocondensation of sulfone-substituted nitroethene **11j**. Utilizing the general reaction conditions (excess **12**), none of the expected product **8j** or the starting nitroethene **11j** was detected during analysis of the crude reaction mixture by ^{1}H NMR. We then revisited this reaction by using excess nitroalkene **11j** and obtained a 40% yield of **8j**. We speculated that the electron-withdrawing sulfone might be responsible for the low yield. To test this idea, we prepared both *p*- and *m*-nitro-substituted nitroethenes **11m** and **11n** and submitted them to the Barton—Zard pyrrole cyclocondensation conditions. Interestingly, the yields were fairly consistent with our previous results (with **12** in excess); thus, **11j** appears to be an exceptional case.

Due to the lower yield obtained for **8j**, we explored an alternate synthesis; **8j** is the precursor to **10j**, the lactam analogue of the selective COX-II inhibitor rofecoxib. We found that **8j** could alternately be obtained by oxidation of thioether **8e** with *m*-CPBA[43] in 95% yield. With a reliable route to **8j**, the synthesis of the rofecoxib analogue **10j** was achieved by reduction with $LiAlH_4$ followed by oxidation with H_2O_2 in the same manner previously used (Scheme 3). Newly synthesized compound **10j** was identical with an authentic sample that was prepared in our lab using a different method.[20a] Interestingly, the synthesis of isomeric 3-pyrrolin-2-one **10k** was not as successful. Although **9k** could be obtained in two reasonable yielding steps from nitroethene **11k** (or three steps from **11c**), subsequent oxidation with H_2O_2 gave **10k** in only trace amounts. The low yield, in part, could possibly be due to the low solubility of **9k** in methanol; in one run, 80% of the starting material was recovered unchanged. Heating the reaction did not improve matters. A brief exploration of this reaction in acetone gave a slightly better result (5% yield) and allowed for the preparation of the analytical sample.

CONCLUSION

A new method for the regiocontrolled construction of both symmetrical and unsymmetrical 3,4-diaryl-3-pyrrolin-2-ones **10**

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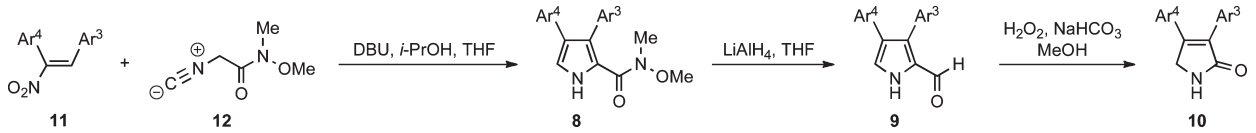
Table 2. Pyrrole-2-carboxamides, Pyrrole-2-carboxaldehydes, and 3-Pyrrolin-2-ones

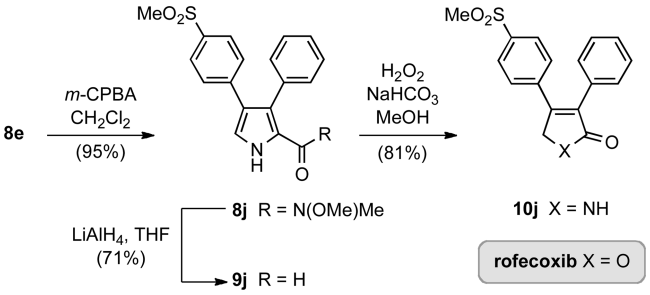


11 12 8 9 10

substrates	Ar^3	Ar^4	amide **8**, yield (%)[a]	aldehyde **9**, yield (%)	3-pyrrolin-2-one **10**, yield (%)
a	Ph	Ph	87	72	91
b	4-MeOPh	Ph	89	68	90
c	4-MeSPh	Ph	79	81	0[b]
d	Ph	4-MeOPh	89	73	90
e	Ph	4-MeSPh	78	72	0[b]
f	Ph	4-FPh	69	70	66
g	Ph	4-ClPh	66	82	73
h	4-MeOPh	4-MeOPh	82	63	72[c]
i	4-MeSPh	4-MeSPh	75	—[d]	—[d]
j	Ph	4-$MeSO_2$Ph	40[e] (95[f])	71	81
k	4-$MeSO_2$Ph	Ph	65 (69[f])	64	5[g]
m	Ph	4-NO_2Ph	64	—[d]	—[d]
n	Ph	3-NO_2Ph	60	—[d]	—[d]

[a] 1.0 equiv of **11** and 1.5 equiv of **12** used. [b] Reactions were run both with 3−5 equiv of *m*-CPBA in addition to large excess of H_2O; analysis of crude reaction mixtures by ^{1}H NMR revealed no 3-pyrrolin-2-one product and possible partial oxidation of the thioether moiety. [c] Yield based on recovered starting material. [d] Not attempted. [e] 1.2 equiv of **11** and 1.0 equiv of **12** used. [f] Yield of reaction involving oxidation of the corresponding thioether-substituted pyrrole-2-carboxamide **8c** or **8e** with 2 equiv of *m*-CPBA. [g] Up to 80% of the starting material recovered unchanged.

Scheme 3. Synthesis of Rofecoxib Analogue



has been achieved starting from β-nitrostyrenes **21** with pyrrole-2-carboxamides (pyrrole Weinreb amides) **8** serving as the key intermediates. Suzuki−Miyaura cross-coupling reactions of 2-aryl-1-bromo-1-nitroethenes **22** with arylboronic acids provided a superior route to 1,2-diaryl-1-nitroethenes **11** compared to our initial approach, which used a modified Henry reaction involving arylnitromethanes (e.g., **15**) that proved to be difficult to prepare. Pyrrole-2-carboxamides **8** were synthesized using a Barton−Zard pyrrole cyclocondensation; these were then converted into the corresponding 3,4-diaryl-3-pyrrolin-2-ones **10** in two steps. This methodology was then used to prepare eight 3,4-diaryl-3-pyrrolin-2-ones **10** including the *N*-H lactam analogue of rofecoxib **10j**. We will continue to explore the use of this methodology for the synthesis of biologically active 3,4-diaryl-3-pyrrolin-2-ones, such as those depicted in Figure 1.

EXPERIMENTAL SECTION

2-Isocyano-*N*-methoxy-*N*-methylacetamide (12).[19,45] Our previously reported procedure[19] was followed with a slight modification.[44] To a 0 °C stirred solution of 2-formamido-*N*-methoxy-*N*-methylacetamide[19] (2.4 g, 16 mmol) in CH_2Cl_2 (50 mL) and diisopropylamine (4.5 g, 44 mmol) was added neat phosphorus oxychloride (2.8 g, 18 mmol) dropwise via syringe over the course of 5 min. This was stirred at 0 °C for 2 h, and then a saturated solution of Na_2CO_3 (15 mL) was added dropwise via addition funnel. The resulting mixture was stirred at rt for 1.5 h and then was transferred to a separatory funnel with the aid of deionized water and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 50 mL). The combined organic layers were washed with deionized water (4 × 100 mL) and dried over sodium sulfate. Removal of the solvent in vacuo gave the desired product as a tan amorphous solid (1.9 g, 92% yield) which could be used directly without further purification: mp 81−82 °C (lit.[19] mp 85−86 °C); R_f (1:1 ethyl acetate/petroleum ether) = 0.20 (visualized with I_2); IR (ATR, neat) 2982, 2954, 2160, 1670, 1467, 1435, 1400, 1326, 1200, 1183, 1158, 1112, 1011, 960, 915, 798 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.41 (s, 2H), 3.72 (s, 3H), 3.23 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.1, 161.1, 61.9, 44.0, 33.0 ppm.

4-(Methylsulfonyl)benzyl Alcohol[53]. A modification of the procedure reported by Wayner and Arnold was followed.[54] To a 0 °C stirred solution of 4-(thiomethyl)benzyl alcohol (7.0 g, 45 mmol) in CH_2Cl_2 (100 mL) was added *m*-CPBA (77% purity, 10.4 g, 136 mmol). The solution was then stirred at rt for 6 h. The reaction mixture was treated with a saturated solution of $NaHCO_3$ (200 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with saturated solutions of $NaHCO_3$ (2 × 100 mL) and dried over sodium sulfate. Removal of the solvent gave the title product as a white powder (5.0 g, 27 mmol, 60% yield) which could be used without further purification: mp 81−82 °C (lit.[53] mp 83.5−84 °C); R_f (1:1 ethyl acetate/petroleum ether) = 0.10; IR (ATR, neat) 3483, 3006, 2923, 1597, 1449, 1411, 1328, 1277, 1196, 1141, 1089, 1049, 1015, 965, 947, 817, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (d, 2H, *J* = 8.5 Hz), 7.55 (d, 2H, *J* = 8.5 Hz), 4.80 (s, 2H), 3.04 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ 147.6, 139.5, 127.8, 127.5, 64.4, 44.8 ppm.

General Method. Synthesis of Benzyl Bromides 13. A modification of the procedure reported by Bjørnholm et al. was followed.[55] To a

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0 °C stirred solution of benzyl alcohol (20 mmol) in CH_2Cl_2 (40 mL) was added neat PBr_3 (1.9 mL, 5.4 g, 20 mmol) dropwise over the course of 5 min. The reaction mixture was stirred at rt for 1 h (monitored by TLC) and then poured into a mixture of ice and deionized water (50 mL). After being warmed to rt, the organic layer was separated and washed with deionized water (50 mL) and dried over sodium sulfate. Removal of the solvent in vacuo gave the benzyl bromides as amorphous solids which could be used directly without further purification.

