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An Expedient, Direct, Three-Component Approach for the Synthesis of 4-Thioarylpyrroles

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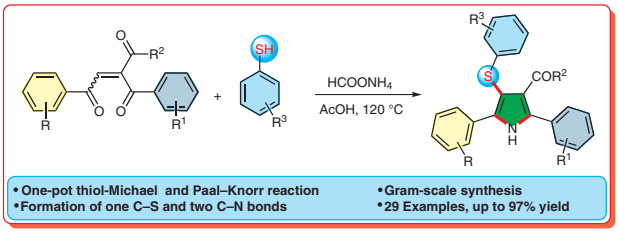

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Abstract A three-component strategy for the synthesis of 4-thioarylpyrroles from 1,4-enediones, thiols, and ammonium formate in one-pot has been developed. The reaction proceeds through the sequential thiol-Michael/Paal–Knorr reaction of 1,4-enediones with the formation of one new C–S and two C–N bonds. The operationally simple protocol provides direct access to the highly functionalized 4-thioarylpyrroles with free-NH in good to excellent yields. The synthetic application of resulting 4-thioarylpyrroles was demonstrated by oxidation of the sulfur atom to the corresponding sulfoxide and sulfone.

Key words metal-free synthesis, 1,4-enediones, 4-thioarylpyrroles, thiol-Michael reaction, C–S bond formation

Pyrrole is a prominent heterocyclic motif that is found extensively in numerous natural products, bioactive drug molecules, and functional organic materials.[1] Its derivatives exhibit a broad range of biological action such as antibacterial, antifungal, anti-inflammatory, and anticancer activities.[2–3] For instance, Atorvastatin[4a–d] is a pyrrole-based top-selling drug molecule that is widely used as a cholesterol-lowering agent that acts by inhibiting HMG-CoA reductase. Interestingly, the corresponding 4-sulfamoyl pyrroles[4e] also display potential activity as antihypolipidemic agents, which illustrates the importance of sulfur substitution in diversifying the statins (Figure 1).

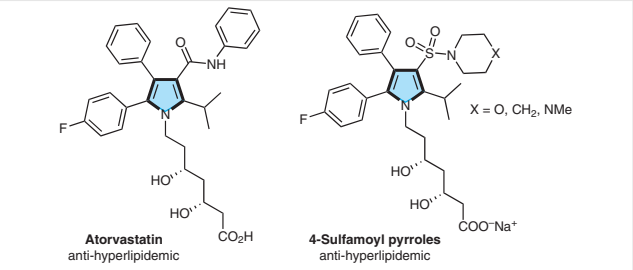

Figure 1 Representative examples of pyrrole-containing bioactive molecules

Owing to the prominence of these molecules, the development of efficient and practical protocols for the construction of highly functionalized pyrrole rings has been an attractive area of research. In general, classical methods such as Hantzsch, Knorr, and Paal–Knorr are widely used for the synthesis of pyrroles.[5] However, these methods offer limited access to pyrrole ring with different functionalities because of the restricted availability of starting materials. Over the past decades, a variety of elegant methods have been developed for the synthesis of pyrroles, which include transition-metal-mediated reactions,[6] multicomponent coupling reactions,[7] and cycloaddition reactions.[8] Recently, iodine-mediated synthetic transformations have emerged as a potential tool for the construction of various heterocyclic systems.[9] In this context, various research groups have reported the iodine-mediated synthesis of polysubstituted pyrroles from readily available substrates.[10] Very recently, Gandon and Sahoo demonstrated the use of yne-ynamides as precursors for the synthesis of 4-sulfinylated pyrroles[11a] and 4-thioarylpyrroles[11b] via Au(I)-catalyzed cycloisomerization and sulfur radical-triggered cyclization approaches, respectively (Scheme 1a). However, these methods involve multistep synthesis of starting materials. Herein, we describe a new approach to synthesize 4-thioarylpyrroles through the combination of thiol-Michael and Paal–Knorr reactions of 1,4-enediones (Scheme 1b).

On the other hand, the reduction followed by Paal–Knorr cyclization of methylthio-substituted 1,4-enediones was observed for the synthesis of methylthio-substituted pyrroles.[11c] Furthermore, the prevalence of organosulfur compounds in bioactive molecules and pharmaceuticals has inspired the scientific community to develop valuable

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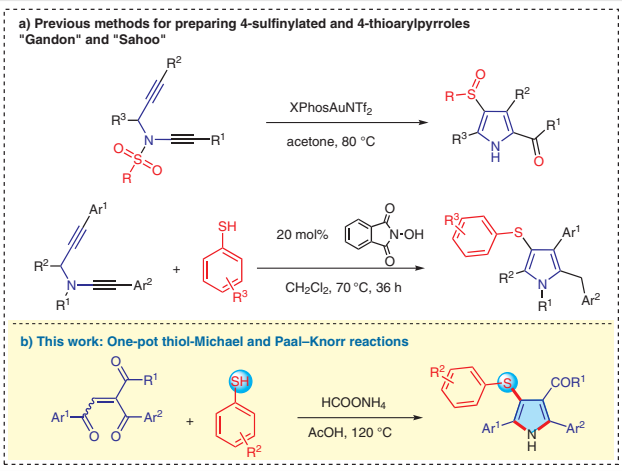
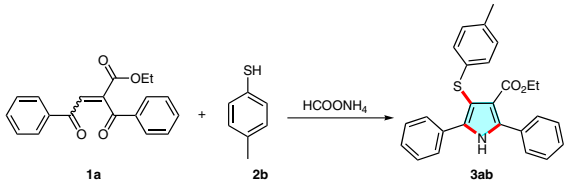


Scheme 1 Methods for the synthesis of polysubstituted pyrroles

new synthetic routes to access these compounds.[12] During the last decade, transition-metal-catalyzed coupling reactions have become efficient tools to build C–S bonds and they are utilized extensively in the synthesis of valuable products.[13] To avoid use of metal catalyst and to construct C–S bonds, recently, iodine-mediated sulfenylation of electron-rich aromatic systems such as indoles, benzofurans, pyrazolones, naphthols, and naphthylamines have been developed by using sulfonyl hydrazides as sulfenylating agents.[14] Despite the advances made, most of these methods have shortcomings such as substrate availability or they are limited to electron-rich systems. Thus, the development of an alternative route for the construction of aryl thioethers is highly desirable. In this perspective, here, we report a practical route for the synthesis of 4-thioarylpyrroles from readily accessible starting materials such as 1,4-enediones and thiols under metal-free reaction conditions (Scheme 1b).

We started by examining the reaction conditions for the formation of 4-thioarylpyrrole **3ab** with the model substrates 1,4-enedione **1a** and thiol **2b**, with ammonium formate as nitrogen source (Table 1). The initial attempt at the formation 4-thioarylpyrrole **3ab** was unsuccessful when the reaction was carried out in toluene at 110 °C for 24 h. However, we achieved a satisfactory yield of 85% of the desired product **3ab** when we performed the reaction in a mixture of toluene/AcOH (2:1) as solvent (entry 2). Furthermore, the yield of the reaction was enhanced to 92% when the reaction was carried out in acetic acid as the sole solvent at 120 °C for 24 h (entry 3). The screening of other acids such as formic acid (HCOOH), trifluoroacetic acid (TFA) and trifluoromethanesulfonic acid (CF_3SO_3H) as reaction solvent for the present transformation was not efficient (entries 4–6). Decreasing the temperature of the reaction or reducing the amount of ammonium formate resulted in lower yields (entries 7 and 8).