4-(Thiomethyl)benzyl Bromide (13i).[55] Off-white amorphous solid: 92% yield; mp 41−42 °C (lit.[55] mp 43−44 °C); R_f (1:2 CH_2Cl_2/petroleum ether) = 0.50; IR (ATR, neat) 3021, 2979, 2917, 1598, 1562, 1489, 1432, 1402, 1326, 1226, 1204, 1185, 1128, 1090, 1012, 970, 954, 873, 826, 810, 717 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.31 (d, 2H, J = 8.6 Hz), 7.21 (d, 2H, J = 8.6 Hz), 4.48 (s, 2H), 2.48 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.5, 134.6, 129.8, 126.7, 33.7, 15.8 ppm.

4-(Methylsulfonyl)benzyl Bromide (13ii).[54] White powder: 51% yield; mp 95−97 °C (lit.[54] mp 94−96 °C); R_f (1:3 ethyl acetate/petroleum ether) = 0.43; IR (ATR, neat) 3006, 2925, 1598, 1445, 1325, 1289, 1228, 1146, 1089, 1020, 963, 848, 816, 766, 719 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (d, 2H, J = 8.5 Hz), 7.59 (d, 2H, J = 8.5 Hz), 4.51 (s, 2H), 3.06 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.0, 140.6, 130.2, 128.2, 44.8, 31.6 ppm.

General Method. Synthesis of Arylnitromethanes 14 and 15. A modification of the procedure reported by Kornblum et al. was followed.[30] To a rt stirred solution of DMF (100 mL) and $NaNO_2$ (10.4 g, 150 mmol) was added urea (12.0 g, 200 mmol). The urea was allowed to dissolve completely, and the solution was cooled to −10 °C. A solution of benzyl bromide **13** (100 mmol) dissolved in DMF (100 mL) was then added dropwise via addition funnel. The reaction mixture was stirred at −10 °C for 2−6 h (monitored by TLC). The reaction solution was poured onto ice-cooled H_2O (500 mL). The aqueous layer was extracted with cold ether (3 × 200 mL). The combined organic layers were then washed with ice-cooled brine (500 mL) and dried over Na_2SO_4. The solvent was removed in vacuo to give the crude product. Crude oils were purified by vacuum distillation, and crude solids were purified by flash column chromatography (ethyl acetate/petroleum ether gradient).

Phenylnitromethane (14). Light yellow oil: 53% yield; bp 50−60 °C (15 mmHg); lit.[30] bp 76−78 °C (2 mmHg); R_f (1:10 CH_2Cl_2/petroleum ether) = 0.23; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.46−7.40 (m, 5H), 5.42 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 130.3, 130.2, 130.0, 129.4, 80.3 ppm.

4′-(Thiomethyl)phenylnitromethane (15). Orange amorphous solid: 20% yield; mp 1−42 °C; R_f (1:1 CH_2Cl_2/petroleum ether) = 0.57; IR (ATR, neat) 2961, 2926, 1602, 1543, 1494, 1424, 1405, 1368, 1307, 1221, 1191, 1122, 1089, 1018, 966, 950, 890, 861, 838, 810, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34 (d, 2H, J = 8.5 Hz), 7.25 (d, 2H, J = 8.5 Hz), 5.36 (s, 2H), 2.47 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.8, 130.7, 126.6, 126.2, 79.9, 15.5 ppm; HRMS (EI) calcd for $C_8H_9NO_2S$: 183.0354, found 183.0343.

General Method. Synthesis of Nitrophenylnitromethanes. A modification of the procedure reported by Kornblum et al. was followed.[33] To a 0 °C stirred mixture of silver nitrite (33 mmol) in ether (50 mL) was added a solution of nitrobenzyl bromide dissolved in ether (80 mL) dropwise via addition funnel over a period of 1 h. The reaction mixture was stirred at 4 °C for 24−48 h (cold room) monitored by TLC. The reaction mixture was filtered through Celite with the aid of ether. The organic layer was dried over sodium sulfate, and solvent was concentrated on a rotary evaporator until crystallization was observed. The crystals were then isolated by filtration (multiple crops), giving the desired products which could be used directly without further purification.

4′-Nitrophenylnitromethane (17).[37,56] Yellow crystals (ether); 57% yield; mp 84−85 °C (lit.[37,56] mp 90−91 °C); R_f (1:1 CH_2Cl_2/petroleum ether) = 0.33; IR (ATR, neat) 1613, 1553, 1538, 1373, 1347, 1314, 1299, 1196, 1106, 1015, 904, 858, 826, 767, 721 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.32 (d, 2H, J = 8.8 Hz), 7.67 (d, 2H, J = 8.8 Hz), 5.56 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.2, 136.0, 131.4, 124.6, 79.0 ppm.

3′-Nitrophenylnitromethane (18).[37] Yellow crystals (ether); 62% yield; mp 92.5−94 °C (lit.[37] 91−93 °C); R_f (1:1 CH_2Cl_2/petroleum ether) = 0.22; IR (ATR, neat) 3080, 1543, 1518, 1430, 1348, 1315, 1216, 1100, 1081, 931, 886, 832, 815, 713 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.33−8.36 (m, 2H), 7.81−7.83 (m, 1H), 7.67 (t, 1H, J = 8.0 Hz), 5.56 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.8, 136.3, 131.4, 130.6, 125.5, 125.3, 78.9 ppm.

General Method. Synthesis of Benzylidenimines 19. To a rt stirred solution of an aldehyde (10.0 mmol) in benzene (100 mL) was added *n*-butylamine (10.0 mmol). A Dean−Stark apparatus was attached, and the reaction mixture was heated to reflux and stirred for 12−24 h. The solvent was removed in vacuo to give a crude oil that was purified by fractional vacuum distillation.

***N*-(Benzylidene)butan-1-amine (19i).**[31,57] Light yellow oil; 91% yield; bp 130−134 °C (15 mmHg); lit.[57] bp 74 °C (0.7 mmHg); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.27 (s, 1H), 7.71−7.73 (m, 2H), 7.39−7.42 (m, 3H), 3.61 (t, 2H, J = 7.2 Hz), 1.69 (quint, 2H, J = 7.2 Hz), 1.40 (sext, 2H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 136.7, 130.7, 128.8, 128.3, 61.7, 33.3, 20.7, 14.2 ppm.

***N*-(4′-Methoxybenzylidene)butan-1-amine (19ii).**[31,58] Clear oil; 90% yield; bp 155−160 °C (15 mmHg); lit.[58] bp 126−127 °C (3.5 mmHg); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.18 (s, 1H), 7.64 (d, 2H, J = 8.8 Hz), 6.90 (d, 2H, J = 8.8 Hz), 3.82 (s, 3H), 3.55 (t, 2H, J = 7.0 Hz), 1.64 (tt, 2H), 1.36 (tq, 2H), 0.92 (t, 3H, J = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.7, 160.3, 129.8, 129.6, 114.2, 61.7, 55.6, 33.4, 20.7, 14.2 ppm.

***N*-[4′-(Methylthio)benzylidene]butan-1-amine (19iii).**[59] Clear oil; 95% yield; bp 170−178 °C (3 mmHg); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.21 (s, 1H), 7.62 (d, 2H, J = 8.6 Hz), 7.24 (d, 2H, J = 8.6 Hz), 3.6 (t, 2H, J = 7.2 Hz), 2.49 (s, 3H), 1.65 (tt, 2H), 1.39 (tq, 2H), 0.94 (t, 3H, J = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.4, 142.0, 133.4, 128.6, 126.1, 61.8, 33.3, 20.7, 15.6, 14.2 ppm.

General Method. General Procedure to *β*-Nitrostyrenes 21. A modification of the procedure reported by Namboothiri et al. was followed.[39a] To a 5 °C solution of aldehyde **20** (50 mmol) in MeOH (10 mL) was added a solution of nitromethane (50 mmol) in MeOH (10 mL). Ice-cooled 4 M NaOH (10 mL) was then added dropwise via addition funnel while maintaining an internal temperature of 5 °C. The cloudy yellow/white reaction mixture was stirred at 5 °C for 1 h. It was then diluted with ice-cooled H_2O (20 mL), and the resulting mixture was then added dropwise to ice-cooled 4 M HCl (25 mL). The resulting yellow mixture stirred at 5 °C until TLC showed the absence of starting material. The yellow mixture was filtered through sintered glass and washed with water, giving a crude yellow, amorphous solid that was purified by flash column chromatography (CH_2Cl_2/petroleum ether gradient). Recrystallization then gave analytically pure samples.

***(E)*-1-(4′-Methoxyphenyl)-2-nitroethene (21ii).**[60] Yellow crystals (EtOH): 62% yield; mp 87−88 °C (lit.[60] mp 86−88 °C); R_f (1:2 CH_2Cl_2/petroleum ether) = 0.41; IR (ATR, neat) 3108, 2906, 2839, 1623, 1600, 1570, 1515, 1493, 1424, 1323, 1307, 1274, 1247, 1172, 1122, 1029, 964, 940, 865, 843, 832, 818, 806, 779 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.97 (d, 2H, J = 13.6 Hz), 7.48−7.54 (m, 3H), 6.96 (d, 2H, J = 8.8 Hz), 3.87 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.2, 139.2, 135.3, 131.4, 122.8, 115.2, 55.8 ppm.

***(E)*-1-[4′-(Methylthio)phenyl]-2-nitroethene (21iii).**[61] Yellow crystals: 53% yield; mp 84−86 °C (lit.[61] mp 84−86 °C); R_f (1:2 CH_2Cl_2/petroleum ether) = 0.33; IR (ATR, neat) 3106, 1619, 1588, 1546, 1489, 1406, 1325, 1262, 1186, 1124, 1088, 963, 811, 747, 730 cm^{-1}; ^1H NMR

($CDCl_3$, 400 MHz) δ 7.97 (d, 1H, J = 13.6 Hz), 7.58 (d, 1H, J = 13.6 Hz), 7.46 (d, 2H, J = 8.4 Hz), 7.27 (d, 2H, J = 8.4 Hz), 2.51 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.4, 139.0, 136.4, 129.7, 129.5, 126.2, 15.1 ppm.

General Method. Synthesis of 2-Aryl-1-bromo-1-nitroethenes 22. A modification of the procedure reported by Namboothiri et al. was followed.[38] To a rt stirred solution of β-nitrostyrene **21** (5.0 mmol) in pyridine (6.5 mmol) and cyclohexane (20 mL) was added neat Br_2 (6.0 mmol) dropwise over 5 min. The cloudy yellow reaction was then heated to reflux and stirred for 4−12 h (monitored by TLC). The reaction mixture was then transferred to a single-neck round-bottom flask with the aid of ethyl acetate. The solvent was removed, and the resulting residue was taken up in ethyl acetate (50 mL). The organic layer was washed with aqueous $Na_2S_2O_3$ (1.0 M, 2 × 20 mL), H_2O (20 mL), and brine (20 mL) and then dried over Na_2SO_4. The solvent was removed in vacuo to give a crude solid that was purified by flash chromatography (CH_2Cl_2/petroleum ether gradient).

(*Z*)-1-Bromo-1-nitro-2-phenylethene (22i).[38] Yellow needles (EtOH); 78% yield; mp 62−64 °C (lit.[38] mp 63−64 °C); R_f (1:10 CH_2Cl_2/petroleum ether) = 0.16; IR (ATR, neat) 3032, 1596, 1572, 1526, 1446, 1305, 1284, 1209, 1161, 1056, 1033, 955, 930, 904, 859, 763, 753, 688 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.65 (s, 1H), 7.88−7.90 (m, 2H), 7.50−7.53 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.0, 132.1, 131.2, 130.4, 129.2, 128.4 ppm.

(*Z*)-1-Bromo-2-(4′-methoxyphenyl)-1-nitroethene (22ii).[38] Yellow crystals (EtOH): 88% yield; mp 64−65 °C (lit.[38] mp 67−68 °C); R_f (1:2 CH_2Cl_2/petroleum ether) = 0.42; IR (ATR, neat) 2942, 1591, 1564, 1519, 1426, 1307, 1293, 1261, 1180, 1055, 1033, 1021, 957, 912, 866, 825, 793, 713 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (br s, 1H), 7.93 (d, 2H, J = 8.8 Hz), 7.01 (d, 2H, J = 8.8 Hz), 3.89 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.1, 136.6, 133.7, 125.7, 122.7, 114.8, 55.8 ppm.

(*Z*)-1-Bromo-2-[4′-(methylthio)phenyl]-1-nitroethene (22iii). Yellow needles (EtOH): 81% yield; mp 86−88 °C; R_f (1:5 CH_2Cl_2/petroleum ether) = 0.20; IR (ATR, neat) 2919, 1601, 1586, 1549, 1518, 1492, 1406, 1291, 1213, 1197, 1134, 1088, 1010, 947, 906, 862, 827, 810, 763, 727, 703, 674 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.61 (s, 1H), 7.84 (d, 2H, J = 8.8 Hz), 7.30 (d, 2H, J = 8.8 Hz), 2.54 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.5, 136.3, 131.7, 127.0, 126.3, 125.7, 15.0 ppm. Anal. Calcd for $C_9H_8BrNO_2S$: C, 39.43; H, 2.94; N, 5.11; S, 11.70. Found: C, 39.16; H, 2.86; N, 5.13; S, 11.72.

General Method #1. Synthesis of Nitroethenes 11 via Modified Henry Reaction. A modification of the procedure reported by Robertson was followed.[29] To a rt stirred solution of an arylnitromethane (1.00 mmol) in AcOH (5 mL) was added an imine **17** (1.00 mmol). The light yellow solution was stirred at rt for 1 h, MeOH (50 mL) was added, and the reaction solution was stirred at rt for an additional 1.5 h. The solvent was removed in vacuo to give an oil or amorphous solid. MeOH (50 mL) was added and then partially removed on a rotary evaporator until crystal formation was observed (in some cases, this process was repeated several times). Filtration then gave nitroalkenes **11** as yellow crystals.

General Method #2. Synthesis of Nitroethenes 11 via Suzuki−Miyaura Cross-Coupling. A modification of the procedure reported by Ganesh and Namboothiri was followed.[38] To a rt stirred solution of 2-aryl-1-bromo-1-nitroethene **20** (1.00 mmol) and arylboronic acid (1.50 mmol) in THF (10 mL) was added $Pd(PPh_3)_4$ (0.05 mmol). To the resulting mixture, a solution of Na_2CO_3 (2.50 mmol) in H_2O (1 mL) was added. The light yellow solution was stirred at rt for 40 min and then heated to reflux for 5−30 h until TLC analysis showed complete conversion of **20**. The reaction solution was filtered through Celite with the aid of ethyl acetate. The solvent was removed in vacuo to give crude solids. Purification by flash column chromatography (CH_2Cl_2/petroleum ether gradient) gave nitroethenes **11** as yellow amorphous solids. Recrystallization then gave analytically pure samples.

General Method #3. Oxidation of Thioethers to Sulfones. To a rt stirred solution of thioether compound (1.00 mmol) in CH_2Cl_2 (15 mL) was added *m*-CPBA (2.00 mmol). The yellow reaction solution stirred at rt for 4 h and then was diluted with CH_2Cl_2 (15 mL). The organic layer was washed with 5% Na_2SO_3 (15 mL) and 5% $NaHCO_3$ (15 mL), dried over Na_2SO_4, and then filtered through a sintered glass funnel with the aid of CH_2Cl_2 (10 mL). Removal of the solvent in vacuo gave the desired sulfones as amorphous solids which could be utilized directly without further purification. Recrystallization provided analytically pure samples.

(*E*)-1-Nitro-1,2-diphenylethene (11a).[38] Yellow needles (EtOH): general method #1 (42% yield); general method #2 (77% yield); mp 74−76 °C (lit.[38] mp 72−74 °C); R_f (1:5 CH_2Cl_2/petroleum ether) = 0.33; IR (ATR, neat) 3059, 2973, 1652, 1574, 1508, 1491, 1445, 1370, 1317, 1291, 1214, 1159, 1055, 1033, 1001, 967, 936, 915, 860, 793, 776, 759, 738, 709 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24 (s, 1H), 7.49−7.51 (m, 3H), 7.30−7.38 (m, 3H), 7.20−7.26 (m, 2H), 7.10 (d, 2H, J = 8.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.9, 135.1, 131.5, 131.4, 131.0, 130.85, 130.83, 130.3, 129.5, 129.0 ppm.

(*E*)-2-(4′-Methoxyphenyl)-1-nitro-1-phenylethene (11b).[38] Yellow crystals (EtOH): general method #1 (62% yield); general method #2 (77% yield); mp 152−154 °C (lit.[38] mp 152−153 °C); R_f (1:2 CH_2Cl_2/petroleum ether) = 0.21; IR (ATR, neat) 3057, 2939, 2844, 1642, 1601, 1567, 1517, 1493, 1455, 1442, 1424, 1381, 1308, 1256, 1177, 1119, 1073, 1021, 972, 942, 931, 920, 869, 831, 804, 783, 740, 725, 709 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23 (s, 1H), 7.50−7.52 (m, 3H), 7.33−7.35 (m, 2H), 7.04 (d, 2H, J = 9.0 Hz), 6.74 (d, 2H, J = 9.0 Hz), 3.78 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.0, 147.7, 135.3, 133.5, 131.3, 130.9, 130.2, 129.6, 123.9, 114.6, 55.7 ppm.

(*E*)-2-[4′-(Methylthio)phenyl]-1-nitro-1-phenylethene (11c). Yellow crystals (EtOH): general method #1 (70% yield); general method #2 (83% yield); mp 119−120 °C; R_f (1:1 CH_2Cl_2/petroleum ether) = 0.42; IR (ATR, neat) 3057, 1638, 157, 1506 1488, 1443, 1430, 1407, 1378, 1303, 1223, 1191, 1164, 1090, 1031, 1012, 1001, 969, 942, 918, 865, 813, 775, 721, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20 (s, 1H), 7.49−7.51 (m, 3H), 7.32−7.34 (m, 2H), 7.05 (d, 2H, J = 8.6 Hz), 6.99 (d, 2H, J = 8.6 Hz), 2.44 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 143.7, 134.9, 131.7, 131.1, 130.8, 130.3, 129.6, 127.6, 125.6, 15.0 ppm. Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16; S, 11.82. Found: C, 66.22; H, 4.63; N, 5.29; S, 11.56.