Table 1 Optimization of Reaction Conditions[a]



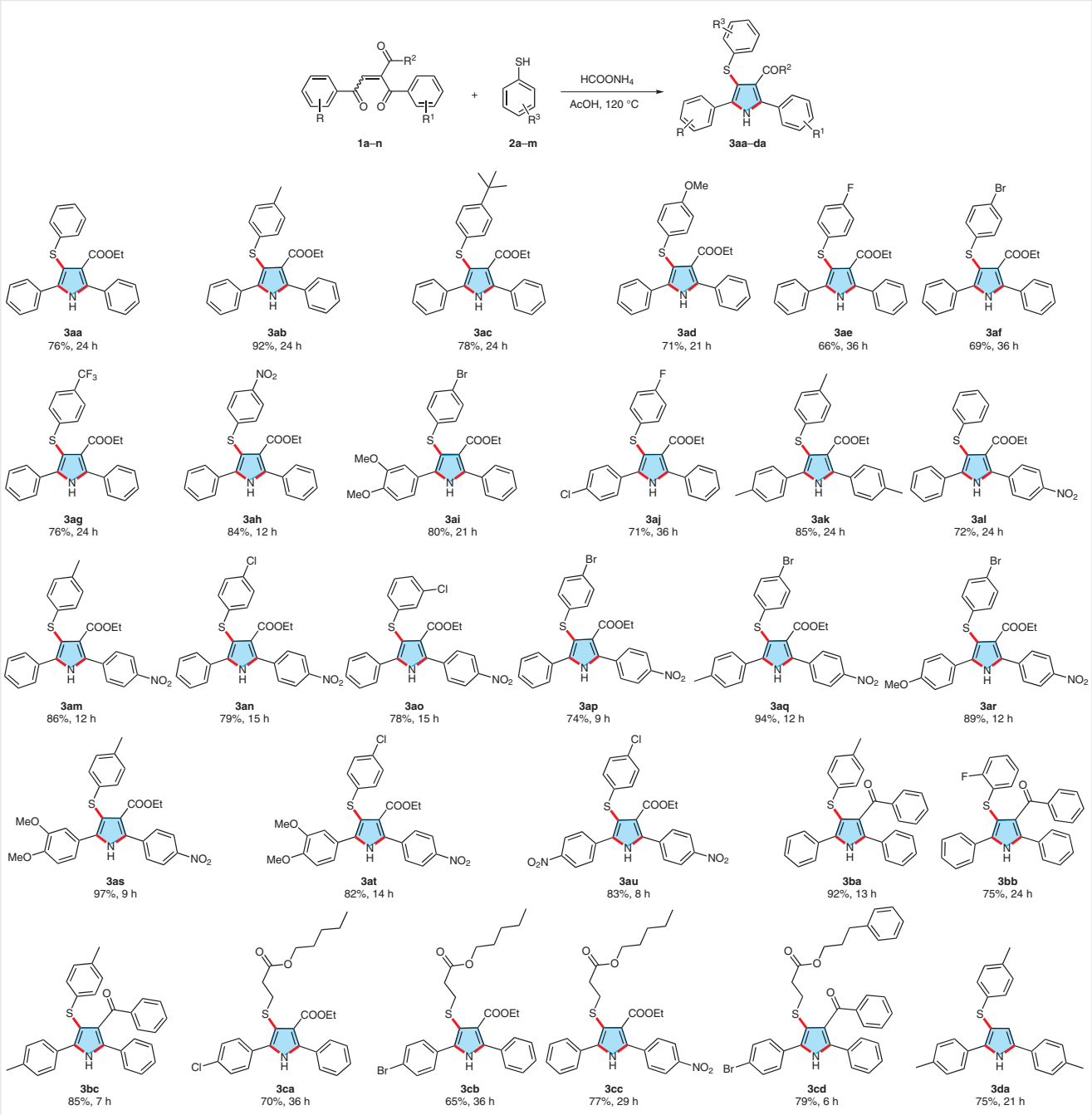
Entry	Solvent (mL)	Temp (°C)	Time (h)	Yield (%)[b]
1	toluene	110	24	trace
2	toluene/AcOH (2:1)	120	18	85
3	AcOH	120	24	92
4	HCOOH	120	42	26
5	TFA	120	36	68
6	CF_3SO_3H	120	36	0
7	AcOH	100	48	83
8	AcOH	120	48	76[c]

[a] Reaction conditions: **1a** (100 mg, 0.324 mmol), **2b** (44 mg, 0.356 mmol), $HCOONH_4$ (51 mg, 0.811 mmol), solvent (2 mL), sealed tube.
[b] Isolated yield.
[c] Ammonium formate (1 equiv) was used.

After the optimal reaction conditions for the formation of 4-thioarylpyrrole had been established, the scope and generality of this protocol were explored. As shown in Scheme 2, numerous 4-thioarylpyrroles were synthesized in good to high yields by treating various 1,4-enediones with thiols under the standard reaction conditions. Initially, we employed simple 1,4-enedione **1a** to react with various thiols bearing different substituents. The electron-donating groups on the thiols such as **2a–d** underwent reaction with **1a** to afford 4-thioarylpyrroles **3aa–ad** in 71–92% yields. The thiols equipped with halogen substitutions also reacted efficiently to produce the corresponding products **3ae–af** in good yields (66–69%). It is noteworthy that the reaction proceeded smoothly in the case of thiols bearing strong electron-withdrawing groups such as trifluoromethyl (CF_3) and nitro (NO_2), to give the desired products **3ag–ah** in 76 and 85% yield, respectively. 1,4-Enedione **1b**, containing a dimethoxy group, reacted efficiently to afford the product **3ai** in 80% yield. Next, 1,4-enedione **1c**, possessing a chloro substituent, underwent the reaction to give the product **3aj** in 71% yield. The substrate **1e**, containing a dimethyl group, reacted with *p*-thiocresol to give the product **3ak** in 85% yield. 1,4-Enedione **1f**, bearing a highly electron-withdrawing NO_2 group, was compatible with the present reaction, delivering various products **3al–ap** in good yields (72–86%). Furthermore, the 1,4-enedione substrates **1g–i**, containing both electron-donating (Me, OMe) and electron-withdrawing (NO_2) groups, were investigated for this protocol. These substrates reacted with various thiols efficiently and furnished 4-thioarylpyrroles **3aq–at** in 82–97% yields. Next,

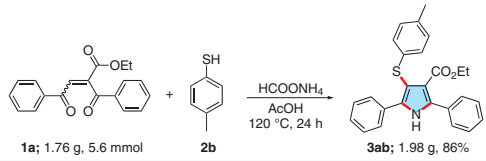
the 1,4-enedione **1j**, having two nitro groups, was also tolerated in the reaction, affording the desired product **3au** in 83% yield.

Encouraged by the good tolerance of a variety of 1,4-enedione substrates, we further turned our attention to investigate the scope of the reaction with 1,4-enediones possessing a keto group instead of an ester group (Scheme 2). The substrates **1k–l**, having a keto group, reacted with different thiols to give the 4-thioarylpyrroles **3ba–bc** in good to excellent yields. In addition, the scope of the reaction was also examined with alkyl thiols. Notably, the alkyl thiols **2l–m** proved to be a good substrates for the present reaction to afford the products **3ca–cd** in 65–79% yield. Furthermore, substrate **1n**, without having either a keto or ester group in the system, also reacted efficiently to afford the product **3da** in 75% yield.



Scheme 2 Substrate scope for the synthesis of 4-thioarylpyrroles. *Reagents and conditions*: **1a–n** (100 mg), **2a–m** (1.1 equiv), $HCOONH_4$ (2.5 equiv), acetic acid (2 mL), 120 °C for the time indicated. Isolated yields are reported.