(*E*)-1-(4′-Methoxyphenyl)-1-nitro-2-phenylethene (11d).[38] Yellow needles (EtOH): general method #2 (84% yield); mp 100−102 °C (lit.[38] mp 95−96 °C); R_f (1:2 CH_2Cl_2/petroleum ether) = 0.24; IR (ATR, neat) 2937, 1648, 1606, 1509, 1447, 1370, 1315, 1292, 1245, 1210, 1168, 1113, 1056, 1027, 968, 932, 912, 860, 832, 811, 765, 742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.18 (s, 1H), 7.22−7.32 (m, 5H), 7.14 (d, 2H, J = 8.8 Hz), 6.99 (d, 2H, J = 8.8 Hz), 3.88 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.1, 150.0, 134.7, 132.3, 131.8, 131.4, 130.9, 129.0, 122.8, 115.0, 55.6 ppm.

(*E*)-1-[4′-(Methylthio)phenyl]-1-nitro-2-phenylethene (11e). Yellow crystals (EtOH): general method #1 (25% yield); general method #2 (81% yield); mp 103−105 °C; R_f (1:1 CH_2Cl_2/petroleum ether) = 0.30; IR (ATR, neat) 3071, 2916, 1645, 1593, 1518, 1489, 1450, 1431, 1398, 1369, 1313, 1210, 1187, 1167, 1120, 1090, 1032, 1017, 965, 933, 916, 861, 819, 785, 772, 747 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20 (s, 1H), 7.23−7.33 (m, 7H), 7.15 (d, 2H, J = 7.6 Hz), 2.54 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.5, 141.9, 135.0, 131.5, 131.3, 131.2, 131.0, 129.0, 126.8, 126.5, 15.3 ppm. Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16; S, 11.82. Found: C, 66.53; H, 4.84; N, 5.15; S, 11.79.

(*E*)-1-(4′-Fluorophenyl)-1-nitro-2-phenylethene (11f).[62] Light yellow crystals (EtOH): general method #2 (76% yield); mp 88−90 °C; R_f (1:2 CH_2Cl_2/petroleum ether) = 0.33; IR (ATR, neat) 3070, 1647, 1600, 1508, 1490, 1146, 1363, 1322, 1300, 1214, 1161, 1104, 1074, 1029, 977, 941, 926, 907, 863, 841, 822, 773, 763, 732 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ

8.24 (s, 1H), 7.30−7.36 (m, 3H), 7.23−7.27 (m, 2H), 7.16−7.21 (m, 2H), 7.09−7.11 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.4 (d, J_{C-F} = 250.6 Hz), 148.9, 135.6, 133.1 (d, J_{C-F} = 8.2 Hz), 131.4, 131.3, 131.2, 129.1, 126.8 (d, J_{C-F} = 3.7 Hz), 116.8 (d, J_{C-F} = 22.5 Hz) ppm. Anal. Calcd for $C_{14}H_{10}FNO_2$: C, 69.13; H, 4.14; N, 5.76. Found: C, 69.27; H, 4.10; N, 5.82.

(*E*)-1-(4′-Chlorophenyl)-1-nitro-2-phenylethene (11g).[63] Yellow crystals (EtOH): general method #2 (75% yield); mp 105−107 °C; R_f (1:5 ethyl acetate/petroleum ether) = 0.33; IR (ATR, neat) 3060, 1915, 1648, 1594, 1519, 1489, 1445, 1399, 1365, 1319, 1211, 1183, 1168, 1087, 1030, 1018, 973, 946, 928, 908, 861, 834, 786, 768, 748, 732, 689 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.22 (s, 1H), 7.44 (d, 2H, J = 8.8 Hz), 7.22−7.32 (m, 5H), 7.09 (d, 2H, J = 8.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.7, 136.6, 135.7, 132.4, 131.4, 131.3, 131.2, 129.9, 129.22, 129.17 ppm. Anal. Calcd for $C_{14}H_{10}ClNO_2$: C, 64.75; H, 3.88; N, 5.39. Found: C, 64.63; H, 3.94; N, 5.38.

(*E*)-1,2-Bis(4′-methoxyphenyl)-1-nitroethene (11h).[64] Fine yellow crystals (EtOH): general method #2 (70% yield); mp 142−144 °C (lit.[64] mp 140−141 °C); R_f (1:1 CH_2Cl_2/petroleum ether) = 0.30; IR (ATR, neat) 2936, 2840, 1642, 1599, 1569, 1502, 1451, 1440, 1425, 1378, 1303, 1249, 1177, 1118, 1033, 1021, 965, 952, 932, 919, 869, 847, 813, 789, 756, 746, 722, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20 (s, 1H), 7.26 (d, 2H, J = 8.8 Hz), 7.09 (d, 2H, J = 8.8 Hz), 7.03 (d, 2H, J = 8.8 Hz), 6.77 (d, 2H, J = 8.8 Hz), 3.89 (s, 3H), 3.80 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.9, 160.9, 147.7, 135.0, 133.4, 132.3, 124.2, 123.3, 115.1, 114.6, 55.64, 55.63. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.15; H, 5.27; N, 4.95.

(*E*)-1,2-Bis[4′-(methylthio)phenyl]-1-nitroethene (11i). Yellow crystals (EtOH): general method #2 (68% yield); mp 108−110 °C; R_f (1:2 CH_2Cl_2/petroleum ether) = 0.23; IR (ATR, neat) 3065, 2916, 2166, 1641, 1587, 1485, 1421, 1404, 1375, 1302, 1218, 1189, 1168, 1126, 1085, 1012, 968, 957, 939, 926, 865, 843, 826, 818, 788, 757, 713, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17 (s, 1H), 7.32 (d, 2H, J = 8.8 Hz), 7.23 (d, 2H, J = 8.8 Hz), 7.06 (d, 2H, J = 9.2 Hz), 7.02 (d, 2H, J = 9.2 Hz), 2.54 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5, 143.8, 141.8, 134.9, 131.7, 131.2, 127.6, 127.1, 126.6, 125.7, 15.3, 15.0 ppm. Anal. Calcd for $C_{16}H_{15}NO_2S_2$: C, 60.54; H, 4.76; N, 4.41; S, 20.20. Found: C, 60.73; H, 4.80; N, 4.39; S, 20.02.

(*E*)-1-[4′-(Methylsulfonyl)phenyl]-1-nitro-2-phenylethene (11j). Yellow crystals (ethyl acetate): general method #2 (48% yield); general method #3 (84% yield); mp 165−167 °C; R_f (4:1 CH_2Cl_2/petroleum ether) = 0.16; IR (ATR, neat) 3066, 3006, 2925, 1657, 1518, 1449, 1415, 1400, 1376, 1326, 1311, 1293, 1278, 1215, 1180, 1170, 1144, 1105, 1088, 1029, 1019, 983, 957, 932, 907, 868, 847, 790, 777, 765, 745, 731, 714 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.34 (s, 1H), 8.07 (d, 2H, J = 8.8 Hz), 7.57 (d, 2H, J = 8.8 Hz), 7.25−7.37 (m, 3H), 7.07 (d, 2H, J = 8.4 Hz), 3.14 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.6, 142.1, 136.9, 136.5, 132.2., 131.8, 131.4, 130.5, 129.4, 128.6. 44.7 ppm. Anal. Calcd for $C_{15}H_{13}NO_4S$: C, 59.39; H, 4.32; N, 4.62; S, 10.57. Found: C, 59.48; H, 4.22; N, 4.71; S, 10.41.

(*E*)-2-[4′-(Methylsulfonyl)phenyl]-1-nitro-1-phenylethene (11k). Yellow crystals (EtOH): general method #3 (95% yield); mp 152−153 °C; R_f (1:1 CH_2Cl_2/petroleum ether) = 0.09; IR (ATR, neat) 2929, 1658, 1596, 1520, 1409, 1322, 1300, 1213, 1189, 1145, 1088, 950, 917, 867, 832, 760, 729, 706 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.19 (s, 1H), 7.79 (d, 2H, J = 8.6 Hz), 7.50−7.55 (m, 3H), 7.27−7.33 (m, 4H), 3.02 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6, 141.9, 137.0, 132.3, 131.7, 131.0, 130.7, 129.73, 129.65, 127.9, 44.5 ppm. Anal. Calcd for $C_{15}H_{13}NO_4S$: C, 59.39; H, 4.32; N, 4.62; S, 10.57. Found: C, 59.32; H, 4.24; N, 4.72; S, 10.58.

(*E*)-1-(4′-Nitrophenyl)-1-nitro-2-phenylethene (11m).[65] Light yellow crystals (EtOH): general method #1 (36% yield); general method #2 (0% yield); mp 116−118 °C (lit.[65] mp 117.5−118 °C); R_f (1:1 CH_2Cl_2/petroleum ether) = 0.38; IR (ATR, neat) 1648, 1601, 1519, 1446, 1349, 1313, 1287, 1212, 979, 958, 934, 832, 776, 754, 720, 689 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (s, 1H), 8.33 (d, 2H, J = 8.8 Hz), 7.54 (d, 2H, J = 8.8 Hz), 7.35−7.37 (m, 1H), 7.24−7.28 (m, 2H), 7.07 (d, 2H, J = 8.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 147.3, 137.3, 137.0, 132.3, 131.8, 131.3, 130.5, 129.3, 124.6 ppm.

(*E*)-1-(3′-Nitrophenyl)-1-nitro-2-phenylethene (11n).[65] Light yellow crystals (EtOH): general method #1 (12% yield); general method #2 (52% yield); mp 106−107 °C (lit.[65] mp 107−108 °C); R_f (1:1 CH_2Cl_2/petroleum ether) = 0.50; IR (ATR, neat) 1650, 1614, 1527, 1515, 1489, 1446, 1347, 1321, 1288, 1182, 985, 943, 882, 815, 789, 775, 758, 720 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38−8.40 (m, 1H), 8.38 (s, 1H), 8.24 (s, 1H), 7.68−7.70 (m, 2H), 7.35−7.39 (m, 1H), 7.25−7.29 (m, 2H), 7.09 (d, 2H, J = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 147.1, 137.2, 137.1, 132.5, 131.8, 131.4, 130.6, 130.5, 129.4, 126.3, 125.2 ppm. Anal. Calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.00; H, 3.64; N, 10.33.

General Method. Synthesis of Pyrrole-2-carboxamides 8. A modification of our previously reported literature procedure was followed.[19] To a 0 °C stirred solution of **12** (1.5 mmol), DBU (1.5 mmol), and *i*-PrOH (1.5 mmol) in inhibitor-free THF[46] (15 mL) was added a solution of **11** (1.0 mmol) in THF (15 mL) dropwise via addition funnel. The yellow solution stirred at 0 °C for 30 min then at rt until analysis by TLC showed complete conversion of the starting material **11** (usually 6−24 h). The solvent was removed in vacuo, giving a crude oil or solid. Purification by flash column chromatography (ethyl acetate/petroleum ether gradient) then gave pyrrole-2-carboxamides **8**. The TLC plates used in the analysis were visualized with UV and then by staining with I_2 (the latter is necessary to observe unreacted **12**). Recrystallization then gave analytically pure samples.

***N*-Methoxy-*N*-methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxamide (8a).**[19] White crystals (EtOH): 87% yield; mp 163−164 °C (lit.[19] mp 137−140 °C); R_f (2:1 ethyl acetate/petroleum ether) = 0.36; IR (ATR, neat) 3240, 1612, 1599, 1526, 1481, 1427, 1393, 1228, 1186, 1080, 1018, 971, 941, 912, 866, 784, 747 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.62 (br s, 1H), 7.14−7.30 (m, 8H), 7.04 (d, 1H, J = 3.2 Hz), 7.01 (d, 2H, J = 8.4 Hz), 3.58 (s, 3H), 3.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.1, 135.5, 135.0, 130.6, 128.8, 128.4, 128.2, 128.1, 127.0, 126.2, 126.0, 121.7, 119.5, 61.2, 35.0 ppm.

***N*-Methoxy-3-(4′-methoxyphenyl)-*N*-methyl-4-phenyl-1*H*-pyrrole-2-carboxamide (8b).** White crystals (EtOH): 89% yield; mp 141−142 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.22; IR (ATR, neat) 3331, 1649, 1600, 1529, 1476, 1462, 1421, 1387, 1288, 1239, 1180, 1125, 1035, 1018, 970, 936, 867, 845, 769, 749, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.43 (br s, 1H), 7.10−7.22 (m, 7H), 7.04 (d, 1H, J = 3.1 Hz), 6.84 (d, 2H, J = 9.0 Hz), 3.81 (s, 3H), 3.63 (s, 3H), 3.05 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.2, 158.7, 135.1, 131.6, 128.7, 128.4, 128.0, 127.6, 126.2, 125.9, 121.5, 119.5, 113.7, 61.3, 55.4, 35.1 ppm. Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.15; H, 6.06; N, 8.26.

***N*-Methoxy-*N*-methyl-3-(4′-(methylthio)phenyl)-4-phenyl-1*H*-pyrrole-2-carboxamide (8c).** Tan crystals (ethyl acetate): 79% yield; mp 137−139 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.19; IR (ATR, neat) 3200, 1638, 1605, 1490, 1472, 1436, 1377, 1226, 1100, 1069, 1027, 958, 932, 861, 821, 768, 741, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.48 (br s, 1H), 7.08−7.23 (m, 9H), 7.04 (d, 1H, J = 3.1 Hz), 3.63 (s, 3H), 3.09 (s, 3H), 2.48 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.9, 136.8, 134.9, 132.1, 131.0, 128.8, 128.5, 128.0, 126.3, 126.2, 126.0, 121.5, 119.5, 61.4, 34.8, 16.0 ppm. Anal. Calcd for $C_{20}H_{20}N_2O_2S$: C, 68.16; H, 5.72; N, 7.95; S, 9.10 Found: C, 68.37; H, 5.62; N, 8.08; S, 8.87.

***N*-Methoxy-4-(4′-methoxyphenyl)-*N*-methyl-3-phenyl-1*H*-pyrrole-2-carboxamide (8d).** White crystals (EtOH): 89% yield; mp 142−144 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.18; IR (ATR, neat) 3183, 2966, 1605, 1577, 1559, 1534, 1488, 1457, 1436, 1426, 1391, 1281, 1242, 1173, 1139, 1101, 1079, 1025, 1005, 993, 963, 941, 918, 871,

830, 776, 754, 718, 698 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.54 (br s, 1H), 7.20−7.27 (m, 5H), 7.01 (d, 2H, J = 8.8 Hz), 7.00 (d, 1H, J = 2.9 Hz), 6.72 (d, 2H, J = 9.0 Hz), 3.74 (s, 3H), 3.58 (s, 3H), 3.00 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.1, 158.2, 136.0, 130.6, 129.8, 128.2, 128.0, 127.4, 126.9, 125.6, 121.5, 119.1, 113.8, 61.2, 55.4, 34.9 ppm. Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.52; H, 5.89; N, 8.48.

***N*-Methoxy-*N*-methyl-4-(4′-(methylthio)phenyl)-3-phenyl-1*H*-pyrrole-2-carboxamide (8e).** White crystals (ethyl acetate): 78% yield; mp 153−154 °C; R_f = 0.19 (1:1 ethyl acetate/petroleum ether); IR (ATR, neat) 3233, 2923, 1623, 1600, 1557, 1541, 1522, 1473, 1424, 1381, 1264, 1176, 1145, 1087, 1075, 1023, 972, 937, 863, 839, 817, 757, 739, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.60 (br s, 1H), 7.20−7.31 (m, 5H), 7.00−7.09 (m, 4H), 7.03 (d, 1H, J = 2.8 Hz), 3.58 (s, 3H), 3.02 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 135.9, 135.4, 132.0, 130.5, 129.1, 128.3, 127.9, 127.0, 126.7, 125.3, 121.7, 119.5, 61.2, 35.0, 16.2 ppm. Anal. Calcd for $C_{20}H_{20}N_2O_2S$: C, 68.16; H, 5.72; N, 7.95; S, 9.10. Found: C, 68.25; H, 5.76; N, 7.97; S, 9.03.

4-(4′-Fluorophenyl)-*N*-methoxy-*N*-methyl-3-phenyl-1*H*-pyrrole-2-carboxamide (8f). White crystals (ethyl acetate): 69% yield; mp 152−153 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.24; IR (ATR, neat) 3221, 3007, 2936, 2160, 1625, 1602, 1552, 1529, 1504, 1480, 1602, 1552, 1529, 1504, 1480, 1443, 1473, 1386, 1302, 1274, 1220, 1179, 1165, 1144, 1100, 1090, 1079, 1019, 999, 972, 939, 920, 867, 840, 814, 778, 756, 720, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.72 (br s, 1H), 7.26−7.30 (m, 3H), 7.19−7.21 (m, 2H), 7.01−7.06 (m, 3H), 6.86−6.90 (m, 2H), 3.59 (s, 3H), 3.02 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 161.7 (d, J_{C-F} = 245 Hz), 135.3, 131.0 (d, J_{C-F} = 3.8 Hz), 130.5, 130.2 (d, J_{C-F} = 7.5 Hz), 128.3, 127.9, 127.1, 125.0, 121.7, 119.4, 115.3 (d, J_{C-F} = 21 Hz), 61.2, 35.0 ppm. Anal. Calcd for $C_{19}H_{17}FN_2O_2$: C, 70.36; H, 5.28; N, 8.64. Found: C, 70.08; H, 5.42; N, 8.40.

4-(4′-Chlorophenyl)-*N*-methoxy-*N*-methyl-3-phenyl-1*H*-pyrrole-2-carboxamide (8g). White crystals (ethyl acetate): 66% yield; mp 175−176 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.23; IR (ATR, neat) 3315, 2937, 1639, 1599, 1823, 1437, 1438, 1420, 1381, 1323, 1227, 1180, 1136, 1094, 1068, 1016, 998, 967, 940, 912, 864, 798, 776, 762, 747, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.62 (br s, 1H), 7.09−7.28 (m, 9H), 7.06 (d, 2H, J = 2.8 Hz), 3.60 (s, 3H), 3.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.4, 135.5, 135.1, 130.5, 128.7, 128.3, 128.2, 127.7, 126.9, 126.1, 125.6, 121.7, 119.8, 61.1, 35.2 ppm. Anal. Calcd for $C_{19}H_{17}ClN_2O_2$: C, 66.96; H, 5.03; N, 8.22. Found: C, 66.83; H, 5.03; N, 8.26.