Considering the importance of pyrroles and thio compounds in pharmaceutical industries and in biological sciences,[2–4,12] a larger scale reaction was carried out to highlight the synthetic potential of the current protocol. The reaction worked well with 1,4-enedione **1a** (1.71 g, 5.6 mmol) and 4-methylbenzenethiol **2b** (758 mg, 6.1 mmol) under the standard reaction conditions to produce 4-thioarylpyrrole **3ab** in 86% yield (Scheme 3).



Scheme 3 Gram-scale synthesis of 4-thioarylpyrrole **3ab**

All the compounds were characterized by IR, ^{1}H, and ^{13}C NMR spectroscopy and by HRMS (ESI) analysis. In addition, the structure of compound **3ap** was confirmed by single-crystal X-ray analysis (Figure 2).[15]

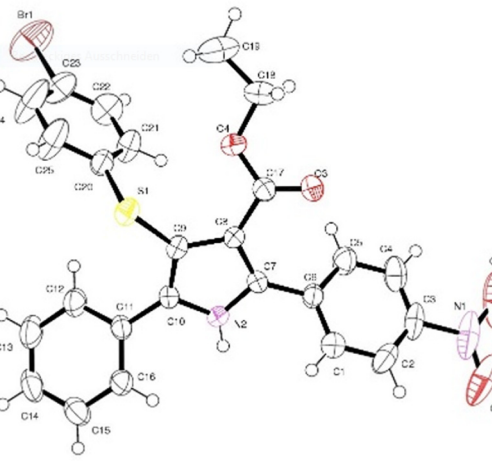
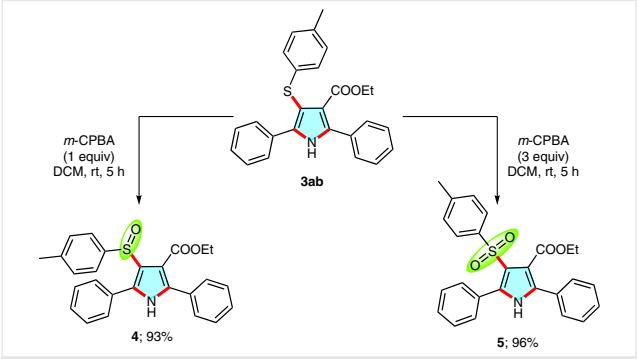


Figure 2 X-ray crystal structure of compound **3ap** (CCDC 1895966)

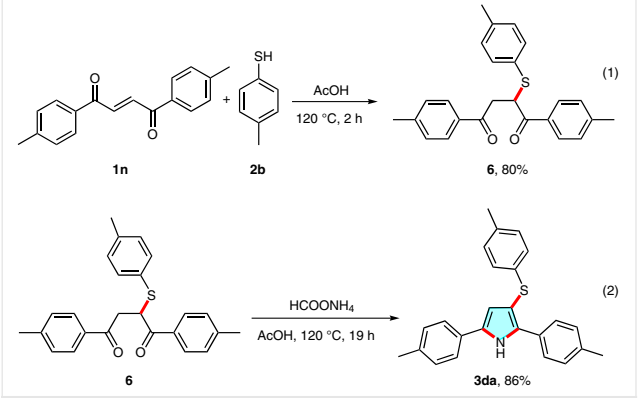
A synthetic application of this protocol was demonstrated by the oxidation of 4-thioarylpyrrole **3ab** using *m*-CPBA (Scheme 4). Upon treatment of compound **3ab** with one equivalent of *m*-CPBA, the sulphenyl group was oxidized to the corresponding sulfoxide **4** in 93% yield. Similarly, sulfone **5** was obtained in 96% yield when three equivalents of *m*-CPBA were used.[16]

Control experiments were carried out in order to better understand the mechanism. First, the reaction of 1,4-enedione **1n** with 4-methylbenzenethiol **2b** was performed under the standard reaction conditions in the absence of ammonium formate (Scheme 5). Interestingly, the thiol-Michael addition proceeded efficiently to form thioaryl



Scheme 4 Conversion of 4-thioarylpyrrole **3ab** into the corresponding sulfoxide **4** and sulfone **5**

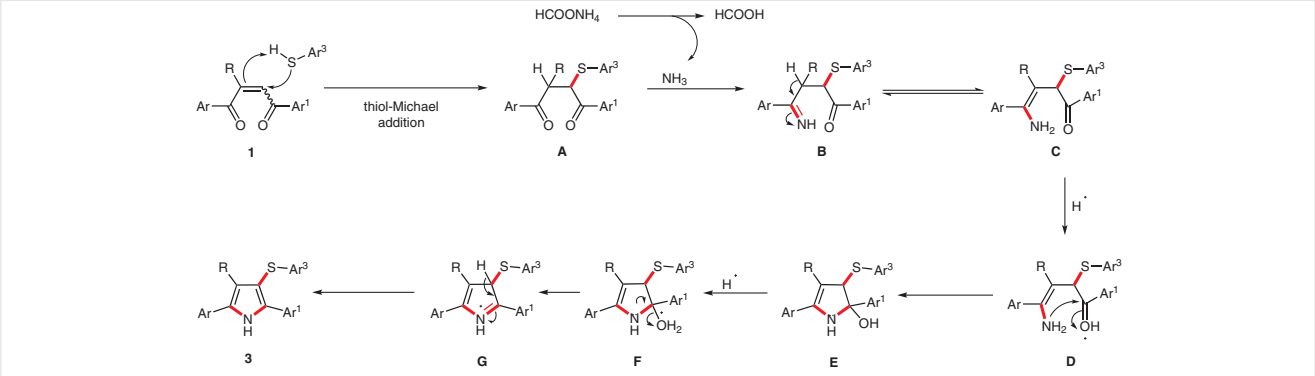
substituted 1,4-diketone **6** in 80% yield.[17] Next, we treated the resulting 1,4-diketone **6** with ammonium formate in acetic acid. The product **3da** was obtained in 86% yield. These results clearly show that the present protocol proceeds through the sequential thiol-Michael and Paal–Knorr reaction to provide 4-thioarylpyrroles. In addition to this, the Paal–Knorr reaction of methylthio-substituted diketones were absorbed to form the methylthio-substituted pyrroles.[11c]



Scheme 5 Control experiments

Based on our experimental results and on previous reports,[18] a reaction mechanism for the formation of 4-thioarylpyrrole is proposed as shown in Scheme 6.

1,4-Enediones **1** react with thiols to form thio-tethered diketones **A** through thiol-Michael addition. Subsequently, the imine intermediate **B** is formed by the reaction of **A** with NH_3, which is generated in situ by decomposition of ammonium formate under the reaction conditions. Intramolecular nucleophilic attack of the amino group of enamine **C** on the keto group then results in the formation of a new C–N bond to produce cyclic intermediate **E**, which undergoes dehydration and aromatization to give 4-thioarylpyrrole **3**.



Scheme 6 Reaction mechanism

In conclusion, we have developed a one-pot thiol-Michael/Paal–Knorr reaction for the synthesis of 4-thioarylpyrroles from readily available starting materials such as 1,4-enediones, thiols, and ammonium formate. This protocol is operationally simple and avoids the use of metal catalysts for C–S bond formation. A wide range of structurally diverse 4-thioarylpyrroles were obtained in good to excellent yields. Furthermore, the synthetic transformation of 4-thioarylpyrrole was demonstrated for the synthesis of sulfoxide and sulfone moieties by simple oxidation in excellent yields.