***N*-Methoxy-3,4-bis(4′-methoxyphenyl)-*N*-methyl-1*H*-pyrrole-2-carboxamide (8h).** White crystals (EtOH); 82% yield; mp 167−168 °C; R_f (2:1 ethyl acetate/petroleum ether) = 0.43; IR (ATR, neat) 3223, 1608, 1534, 1512, 1436, 1380, 1284, 1244, 1177, 1140, 1025, 1000, 971, 932, 877, 829, 817, 791, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.42 (br s, 1H), 7.14 (d, 2H, J = 8.8 Hz), 7.03 (d, 2H, J = 8.8 Hz), 6.98 (d, 1H, J = 2.9 Hz), 6.84 (d, 2H, J = 8.8 Hz), 6.75 (d, 2H, J = 8.8 Hz), 3.81 (s, 3H), 3.77 (s, 3H), 3.63 (s, 3H), 3.04 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 158.7, 158.2, 131.7, 129.8, 127.84, 127.76, 127.6, 125.6, 121.3, 119.1, 113.9, 61.3, 55.45, 55.41, 35.1 ppm. Anal. Calcd for $C_{21}H_{22}N_2O_4$: C, 68.84; H, 6.05; N, 7.65. Found: C, 68.64; H, 6.03; N, 7.76.

***N*-Methoxy-3,4-bis(4′-(methylthio)phenyl)-*N*-methyl-1*H*-pyrrole-2-carboxamide (8i).** White crystals (ethyl acetate); 75% yield; mp 169−170 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.16; IR (ATR, neat) 3274, 1617, 1559, 1519, 1472, 1423, 1382, 1321, 1259, 1188, 1146, 1103, 1088, 1031, 1015, 973, 934, 861, 834, 824, 813, 759, 738, 715 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.53 (br s, 1H), 7.09−7.17 (m, 6H), 7.01−7.03 (m, 3H), 3.62 (s, 3H), 3.08 (s, 3H), 2.49 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 136.9, 136.0, 132.1, 131.9, 131.0, 129.1, 127.6, 126.8, 126.3, 125.3, 121.6, 119.5, 61.3, 34.9, 16.2, 15.9 ppm. Anal. Calcd for $C_{21}H_{22}N_2O_2S_2$: C, 63.29; H, 5.56; N, 7.03; S, 16.09. Found: C, 63.06; H, 5.66; N, 6.86; S, 16.04.

***N*-Methoxy-*N*-methyl-4-(4′-(methylsulfonyl)phenyl)-3-phenyl-1*H*-pyrrole-2-carboxamide (8j).** White crystals (ethyl acetate); general method #3 (95% yield) from **8c**; modification of general method #4 (40% yield) that involved 1.0 equiv of isocyanide **12**, 1.2 equiv of nitroalkene **11j**, and 1.5 equiv of DBU; mp 203−205 °C; R_f (2:1 ethyl acetate/petroleum ether) = 0.29; IR (ATR, neat) 3360, 2927, 1644, 1595, 1548, 1492, 1474, 1416, 1376, 1313, 1291, 1279, 1156, 1126, 1089, 1005, 996, 957, 937, 864, 843, 799, 783, 753, 724, 703 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.80 (br s, 1H), 7.72 (d, 2H, J = 8.8 Hz), 7.19−7.32 (m, 7H), 7.14 (d, 1H, J = 3.1 Hz), 3.58 (s, 3H), 3.05 (s, 3H), 3.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.7, 141.1, 137.7, 134.8, 130.4, 129.0, 128.6, 128.3, 127.54, 127.48, 124.0, 122.4, 120.2, 61.3, 44.8, 34.7 ppm. Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29; S, 8.34; Found: C, 62.51; H, 5.14; N, 7.31; S, 8.60.

***N*-Methoxy-*N*-methyl-3-(4′-(methylsulfonyl)phenyl)-4-phenyl-1*H*-pyrrole-2-carboxamide (8k).** White crystals (EtOH); general method #3 (69% yield) from **8e**; general method #4 (65% yield); mp 202−203 °C; R_f (2:1 ethyl acetate/petroleum ether) = 0.17; IR (ATR, neat) 3275, 1603, 1548, 1471, 1435, 1383, 1302, 1147, 1088, 955, 937, 863, 835, 768, 695 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.76 (br s, 1H), 7.83 (d, 2H, J = 8.6 Hz), 7.44 (d, 2H, J = 8.6 Hz), 7.19−7.21 (m, 3H), 7.05 (d, 1H, J = 3.1 Hz), 7.01−7.03 (m, 2H), 3.69 (s, 3H), 3.23 (s, 3H), 3.07 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.9 141.9, 138.5, 134.1, 131.6, 128.8, 128.7, 127.9, 127.1, 126.7, 126.6, 121.5, 119.7, 61.9, 44.9, 33.9 ppm. Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29; S, 8.34; Found: C, 62.58; H, 5.32; N, 7.36; S, 8.29.

***N*-Methoxy-*N*-methyl-4-(4′-nitrophenyl)-3-phenyl-1*H*-pyrrole-2-carboxamide (8m).** Yellow crystals (EtOH); 64% yield; mp 219−220.5 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.23; IR (ATR, neat) 3213, 1592, 1499, 1430, 1393, 1330, 1148, 1079, 1013, 966, 938, 857, 758, 745, 727 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.86 (br s, 1H), 8.03 (d, 2H, J = 8.8 Hz), 7.31−7.35 (m, 3H), 7.18−7.22 (m, 4H), 7.16 (d, 1H, J = 3.2 Hz), 3.58 (s, 3H), 3.06 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 146.0, 142.3, 134.8, 130.4, 128.7, 128.6, 128.2, 127.6, 123.8, 123.7, 122.5, 120.4, 61.3, 34.7 ppm. Anal. Calcd for $C_{19}H_{17}N_3O_4$: C, 64.95; H, 4.88; N, 11.96; Found: C, 65.04; H, 4.77; N, 12.06.

***N*-Methoxy-*N*-methyl-4-(3′-nitrophenyl)-3-phenyl-1*H*-pyrrole-2-carboxamide (8n).** Yellow amorphous solid: 60% yield; mp 196−199 °C; R_f (2:1 ethyl acetate/petroleum ether) = 0.61; IR (ATR, neat) 3207, 1612, 1556, 1534, 1512, 1478, 1440, 1392, 1346, 1302, 1231, 1179, 1147, 1086, 1072, 1016, 1000, 974, 956, 915, 904, 864, 804, 778, 756, 734, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.78 (br s, 1H), 8.03−8.04 (m, 1H), 7.97−8.00 (m, 1H), 7.28−7.32 (m, 4H), 7.19−7.22 (m, 2H), 7.16 (d, 2H, J = 3.1 Hz), 3.59 (s, 3H), 3.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 148.5, 136.9, 134.7, 134.6, 130.4, 129.1, 128.6, 128.3, 127.5, 123.7, 123.1, 122.2, 121.0, 119.9, 61.3, 34.7 ppm. Anal. Calcd for $C_{19}H_{17}N_3O_4$: C, 64.95; H, 4.88; N, 11.96; Found: C, 64.67; H, 4.97; N, 11.85.

General Method. Synthesis of Pyrrole-2-carboxaldehydes 9. A modification of our previously reported literature procedure was followed.[19] To a 0 °C stirred solution of $LiAlH_4$ (1.5 mmol) in THF (5 mL) was added a solution of pyrrole-2-carboxamide **8** (1.0 mmol) in THF (5 mL) dropwise via addition funnel. The yellow reaction solution was stirred at 0 °C for 1 h. The reaction solution was diluted with ether (15 mL), and then 6.0 equiv of $KHSO_4$ (1.2 g, 8.4 mmol) in H_2O (15 mL) was added dropwise via addition funnel. The aqueous layer was extracted with ether (3 × 15 mL), and the combined organic layers were washed with 5% citric acid (50 mL), sat. $NaHCO_3$ (50 mL), and brine (50 mL) and then dried over Na_2SO_4. Removal of the solvent in vacuo

gave crude amorphous solids that were purified by flash column chromatography (ethyl acetate/petroleum ether gradient). In some cases, analytical samples were obtained by recrystallization.

3,4-Diphenyl-1*H*-pyrrole-2-carboxaldehyde (9a).[19] Brown-red amorphous solid: 72% yield; mp 169−170 °C (lit.[19] mp 168−172 °C); R_f (ethyl acetate) = 0.43; IR (ATR, neat) 3243, 3195, 2870, 1636, 1601, 1545, 1527, 1449, 1407, 1372, 1344, 1309, 1286, 1179, 1141, 1071, 1029, 1008, 940, 911, 793, 776, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.62 (br s, 1H), 9.46 (d, 1H, J = 1.0 Hz), 7.15−7.37 (m, 11H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 134.1, 133.9, 132.5, 130.9, 130.5, 128.69, 128.67, 128.63, 128.0, 126.82, 126.75, 124.1 ppm.

3-(4′-Methoxyphenyl)-4-phenyl-1*H*-pyrrole-2-carboxaldehyde (9b). Yellow-orange amorphous solid: 68% yield; mp 154−156 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.64; IR (ATR, neat) 3241, 1634, 1603, 1532, 1504, 1449, 1406, 1374, 1340, 1286, 1240, 1177, 1149, 1109, 1030, 1000, 913, 835, 804, 777, 760, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.84 (br s, 1H), 9.45 (d, 1H, J = 1.0 Hz), 7.17−7.28 (m, 8H), 6.90 (d, 2H, J = 8.8 Hz), 3.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 159.5, 134.2, 134.1, 132.0, 130.5, 128.7, 128.6, 126.7, 126.6, 124.5, 124.5, 114.2, 55.5 ppm; HRMS (ESI) calcd for $C_{18}H_{15}NO_2$: 278.1181 ($[M + H]^+$), found 278.1179 ($[M + H]^+$).

3-(4′-(Methylthio)phenyl)-4-phenyl-1*H*-pyrrole-2-carboxaldehyde (9c). Tan crystals (CH_2Cl_2/petroleum ether): 81% yield; mp 165−166 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.68; IR (ATR, neat) 3263, 2914, 2835, 1631, 1599, 1556, 1527, 1495, 1447, 1431, 1403, 1375, 1339, 1312, 1285, 1225, 1156, 1141, 1099, 1081, 1035, 1019, 1000, 985, 965, 953, 933, 910, 843, 815, 794, 763, 728, 711, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.80 (br s, 1H), 9.49 (s, 1H), 7.20 −7.29 (m, 10H), 2.54 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.6, 138.6, 134.0, 133.7, 131.3, 130.6, 129.1, 128.8, 128.7, 126.9, 126.7, 126.4, 124.5, 15.8 ppm. Anal. Calcd for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77; S, 10.93. Found: C, 73.54; H, 5.12; N, 4.86; S, 10.84.

4-(4′-Methoxyphenyl)-3-phenyl-1*H*-pyrrole-2-carboxaldehyde (9d). Off-white crystals (CH_2Cl_2/petroleum ether); 73% yield; mp 155−157 °C; R_f (1:4 ethyl acetate/petroleum ether) = 0.17; IR (ATR, neat) 3246, 2967, 1633, 1548, 1526, 1505, 1479, 1456, 1442, 1443, 1400, 1370, 1341, 1291, 1276, 1243, 1175, 1057, 1032, 940, 833, 821, 772, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.96 (br s, 1H), 9.45 (s, 1H), 7.30−7.37 (m, 5H), 7.22 (d, 1H, J = 2.4 Hz), 7.08 (d, 2H, J = 8.8 Hz), 6.79 (d, 2H, J = 8.8 Hz), 3.78 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 158.6, 134.1, 132.7, 130.9, 130.5, 129.7, 128.6, 127.9, 126.43, 126.39, 124.1, 114.1, 55.5 ppm; HRMS (ESI) calcd for $C_{18}H_{15}NO_2$: 278.1181 ($[M + H]^+$), found 278.1180 ($[M + H]^+$).

4-(4′-(Methylthio)phenyl)-3-phenyl-1*H*-pyrrole-2-carboxaldehyde (9e). Brownish-red amorphous solid: 72% yield; mp 191−192 °C; R_f (1:4 ethyl acetate/petroleum ether) = 0.24; IR (ATR, neat) 3231, 2922, 2872, 1628, 1600, 1538, 1522, 1498, 1474, 1456, 1440, 1416, 1392, 1372, 1338, 1312, 1301, 1278, 1220, 1188, 1146, 1102, 1084, 1071, 1016, 1006, 963, 938, 918, 837, 815, 787, 773, 742, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.22 (br s, 1H), 9.44 (s, 1H), 7.35−7.39 (m, 3H), 7.30−7.33 (m, 2H), 7.26−7.28 (m, 1H), 7.13 (d, 2H, J = 8.8 Hz), 7.08 (d, 2H, J = 8.8 Hz), 2.46 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 136.7, 134.3, 132.5, 130.9, 130.8, 130.6, 128.9, 128.7, 128.0, 126.7, 126.1, 124.6, 16.0 ppm; HRMS (ESI) calcd for $C_{18}H_{15}NOS$: 294.0953 ($[M + H]^+$), found 294.0952 ($[M + H]^+$).

4-(4′-Fluorophenyl)-3-phenyl-1*H*-pyrrole-2-carboxaldehyde (9f). Orange-red amorphous solid: 70% yield; 185−186 mp °C; R_f (1:3 ethyl acetate/petroleum ether) = 0.56; IR (ATR, neat) 3269, 3062, 2925, 1678, 1627, 1604, 1577, 1547, 1526, 1504, 1478, 1455, 1442, 1420, 1393, 1366, 1338, 1301, 1275, 1220, 1162, 1139, 1095, 1069, 1007, 993, 940, 915, 849, 832, 789, 765, 734, 720, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.26 (br s, 1H), 9.44 (d, 1H, J = 1.0 Hz), 7.34−7.38 (m, 3H), 7.27−7.30 (m, 2H), 7.25 (dd, 1H, J = 1.0, 3.0 Hz), 7.08−7.13 (m, 2H), 6.90−6.96 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 162.0 (d, J_{C-F} = 246 Hz), 134.4, 132.4, 130.9, 130.5, 130.2 (d, J_{C-F} = 8.2 Hz), 130.0 (d, J_{C-F} = 3.8 Hz), 128.7, 128.1, 125.7, 124.6, 115.6 (d, J_{C-F} = 20.9 Hz) ppm; HRMS (ESI) calcd for $C_{17}H_{12}FNO$: 266.0981 ($[M + H]^+$), found 266.0978 ($[M + H]^+$).

4-(4′-Chlorophenyl)-3-phenyl-1*H*-pyrrole-2-carboxaldehyde (9g). Off-white amorphous solid: 82% yield; mp 169−170 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.71; IR (ATR, neat) 3250, 1633, 1542, 1443, 1417, 1389, 1335, 1144, 1087, 1013, 918, 840, 818, 789, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.06 (br s, 1H), 9.46 (d, 1H, J = 1.0 Hz), 7.27−7.39 (m, 6H), 7.21 (d, 2H, J = 8.5 Hz), 7.09 (d, 2H, J = 8.5 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 134.3, 132.7, 132.5, 130.8, 130.6, 129.8, 128.9, 128.8, 128.1, 125.5, 124.4 ppm. Anal. Calcd for $C_{17}H_{12}ClNO$: C, 72.47; H, 4.29; Cl, 12.58; N, 4.97. Found: C, 72.25; H, 4.37; N, 4.78.

3,4-Bis(4′-methoxyphenyl)-1*H*-pyrrole-2-carboxaldehyde (9h).[47,66] Yellow amorphous solid: 63% yield; mp 175−176 °C; R_f (1:5 ethyl acetate/petroleum ether) = 0.13; IR (ATR) 3292, 3031, 2935, 2833, 1722, 1635, 1609, 1573, 1536, 1509, 1487, 1456, 1443, 1423, 1394, 1371, 1331, 1307, 1285, 1250, 1236, 1176, 1138, 1110, 1087, 1031, 1016, 998, 960, 935, 837, 824, 814, 803, 776, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.57 (br s, 1H), 9.44 (d, 1H, J = 1.0 Hz), 7.22 (d, 2H, J = 8.8 Hz), 7.18 (dd, 1H, J = 1.0, 3.0 Hz), 7.09 (d, 2H, J = 8.8 Hz), 6.90 (d, 2H, J = 8.8 Hz), 6.80 (d, 2H, J = 8.8 Hz), 3.84 (s, 3H), 3.79 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.6, 159.5, 158.6, 133.8, 132.0, 130.4, 129.7, 126.5, 126.3, 124.8, 123.9, 114.15, 114.11, 55.54, 55.49 ppm; HRMS (ESI) calcd for $C_{19}H_{17}NO_3$: 308.1286 ($[M + H]^+$), found 308.1287 ($[M + H]^+$).

4-(4′-(Methylsulfonyl)phenyl)-3-phenyl-1*H*-pyrrole-2-carboxaldehyde (9j). Off-white crystals (CH_2Cl_2): 71% yield; mp 189−190 °C; R_f (1:1 ethyl acetate/petroleum ether) = 0.27; IR (ATR, neat) 3245, 2844, 1641, 1596, 1545, 1442, 1419, 1391, 1374, 1340, 1303, 1286, 1141, 1095, 1084, 966, 956, 939, 841, 774, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.61 (br s, 1H), 9.47 (d, 1H, J = 1.0 Hz), 7.79 (d, 2H, J = 8.6 Hz), 7.29−7.41 (m, 8H), 3.05 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 139.9, 138.3, 134.4, 131.8, 130.9, 130.8, 129.0, 128.9, 128.5, 127.8, 124.8, 124.6, 44.8 ppm; HRMS (ESI) calcd for $C_{18}H_{15}NO_3S$: 326.0851 ($[M + H]^+$), found 326.0848 ($[M + H]^+$).