Commercially available chemicals were purchased from Alfa Aesar or Sigma–Aldrich and used as received. Thin-layer chromatography (TLC) was performed using Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with a UV lamp for reaction monitoring. Silica gel for column chromatography (particle size 100–200 mesh) was purchased from Avra Synthesis Private Ltd India. ^{1}H and ^{13}C NMR spectra were recorded with Bruker 300 & 400 MHz instruments. Chemical shifts were recorded in parts per million (ppm) relative to tetramethylsilane (δ = 0.00 ppm) or chloroform (δ = 7.26 ppm). ^{1}H NMR splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), m (multiplet), etc. ^{13}C NMR spectral values were reported relative to $CDCl_3$ (δ = 77.00 ppm) and DMSO-d_6 (δ = 39.51 ppm). FTIR spectra were recorded with a JASCO spectrometer and are reported in frequency of absorption (cm^{-1}). High-resolution mass spectra were obtained with a Waters Q-Tof Premier Spectrometer.

4-Thioarylpyrroles 3aa–da; General Procedure

To an oven-dried sealed tube equipped with a magnetic stir bar was added 1,4-enedione **1a–n** (100 mg), thiol **2a–m** (1.1 equiv), ammonium formate (2.5 equiv) and acetic acid (2 mL). The tube was then sealed with a screw-type cap and the resulting reaction mixture was placed in an oil bath at 120 °C with stirring. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was cooled to r.t. and extracted with EtOAc (3 × 15 mL). The extract was then washed with aqueous brine solution. After drying over Na_2SO_4 and evaporation, the crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the corresponding 4-thioarylpyrrole **3aa–da**.

Ethyl 2,5-Diphenyl-4-(phenylthio)-1*H*-pyrrole-3-carboxylate (3aa)

Yield: 99 mg (76%); yellow solid; mp 103–104 °C.

FTIR (KBr): 3230, 3061, 2974, 1673, 1479, 1259, 1149, 764, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (s, 1 H), 7.56 (dd, *J* = 12.0, 7.6 Hz, 4 H), 7.41–7.29 (m, 6 H), 7.24–7.14 (m, 4 H), 7.06 (t, *J* = 6.8 Hz, 1 H), 4.03 (q, *J* = 7.0 Hz, 2 H), 0.93 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.55, 140.06, 137.33, 137.13, 131.61, 130.83, 128.58 (2C), 128.54, 128.47, 128.30, 128.18, 127.72, 125.57, 124.41, 116.94, 107.72, 60.10, 13.60.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{22}NO_2S$: 400.1371; found: 400.1363.

Ethyl 2,5-Diphenyl-4-(*p*-tolylthio)-1*H*-pyrrole-3-carboxylate (3ab)

Yield: 122 mg (91%); white solid; mp 116–117 °C.

FTIR (KBr): 3228, 2974, 2923, 1675, 1479, 1260, 1150, 764, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.93 (s, 1 H), 7.59–7.53 (m, 2 H), 7.48 (dd, *J* = 7.7, 1.4 Hz, 2 H), 7.37–7.24 (m, 6 H), 7.02 (dd, *J* = 21.9, 8.2 Hz, 4 H), 4.01 (q, *J* = 7.2 Hz, 2 H), 2.25 (s, 3 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.69, 137.19, 136.98, 136.38, 134.04, 131.56, 130.83, 129.33, 128.47, 128.46, 128.29, 128.16, 128.00, 127.70, 125.69, 116.77, 108.07, 60.06, 20.84, 13.60.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{24}NO_2S$: 414.1528; found: 414.1528.

Ethyl 4-{[4-(*tert*-butyl)phenyl]thio}-2,5-diphenyl-1*H*-pyrrole-3-carboxylate (3ac)

Yield: 115 mg (78%); white solid; mp 128–129 °C.

FTIR (KBr): 3229, 2959, 2866, 1675, 1479, 1323, 1258, 1144, 764, 689 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (s, 1 H), 7.65–7.55 (m, 4 H), 7.48–7.31 (m, 6 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 7.11 (d, *J* = 8.6 Hz, 2 H), 4.06 (q, *J* = 7.1 Hz, 2 H), 1.26 (s, 9 H), 0.92 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.73, 147.41, 137.17, 137.02, 136.34, 131.60, 130.89, 128.49, 128.45, 128.29, 128.16, 127.97, 127.78, 125.57, 125.52, 116.75, 108.17, 60.02, 34.20, 31.26, 13.47.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{30}NO_2S$: 456.1997; found: 456.2006.

Ethyl 4-[(4-Methoxyphenyl)thio]-2,5-diphenyl-1*H*-pyrrole-3-carboxylate (3ad)

Yield: 99 mg (71%); white solid; mp 90–91 °C.

FTIR (KBr): 3235, 2978, 1674, 1494, 1322, 1246, 1143, 1041, 764, 670 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.73 (s, 1 H), 7.58 (dd, *J* = 25.9, 6.6 Hz, 4 H), 7.48–7.28 (m, 6 H), 7.13 (d, *J* = 7.8 Hz, 2 H), 6.77 (d, *J* = 7.8 Hz, 2 H), 4.09 (q, *J* = 6.5 Hz, 2 H), 3.74 (s, 3 H), 1.01 (t, *J* = 6.7 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.59, 157.35, 136.84, 136.68, 131.63, 130.89, 130.44, 128.54, 128.41, 128.38, 128.27, 128.07, 127.85, 127.71, 116.87, 114.32, 109.34, 60.08, 55.23, 13.70.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{24}NO_3S$: 430.1477; found: 430.1483.

Ethyl 4-[(4-Fluorophenyl)thio]-2,5-diphenyl-1*H*-pyrrole-3-carboxylate (3ae)

Yield: 90 mg (66%); white solid; mp 129–130 °C.

FTIR (KBr): 3281, 2977, 2927, 1685, 1487, 1225, 1156, 1044, 802, 761, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.84 (s, 1 H), 7.61–7.47 (m, 4 H), 7.44–7.29 (m, 6 H), 7.12 (ddd, *J* = 8.3, 5.1, 2.6 Hz, 2 H), 6.90 (t, *J* = 8.7 Hz, 2 H), 4.06 (q, *J* = 7.1 Hz, 2 H), 0.97 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.53, 161.89, 159.47, 137.16 (d, J_{C-F} = 14.0 Hz), 134.93 (d, J_{C-F} = 3.18 Hz), 131.54, 130.73, 128.61, 128.51, 128.30, 128.25, 127.73, 127.52, 127.45, 115.62 (d, J_{C-F} = 22.09 Hz), 115.51, 108.24, 60.15, 13.68.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{21}FNO_2S$: 418.1277; found: 418.1269.

Ethyl 4-[(4-Bromophenyl)thio]-2,5-diphenyl-1*H*-pyrrole-3-carboxylate (3af)

Yield: 107 mg (69%); white solid; mp 113–114 °C.

FTIR (KBr): 3230, 2976, 1676, 1473, 1323, 1259, 1149, 765, 689 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.94 (s, 1 H), 7.52 (t, *J* = 5.8 Hz, 4 H), 7.39–7.27 (m, 8 H), 7.02 (d, *J* = 8.4 Hz, 2 H), 4.03 (q, *J* = 7.2 Hz, 2 H), 0.95 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.45, 139.51, 137.53, 137.34, 131.51, 131.41, 130.56, 128.59, 128.54, 128.52, 128.29, 128.24, 127.68, 127.06, 117.86, 116.61, 106.94, 60.16, 13.63.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{21}BrNO_2S$: 478.0476; found: 478.0469.

Ethyl 2,5-Diphenyl-4-{[4-(trifluoromethyl)phenyl]thio}-1*H*-pyrrole-3-carboxylate (3ag)

Yield: 115 mg (76%); white solid; mp 137–138 °C.