3-(4′-(Methylsulfonyl)phenyl)-4-phenyl-1*H*-pyrrole-2-carboxaldehyde (9k). White amorphous solid: 64% yield; mp 240−241 °C; R_f (1:2 ethyl acetate/petroleum ether) = 0.18; IR (ATR, neat) 3267, 3002, 2920, 2859, 1643, 1597, 1541, 1449, 1402, 1367, 1338, 1295, 1277, 1183, 1141, 1092, 1018, 999, 969, 937, 928, 842, 779, 748, 719, 707 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.60 (br s, 1H), 9.36 (d, 1H, J = 0.8 Hz), 7.90 (d, 2H, J = 8.4 Hz), 7.52−7.58 (m, 3H), 7.10−7.28 (m, 5H), 3.26 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 179.3, 139.5, 138.3, 133.5, 131.2, 130.2, 130.1, 128.5, 128.1, 126.9, 126.4, 125.5, 125.1, 43.4 ppm; HRMS (ESI) calcd for $C_{18}H_{15}NO_3S$: 326.0851 ($[M + H]^+$), found 326.0854 ($[M + H]^+$).

General Method #12. Synthesis of 3-Pyrrolin-2-ones 10. A modification of our previously reported literature procedure was followed.[19] To a rt stirred mixture of pyrrole-2-carboxaldehyde **9** (1.0 mmol) in MeOH (20 mL) was added $NaHCO_3$ (10.0 mmol) followed by H_2O_2 (35% w/v, 9.7 mL, 100 mmol). The solution was stirred at rt for 24−72 h until analysis by TLC showed complete conversion of the starting material **9**. In some cases, additional hydrogen peroxide was added. The reaction mixture was treated with CH_2Cl_2 (20 mL) and aqueous HCl (1.0 M, 20 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 10 mL). The combined organic layers were dried with sodium sulfate. Removal of the solvent in vacuo gave a crude solid that was purified by flash chromatography (ethyl acetate/petroleum ether to ethyl acetate/MeOH gradient). In some cases, analytical samples were obtained by recrystallization.

3,4-Diphenyl-1*H*-pyrrol-2(5*H*)-one (10a).[19] White powder: 91% yield; mp 185−187 °C (lit.[19] mp 182−183 °C); R_f (ethyl acetate) = 0.43; IR

(ATR, neat) 3171, 3053, 1679, 1572, 1487, 1443, 1366, 1337, 1223, 1086, 1030, 973, 889, 786, 763, 743, 688 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.54 (br s, 1H), 7.26−7.35 (m, 10H), 4.37 (d, 2H, J = 1.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 150.4, 133.3, 132.3, 131.7, 129.3, 129.0, 128.6, 128.2, 127.7, 127.6, 47.5 ppm.

3-(4′-Methoxyphenyl)-4-phenyl-1*H*-pyrrol-2(5*H*)-one (10b). Opaque, white amorphous solid: 90% yield; mp 176−177 °C; R_f (4:1 ethyl acetate/petroleum ether) = 0.22; IR (ATR, neat) 3167, 3057, 2921, 2846, 1679, 1606, 1572, 1510, 1446, 1370, 1290, 1246, 1177, 1110, 1032, 974, 891, 829, 781, 763 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 8.46 (s, 1H), 7.33 (s, 5H), 7.22 (d, 2H, J = 8.8 Hz), 6.90 (d, 2H, J = 8.8 Hz), 4.32 (s, 2H), 3.75 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.6, 158.8, 149.3, 133.7, 131.1, 130.6, 128.9, 128.6, 127.5, 124.3, 113.7, 55.0, 47.5 ppm; HRMS (ESI) calcd for $C_{17}H_{15}NO_2$: 266.1181 ($[M + H]^+$), found 266.1179 ($[M + H]^+$).

4-(4′-Methoxyphenyl)-3-phenyl-1*H*-pyrrol-2(5*H*)-one (10d).[20a] Opaque, white amorphous solid: 90% yield; mp 155−157 °C (lit.[20b] mp 169−174 °C); R_f (4:1 ethyl acetate/petroleum ether) = 0.33; IR (ATR, neat) 3167, 3053, 1678, 1607, 1514, 1455, 1416, 1365, 1298, 1254, 1175, 1117, 1079, 1023, 891, 829, 786, 744, 699 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.42 (br s, 1H), 7.24−7.38 (m, 7H), 6.88 (d, 2H, J = 8.8 Hz), 4.34 (s, 2H), 3.74 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.7, 159.8, 150.0, 132.8, 130.2, 129.4, 129.0, 128.3, 127.6, 125.5, 114.1, 55.2, 47.4 ppm.

4-(4′-Fluorophenyl)-3-phenyl-1*H*-pyrrol-2(5*H*)-one (10f). Light yellow amorphous solid: 66% yield; mp 196−198 °C (lit.[20a] 204−207 °C); R_f (1:1 ethyl acetate/petroleum ether) = 0.24; IR (ATR, neat) 3176, 3060, 2924, 2851, 1680, 1603, 1511, 1493, 1454, 1442, 1408, 1363, 1342, 1226, 1161, 1105, 1079, 1059, 1014, 974, 835, 787, 744, 700 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) d 8.57 (br s, 1H), 7.18−7.39 (m, 9H), 4.36 (d, 2H, J = 1.0 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 162.2 (d, J_{C-F} = 247 Hz), 149.3, 132.2, 131.7, 129.81 (d, J_{C-F} = 8.2 Hz), 129.80, 129.3, 128.3, 127.8, 115.6 (d, J_{C-F} = 22 Hz), 47.5 ppm.

4-(4′-Chlorophenyl)-3-phenyl-1*H*-pyrrol-2(5*H*)-one (10g).[48b] White crystals (EtOH): 73% yield; mp 210−212 °C; R_f (4:1 ethyl acetate/petroleum ether) = 0.28; IR (ATR, neat) 3187, 3059, 2850, 1680, 1592, 1498, 1488, 1443, 1401, 1366, 1340, 1223, 1090, 1059, 1012, 974, 890, 825, 787, 742, 725 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.58 (br s, 1H), 7.26−7.42 (m, 9H), 4.36 (s, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.2, 149.2, 133.6, 132.3, 132.2, 132.0, 129.4, 129.3, 128.7, 128.3, 127.9, 47.4 ppm; HRMS (ESI) calcd for $C_{16}H_{12}ClNO$: 270.0686 ($[M + H]^+$), found 270.0687 ($[M + H]^+$).

3,4-bis(4′-Methoxyphenyl)-1*H*-pyrrol-2(5*H*)-one (10h). Bright yellow powder: 72% yield (based on recovered starting material); mp 213-216 °C; R_f (ethyl acetate) = 0.32; IR (ATR, neat) 3171, 3054, 2957, 2933, 2907, 2838, 1672, 1602, 1570, 1516, 1504, 1439, 1416, 1365, 1342, 1302, 1286, 1248, 1226, 1172, 1116, 1107, 1086, 1023, 975, 893, 839, 824, 799, 789, 779, 747, 720 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.38 (br s, 1H), 7.28 (d, 2H, J = 8.8 Hz), 7.22 (d, 2H, J = 8.8 Hz), 6.92 (d, 2H, J = 9.0 Hz), 6.89 (d, 2H, J = 9.0 Hz), 4.29 (s, 2H), 3.76 (s, 3H), 3.74 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.9, 159.7, 158.7, 149.0, 130.6, 129.7, 128.9, 125.8, 124.7, 114.1, 113.7, 55.2, 55.0, 47.3 ppm; HRMS (ESI) calcd for $C_{18}H_{17}NO_3$: 296.1287 ($[M + H]^+$), found 296.1284 ($[M + H]^+$).

4-(4′-(Methylsulfonyl)phenyl)-3-phenyl-1*H*-pyrrol-2(5*H*)-one (10j).[20a] White amorphous solid; 81% yield; mp 203−204 °C (lit.[20a] 197−200 °C); R_f (ethyl acetate) = 0.16; IR (ATR, neat) 3452, 3178, 3056, 2994, 2917, 1677, 1633, 1596, 1564, 1490, 1446, 1403, 1362, 1336, 1302, 1284, 1225, 1181, 1147, 1089, 1060, 1032, 1021, 960, 918, 889, 838, 789, 769, 737, 715 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.70 (br s, 1H), 7.87 (d, 2H, J = 8.6 Hz), 7.56 (d, 2H, J = 8.6 Hz), 7.26−7.38 (m, 5H), 4.42 (s, 2H), 3.23 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.9, 148.7, 140.7, 138.5, 133.9, 131.6, 129.3, 128.5, 128.4, 128.1, 127.2, 47.5, 43.2 ppm.

3-(4′-(Methylsulfonyl)phenyl)-4-phenyl-1*H*-pyrrol-2(5*H*)-one (10k). Yellow amorphous solid; 5% yield; R_f (ethyl acetate) = 0.18; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J = 8.8 Hz), 7.62 (d, 2H, J = 8.8 Hz), 7.30−7.40 (m, 3H), 7.24−7.26 (m, 2H), 6.40 (br s, 1H), 4.43 (d, 2H, J = 1.2 Hz), 3.06 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 153.4, 140.0, 137.8, 132.5, 130.8, 130.7, 130.4, 129.4, 127.88, 127.86, 48.5, 44.8 ppm; HRMS (ESI) calcd for $C_{17}H_{15}NO_3S$: 314.0851 ($[M + H]^+$), found 314.0850 ($[M + H]^+$).

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and spectral data for all other compounds mentioned in the manuscript and copies of ^1H NMR spectra and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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