FTIR (KBr): 3225, 2982, 1671, 1605, 1325, 1259, 1114, 766, 689 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.74 (s, 1 H), 7.57 (ddd, *J* = 13.2, 7.8, 1.6 Hz, 4 H), 7.50–7.34 (m, 8 H), 7.26 (d, *J* = 8.2 Hz, 2 H), 4.07 (q, *J* = 7.1 Hz, 2 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.32, 145.54, 137.78, 137.61, 131.40, 130.48, 128.68, 128.65, 128.61, 128.45, 128.30, 127.69, 126.42 (q, *J* = 32.3 Hz), 125.41 (q, *J* = 3.8 Hz), 125.14, 122.53, 116.64, 106.13, 60.18, 13.53.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{21}F_3NO_2S$: 468.1245; found: 468.1258.

Ethyl 4-[(4-Nitrophenyl)thio]-2,5-diphenyl-1*H*-pyrrole-3-carboxylate (3ah)

Yield: 121 mg (84%); pale-yellow solid; mp 124–125 °C.

FTIR (KBr): 3272, 3064, 2977, 2926, 1684, 1578, 1511, 1338, 1242, 762, 694 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.82 (s, 1 H), 8.09 (d, *J* = 8.8 Hz, 2 H), 7.60 (d, *J* = 6.1 Hz, 2 H), 7.52 (d, *J* = 6.2 Hz, 2 H), 7.42 (dd, *J* = 19.3, 6.7 Hz, 6 H), 7.28 (d, *J* = 9.0 Hz, 1 H), 4.07 (q, *J* = 7.0 Hz, 2 H), 0.95 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.09, 150.74, 144.66, 138.01, 131.23, 130.21, 128.76, 128.71, 128.69, 128.62, 128.28, 127.67, 124.97, 123.81, 116.32, 105.16, 60.21, 13.61.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{21}N_2O_4S$: 445.1222; found: 445.1225.

Ethyl 4-[(4-Bromophenyl)thio]-5-(3,4-dimethoxyphenyl)-2-phenyl-1*H*-pyrrole-3-carboxylate (3ai)

Yield: 117 mg (80%); yellow solid; mp 111–112 °C.

FTIR (KBr): 3246, 2995, 2935, 1673, 1499, 1251, 1133, 1027, 767, 689 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.93 (s, 1 H), 7.56 (d, *J* = 7.5 Hz, 2 H), 7.40 (dt, *J* = 12.3, 6.2 Hz, 3 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.10–7.01 (m, 4 H), 6.84 (d, *J* = 8.3 Hz, 1 H), 4.08 (q, *J* = 7.0 Hz, 2 H), 3.84 (s, 3 H), 3.64 (s, 3 H), 0.99 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.46, 149.14, 149.12, 148.71, 139.81, 137.69, 136.74, 136.72, 131.55, 128.58, 128.50, 128.28, 126.94, 123.37, 119.85, 117.80, 116.90, 111.28, 111.07, 60.17, 55.82, 55.55, 13.69.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{25}BrNO_4S$: 538.0688; found: 538.0696.

Ethyl 5-(4-Chlorophenyl)-4-[(4-fluorophenyl)thio]-2-phenyl-1*H*-pyrrole-3-carboxylate (3aj)

Yield: 94 mg (71%); white solid; mp 162–163 °C.

FTIR (KBr): 3262, 2989, 1683, 1488, 1226, 1166, 1090, 696 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1 H), 7.59–7.48 (m, 4 H), 7.46–7.38 (m, 3 H), 7.35 (d, *J* = 8.5 Hz, 2 H), 7.16–7.08 (m, 2 H), 6.92 (t, *J* = 8.7 Hz, 2 H), 4.08 (q, *J* = 7.2 Hz, 2 H), 0.99 (t, *J* = 7.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$/DMSO-d_6 = 3:1): δ = 163.75, 159.66 (d, *J* = 241.69 Hz), 137.00, 135.60, 134.40 (d, *J* = 3.01 Hz), 132.52, 131.09, 128.88, 128.81, 128.45, 127.41, 127.33, 127.06, 126.41 (d, *J* = 7.65 Hz), 115.82, 114.80 (d, *J* = 21.6 Hz), 106.50, 58.99, 12.91.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{20}ClFNO_2S$: 452.0887; found: 452.0890.

Ethyl 2,5-Di-*p*-tolyl-4-(*p*-tolylthio)-1*H*-pyrrole-3-carboxylate (3ak)

Yield: 112 mg (85%); yellow solid; mp 78–79 °C.

FTIR (KBr): 3434, 2957, 2924, 2855, 1728, 1608, 1491, 1171, 1035, 820 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.54 (s, 1 H), 7.47 (dd, *J* = 7.7, 5.2 Hz, 4 H), 7.21 (dd, *J* = 14.8, 8.0 Hz, 4 H), 7.05 (dd, *J* = 18.9, 8.1 Hz, 4 H), 4.07 (q, *J* = 7.1 Hz, 2 H), 2.40 (s, 3 H), 2.35 (s, 3 H), 2.27 (s, 3 H), 0.99 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.70, 138.31, 137.99, 137.14, 136.92, 136.61, 133.95, 129.32, 129.26, 128.97, 128.83, 128.35, 128.11, 127.55, 125.71, 116.56, 107.69, 59.99, 21.28, 21.22, 20.85, 13.70.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{28}NO_2S$: 442.1841; found: 422.1193.

Ethyl 2-(4-Nitrophenyl)-5-phenyl-4-(phenylthio)-1*H*-pyrrole-3-carboxylate (3al)

Yield: 90 mg (72%); yellow solid; mp 128–129 °C.

FTIR (KBr): 3251, 2927, 2853, 1673, 1512, 1479, 1344, 854, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.34 (s, 1 H), 8.22–8.08 (m, 2 H), 7.71–7.54 (m, 4 H), 7.34 (d, *J* = 5.6 Hz, 3 H), 7.21 (t, *J* = 7.6 Hz, 2 H), 7.16–7.04 (m, 3 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 0.95 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.56, 146.93, 139.50, 139.07, 137.71, 133.93, 130.29, 129.06, 128.67, 128.56, 127.95, 125.62, 124.86, 124.68, 123.43, 118.91, 108.74, 60.62, 13.57.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{21}N_2O_4S$: 445.1222; found: 445.1212.

Ethyl 2-(4-Nitrophenyl)-5-phenyl-4-(*p*-tolylthio)-1*H*-pyrrole-3-carboxylate (3am)

Yield: 111 mg (86%); yellow solid; mp 195–196 °C.

FTIR (KBr): 3256, 2925, 1678, 1519, 1345, 1264, 854, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.90 (s, 1 H), 8.26 (d, *J* = 8.8 Hz, 2 H), 7.73 (d, *J* = 8.9 Hz, 2 H), 7.61 (dd, *J* = 8.0, 1.4 Hz, 2 H), 7.45–7.33 (m, 3 H), 7.04 (q, *J* = 8.4 Hz, 4 H), 4.10 (q, *J* = 7.2 Hz, 2 H), 2.27 (s, 3 H), 1.01 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, DMSO): δ = 164.53, 146.87, 139.26, 137.85, 136.08, 134.59, 133.79, 130.58, 129.94, 129.84, 128.80, 128.77, 128.67, 125.69, 123.72, 119.09, 107.71, 60.56, 20.72, 13.86.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{23}N_2O_4S$: 459.1379; found: 459.1370.

Ethyl 4-[(4-Chlorophenyl)thio]-2-(4-nitrophenyl)-5-phenyl-1*H*-pyrrole-3-carboxylate (3an)

Yield: 107 mg (79%); yellow solid; mp 143–144 °C.

FTIR (KBr): 3230, 2926, 1677, 1600, 1518, 1475, 1344, 855, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.32 (s, 1 H), 8.18 (d, *J* = 8.2 Hz, 2 H), 7.68 (d, *J* = 8.5 Hz, 2 H), 7.59–7.53 (m, 2 H), 7.41–7.34 (m, 3 H), 7.20–7.15 (m, 2 H), 7.09–7.04 (m, 2 H), 4.09 (q, *J* = 7.2 Hz, 2 H), 1.00 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.28, 147.11, 139.11, 138.13, 137.57, 134.03, 130.48, 130.05, 129.08, 128.80, 128.78, 128.71, 127.83, 126.91, 123.52, 118.81, 108.44, 60.72, 13.68.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{20}ClN_2O_4S$: 479.0832; found: 479.0839.

Ethyl 4-[(3-Chlorophenyl)thio]-2-(4-nitrophenyl)-5-phenyl-1*H*-pyrrole-3-carboxylate (3ao)

Yield: 106 mg (78%); yellow solid; mp 125–126 °C.

FTIR (KBr): 3238, 2979, 2926, 2853, 1701, 1600, 1577, 1518, 1343, 855, 771, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 8.25 (dd, *J* = 8.7, 2.8 Hz, 2 H), 7.74 (dd, *J* = 8.8, 2.2 Hz, 2 H), 7.57 (d, *J* = 6.9 Hz, 2 H), 7.44–7.36 (m, 3 H), 7.14 (dd, *J* = 14.2, 6.3 Hz, 2 H), 7.05 (t, *J* = 7.2 Hz, 2 H), 4.11 (q, *J* = 7.0 Hz, 2 H), 0.99 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.35, 147.07, 141.77, 139.25, 137.48, 134.65, 134.18, 129.94, 129.69, 129.08, 128.80, 128.68, 127.81, 125.17, 124.87, 123.66, 123.46, 118.70, 107.73, 60.73, 13.58.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{20}ClN_2O_4S$: 479.0832; found: 479.0828.

Ethyl 4-[(4-Bromophenyl)thio]-2-(4-nitrophenyl)-5-phenyl-1*H*-pyrrole-3-carboxylate (3ap)

Yield: 109 mg (74%); yellow solid; mp 171–172 °C.

FTIR (KBr): 3250, 2995, 2976, 2926, 1683, 1602, 1513, 1471, 1150, 854, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.25 (s, 1 H), 8.16 (d, *J* = 8.9 Hz, 2 H), 7.71–7.63 (m, 2 H), 7.54 (dd, *J* = 7.3, 2.2 Hz, 2 H), 7.38 (ddd, *J* = 7.2, 4.4, 1.6 Hz, 3 H), 7.34–7.29 (m, 2 H), 7.02–6.97 (m, 2 H), 4.08 (q, *J* = 7.2 Hz, 2 H), 0.99 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.29, 147.08, 139.14, 138.82, 137.51, 134.04, 131.65, 129.98, 129.05, 128.83, 128.72, 127.79, 127.17, 123.51, 118.75, 118.25, 108.22, 60.74, 13.66.

HRMS (ESI): *m*/*z* [M + K]$^+$ calcd for $C_{25}H_{19}BrKN_2O_4S$: 560.9886; found: 560.9857.

Ethyl 4-[(4-Bromophenyl)thio]-2-(4-nitrophenyl)-5-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (3aq)

Yield: 138 mg (94%); yellow solid; mp 184–185 °C.

FTIR (KBr): 3228, 2925, 2853, 1683, 1514, 1347, 1235, 813 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1 H), 8.25 (d, *J* = 8.7 Hz, 2 H), 7.73 (d, *J* = 8.8 Hz, 2 H), 7.45 (d, *J* = 8.1 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 2 H), 7.21 (d, *J* = 7.9 Hz, 2 H), 7.02 (d, *J* = 8.5 Hz, 2 H), 4.11 (q, *J* = 7.1 Hz, 2 H), 2.37 (s, 3 H), 1.01 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.22, 147.15, 139.36, 139.01, 137.65, 133.78, 131.64, 129.48, 129.05, 127.68, 127.20, 123.58, 118.86, 118.19, 107.94, 60.67, 21.30, 13.70.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{22}BrN_2O_4S$: 537.0484; found: 537.0471.

Ethyl 4-[(4-Bromophenyl)thio]-5-(4-methoxyphenyl)-2-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (3ar)

Yield: 129 mg (89%); yellow solid; mp 188–189 °C.

FTIR (KBr): 3235, 2977, 2922, 1673, 1519, 1346, 1267, 1163, 834, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.84 (s, 1 H), 8.27 (d, *J* = 8.7 Hz, 2 H), 7.74 (d, *J* = 8.8 Hz, 2 H), 7.49 (d, *J* = 8.7 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 2 H), 7.03 (d, *J* = 8.5 Hz, 2 H), 6.93 (d, *J* = 8.7 Hz, 2 H), 4.12 (q, *J* = 7.2 Hz, 2 H), 3.82 (s, 3 H), 1.01 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.32, 158.55, 145.55, 138.73, 138.67, 136.99, 132.70, 130.37, 128.89, 128.44, 125.91, 122.28, 121.92, 117.42, 116.53, 112.56, 105.04, 59.09, 54.16, 12.64.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{22}BrN_2O_5S$: 553.0433; found: 553.0438.

Ethyl 5-(3,4-Dimethoxyphenyl)-2-(4-nitrophenyl)-4-(*p*-tolylthio)-1*H*-pyrrole-3-carboxylate (3as)

Yield: 112 mg (97%); yellow solid; mp 150–151 °C.

FTIR (KBr): 3245, 2932, 2833, 1677, 1598, 1518, 1493, 1341, 1255, 1026, 849, 699 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.90 (s, 1 H), 8.26 (d, *J* = 8.7 Hz, 2 H), 7.74 (d, *J* = 8.8 Hz, 2 H), 7.20–6.99 (m, 6 H), 6.88 (d, *J* = 8.3 Hz, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 3.88 (s, 3 H), 3.64 (s, 3 H), 2.27 (s, 3 H), 1.04 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.58, 149.22, 148.67, 146.89, 138.98, 137.79, 136.02, 134.43, 133.01, 129.48, 128.86, 125.65, 123.48, 123.14, 119.98, 119.42, 111.52, 111.05, 108.42, 60.65, 55.81, 55.53, 20.83, 13.71.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{27}N_2O_6S$: 519.1590; found: 519.1595.

Ethyl 4-[(4-Chlorophenyl)thio]-5-(3,4-dimethoxyphenyl)-2-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (3at)

Yield: 107 mg (82%); yellow solid; mp 120–121 °C.

FTIR (KBr): 3084, 2980, 1708, 1481, 1283, 1028, 765, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.11 (s, 1 H), 8.23 (d, *J* = 8.8 Hz, 2 H), 7.73 (d, *J* = 8.8 Hz, 2 H), 7.19 (d, *J* = 8.5 Hz, 2 H), 7.14–7.05 (m, 4 H), 6.86 (d, *J* = 8.2 Hz, 1 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.86 (s, 3 H), 3.66 (s, 3 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.30, 149.43, 148.75, 147.03, 139.25, 138.45, 137.66, 133.47, 130.43, 129.04, 128.80, 126.70, 123.50, 122.83, 120.12, 119.08, 111.36, 111.13, 107.38, 60.71, 55.84, 55.58, 13.71.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{24}ClN_2O_6S$: 539.1044; found: 539.1050.

Ethyl 4-[(4-Chlorophenyl)thio]-2,5-bis(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (3au)

Yield: 109 mg (83%); yellow solid; mp 197–198 °C.

FTIR (KBr): 3190, 2924, 2852, 1673, 1596, 1520, 1343, 1164, 854 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$/DMSO-d_6 = 3:1): δ = 12.26 (s, 1 H), 8.17 (dd, *J* = 19.8, 8.9 Hz, 4 H), 7.80 (dd, *J* = 20.1, 8.9 Hz, 4 H), 7.12 (d, *J* = 8.6 Hz, 2 H), 7.01 (d, *J* = 8.6 Hz, 2 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$/DMSO-d_6 = 3:1): δ = 163.69, 146.81, 146.46, 137.36, 137.32, 136.50, 136.02, 135.46, 130.21, 129.56, 128.54, 128.49, 126.57, 123.06, 122.73, 119.10, 109.78, 60.17, 13.35.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{19}ClN_3O_6S$: 524.0683; found: 524.0692.

(2,5-Diphenyl-4-(*p*-tolylthio)-1*H*-pyrrol-3-yl)(phenyl)methanone (3ba)

Yield: 120 mg (92%); yellow solid; mp 162–163 °C.

FTIR (KBr): 3242, 2918, 2856, 1633, 1489, 1233, 906, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (s, 1 H), 7.75–7.63 (m, 4 H), 7.35–7.26 (m, 6 H), 7.15 (t, *J* = 7.7 Hz, 2 H), 7.10 (dd, *J* = 4.8, 2.2 Hz, 3 H), 6.90 (dd, *J* = 22.5, 8.2 Hz, 4 H), 2.17 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.98, 138.23, 136.89, 135.54, 134.45, 134.27, 132.38, 130.87, 130.82, 129.89, 129.27, 128.51, 128.48, 127.85, 127.74, 127.68, 127.44, 127.28, 126.53, 125.53, 108.84, 20.80.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{24}NOS$: 446.1579; found: 446.1577.

{4-[(2-Fluorophenyl)thio]-2,5-diphenyl-1*H*-pyrrol-3-yl}(phenyl)methanone (3bb)

Yield: 99 mg (75%); yellow solid; mp 170–171 °C.

FTIR (KBr): 3234, 2932, 1624, 1615, 1469, 1212, 910, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (s, 1 H), 7.73 (d, *J* = 7.3 Hz, 2 H), 7.68 (d, *J* = 7.3 Hz, 2 H), 7.36 (tt, *J* = 14.7, 7.3 Hz, 6 H), 7.25–7.15 (m, 3 H), 7.06–6.94 (m, 2 H), 6.94–6.80 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.52, 158.98 (d, *J* = 245.21 Hz), 138.15, 137.34, 134.47, 132.56, 130.71 (d, *J* = 19.51 Hz), 129.83, 128.720 (d, *J* = 4.05 Hz), 128.55, 128.55, 128.20, 127.98, 127.86, 127.39, 127.30, 126.39, 126.32, 126.24, 125.80, 124.20 (d, *J* = 3.31 Hz), 114.94 (d, *J* = 21.35 Hz), 106.51.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{21}FNOS$: 450.1328; found: 450.1321.

Phenyl[2-phenyl-5-(*p*-tolyl)-4-(*p*-tolylthio)-1*H*-pyrrol-3-yl]methanone (3bc)

Yield: 110 mg (85%); yellow solid; mp 180–181 °C.

FTIR (KBr): 3250, 2956, 2923, 2853, 1636, 1489, 1234, 908, 712, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.74 (s, 1 H), 7.73 (d, *J* = 7.3 Hz, 2 H), 7.60 (d, *J* = 8.1 Hz, 2 H), 7.37 (dd, *J* = 9.4, 7.6 Hz, 4 H), 7.22 (dd, *J* = 7.6, 4.1 Hz, 6 H), 6.93 (q, *J* = 8.3 Hz, 4 H), 2.37 (s, 3 H), 2.21 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.81, 138.32, 137.97, 137.02, 135.63, 134.48, 133.78, 132.38, 131.04, 129.91, 129.38, 129.30, 128.63, 128.02, 127.77, 127.35, 127.28, 127.20, 126.59, 125.70, 108.66, 21.24, 20.84.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{26}NOS$: 460.1735; found: 460.1747.

Ethyl 5-(4-Chlorophenyl)-4-{[3-oxo-3-(pentyloxy)propyl]thio}-2-phenyl-1*H*-pyrrole-3-carboxylate (3ca)

Yield: 102 mg (70%); white solid; mp 98–99 °C.

FTIR (KBr): 3320, 2952, 2871, 1710, 1481, 1225, 1046, 840, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (s, 1 H), 7.63 (d, *J* = 8.5 Hz, 2 H), 7.47 (dd, *J* = 7.3, 1.6 Hz, 2 H), 7.42–7.33 (m, 3 H), 4.20 (q, *J* = 7.2 Hz, 2 H), 3.90 (t, *J* = 6.8 Hz, 2 H), 2.98 (t, *J* = 7.4 Hz, 2 H), 2.40 (t, *J* = 7.4 Hz, 2 H), 1.59–1.46 (m, 2 H), 1.37–1.21 (m, 4 H), 1.16 (t, *J* = 7.2 Hz, 3 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.11, 164.78, 136.95, 135.05, 133.68, 131.77, 129.61, 129.35, 128.60, 128.54, 128.38, 128.15, 116.84, 111.26, 64.73, 60.18, 34.21, 31.49, 28.11, 27.91, 22.24, 13.90, 13.89.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{31}ClNO_4S$: 500.1662; found: 500.1662.

Ethyl 5-(4-Bromophenyl)-4-{[3-oxo-3-(pentyloxy)propyl]thio}-2-phenyl-1*H*-pyrrole-3-carboxylate (3cb)

Yield: 91 mg (65%); white solid; mp 100–101 °C.

FTIR (KBr): 3321, 2961, 2870, 1710, 1474, 1355, 1225, 1046, 787, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.69 (s, 1 H), 7.56 (q, *J* = 8.6 Hz, 4 H), 7.48 (d, *J* = 6.5 Hz, 2 H), 7.39 (d, *J* = 7.0 Hz, 3 H), 4.21 (q, *J* = 7.0 Hz, 2 H), 3.91 (t, *J* = 6.8 Hz, 2 H), 2.99 (t, *J* = 7.3 Hz, 2 H), 2.41 (t, *J* = 7.3 Hz, 2 H), 1.58–1.48 (m, 2 H), 1.29 (dd, *J* = 15.7, 8.6 Hz, 4 H), 1.16 (t, *J* = 7.1 Hz, 3 H), 0.89 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.09, 164.74, 136.99, 135.04, 131.77, 131.58, 130.06, 129.59, 128.55, 128.43, 128.19, 121.92, 116.94, 111.38, 64.74, 60.20, 34.23, 31.51, 28.13, 27.93, 22.26, 13.91, 13.90.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{31}BrNO_4S$: 544.1157; found: 544.1147.

Ethyl 2-(4-Nitrophenyl)-4-{[3-oxo-3-(pentyloxy)propyl]thio}-5-phenyl-1*H*-pyrrole-3-carboxylate (3cc)

Yield: 111 mg (77%); yellow solid; mp 98–99 °C.

FTIR (KBr): 3309, 2958, 2928, 1698, 1601, 1518, 1345, 1223, 1149, 857, 693 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.33 (s, 1 H), 8.16 (dd, *J* = 8.7, 1.8 Hz, 2 H), 7.71–7.65 (m, 2 H), 7.62 (d, *J* = 8.9 Hz, 2 H), 7.38 (dt, *J* = 24.7, 7.3 Hz, 3 H), 4.25 (q, *J* = 7.2 Hz, 2 H), 3.88 (t, *J* = 6.8 Hz, 2 H), 2.93 (t, *J* = 7.5 Hz, 2 H), 2.39 (t, *J* = 7.5 Hz, 2 H), 1.57–1.46 (m, 2 H), 1.34–1.24 (m, 4 H), 1.22 (t, *J* = 7.2 Hz, 3 H), 0.88 (t, *J* = 7.0 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.10, 164.67, 146.90, 137.99, 137.87, 133.24, 130.60, 128.94, 128.50, 128.31, 128.20, 123.41, 118.81, 111.86, 64.76, 60.67, 34.28, 31.51, 28.07, 27.90, 22.22, 13.98, 13.89.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{31}N_2O_6S$: 511.1903; found: 511.1902.

3-Phenylpropyl 3-{[4-benzoyl-2-(4-bromophenyl)-5-phenyl-1*H*-pyrrol-3-yl]thio}propanoate (3cd)

Yield: 117 mg (79%); yellow solid; mp 94–95 °C.

FTIR (KBr): 3296, 2924, 2853, 1732, 1712, 1639, 1471, 1230, 1009, 908, 695 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 7.84–7.78 (m, 2 H), 7.69 (d, *J* = 8.6 Hz, 2 H), 7.57 (d, *J* = 8.6 Hz, 2 H), 7.42 (dd, *J* = 14.2, 6.9 Hz, 1 H), 7.33–7.26 (m, 5 H), 7.26–7.10 (m, 7 H), 3.92 (t, *J* = 6.6 Hz, 2 H), 2.83 (t, *J* = 7.3 Hz, 2 H), 2.59 (t, *J* = 7.3 Hz, 2 H), 2.36 (t, *J* = 7.3 Hz, 2 H), 1.90–1.76 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.94, 171.79, 141.12, 138.31, 134.94, 134.32, 132.71, 131.78, 130.83, 130.04, 129.97, 129.18, 128.64, 128.37, 128.35, 128.06, 127.97, 127.32, 125.97, 125.93, 121.94, 111.56, 63.87, 34.12, 32.02, 31.92, 29.97.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{35}H_{31}BrNO_3S$: 624.1208; found: 624.1214.

2,5-Di-*p*-tolyl-3-(*p*-tolylthio)-1*H*-pyrrole (3da)

Yield: 105 mg (75%); white solid; mp 121–122 °C.

FTIR (KBr): 3454, 2922, 2854, 1502, 1490, 1463, 808 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.60 (s, 1 H), 7.54 (d, *J* = 8.2 Hz, 2 H), 7.40 (d, *J* = 8.2 Hz, 2 H), 7.19 (dd, *J* = 8.2, 2.5 Hz, 4 H), 7.10 (d, *J* = 8.3 Hz, 2 H), 7.02 (d, *J* = 8.3 Hz, 2 H), 6.61 (d, *J* = 2.8 Hz, 1 H), 2.36 (s, 3 H), 2.35 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.25, 136.60, 136.38, 135.85, 134.42, 132.35, 129.66, 129.53, 129.35, 128.97, 128.83, 126.73, 126.15, 123.67, 113.61, 108.08, 21.20, 21.14, 20.85.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{24}NS$: 370.1629; found: 370.1630.

Ethyl 2,5-Diphenyl-4-(*p*-tolylsulfinyl)-1*H*-pyrrole-3-carboxylate (4)

To a round-bottom flask containing a solution of **3ab** (100 mg, 0.242 mmol) in CH_2Cl_2 (5 mL) was added *m*-chloroperoxybenzoic acid (*m*-CPBA) (41.73 mg, 0.242 mmol). The reaction mixture was stirred at r.t. for 5 h and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was washed with aq. NaOH solution and the layers were separated. The aq. layer was further extracted with CH_2Cl_2 (2 × 20 mL) and the combined organics were washed with brine (30 mL), dried (Na_2SO_4), and concentrated. The crude material was purified by flash chromatography on silica gel (eluent: petroleum ether/EtOAc) to provide product **4**.

Yield: 97 mg (93%); white solid; mp 128–129 °C.

FTIR (KBr): 3084, 2980, 2924, 1708, 1490, 1488, 1238, 1028, 765, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.27 (s, 1 H), 7.60–7.44 (m, 4 H), 7.43–7.28 (m, 8 H), 7.12 (d, *J* = 8.2 Hz, 2 H), 4.14–3.83 (m, 2 H), 2.32 (s, 3 H), 1.06 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.80, 141.32, 139.26, 138.37, 137.73, 130.76, 129.63, 129.44, 128.97, 128.88, 128.62, 128.44, 128.03, 127.96, 124.98, 121.35, 112.71, 60.21, 21.13, 13.74.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{24}NO_3S$: 430.1477; found: 430.1478.

Ethyl 2,5-Diphenyl-4-tosyl-1*H*-pyrrole-3-carboxylate (5)

To a round-bottom flask containing a solution of **3ab** (100 mg, 0.242 mmol) in CH_2Cl_2 (5 mL) was added *m*-chloroperoxybenzoic acid (*m*-CPBA) (125.0 mg, 0.725 mmol). The reaction mixture was stirred at r.t. for 5 h and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was washed with aq. NaOH solution and the layers were separated. The aq. layer was further extracted with CH_2Cl_2 (2 × 20 mL) and the combined organics were washed with brine (30 mL), dried (Na_2SO_4), and concentrated. The crude material was purified by flash chromatography on silica gel (eluent: petroleum ether/EtOAc) to provide product **5**.

Yield: 103 mg (96%); white solid; mp 92–93 °C.

FTIR (KBr): 3259, 3059, 2979, 2925, 1721, 1480, 1382, 1302, 1237, 1139, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.62 (s, 1 H), 7.69 (d, *J* = 8.3 Hz, 2 H), 7.52–7.30 (m, 10 H), 7.17 (d, *J* = 8.2 Hz, 2 H), 4.30 (q, *J* = 7.2 Hz, 2 H), 2.36 (s, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.28, 143.08, 140.38, 136.48, 132.26, 130.01, 129.88, 129.60, 129.19, 129.05, 128.59, 128.44, 127.93, 127.31, 127.09, 120.56, 115.06, 61.48, 21.46, 13.77.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{24}NO_4S$: 446.1426; found: 446.1419.

1,4-Di-*p*-tolyl-2-(*p*-tolylthio)butane-1,4-dione (6)

To an oven-dried sealed tube equipped with a magnetic stir bar was added (*E*)-1,4-di-*p*-tolylbut-2-ene-1,4-dione (**1n**; 200 mg, 0.757 mmol), 4-methylbenzenethiol (**2b**; 103 mg, 0.832 mmol) and acetic acid (5 mL). The tube was then sealed with a screw-type cap and the resulting reaction mixture was placed in the oil bath at 120 °C with stirring. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to r.t. and extracted with EtOAc (3 × 25 mL). The extract was then washed with aqueous brine solution. After drying over Na_2SO_4 and evaporation, the crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford product **6**.

Yield: 234 mg (80%); pale-yellow solid; mp 91–92 °C.

FTIR (KBr): 3060, 2921, 1673, 1604, 1322, 1183, 812 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.1 Hz, 2 H), 7.85 (d, *J* = 8.1 Hz, 2 H), 7.27 (dd, *J* = 14.7, 7.0 Hz, 6 H), 7.12 (d, *J* = 7.9 Hz, 2 H), 5.11 (dd, *J* = 9.4, 4.3 Hz, 1 H), 3.86 (dd, *J* = 17.9, 9.4 Hz, 1 H), 3.47 (dd, *J* = 18.0, 4.4 Hz, 1 H), 2.45 (s, 3 H), 2.42 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.22, 194.54, 144.15, 143.77, 139.29, 135.25, 133.82, 133.25, 129.83, 129.21 (2C), 128.92, 128.22, 127.40, 45.84, 40.71, 21.65 (2C), 21.20.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{25}O_2S$: 389.1575; found: 389.1583.

2,5-Di-*p*-tolyl-3-(*p*-tolylthio)-1*H*-pyrrole (3da)

To an oven-dried sealed tube equipped with a magnetic stir bar was added 1,4-di-*p*-tolyl-2-(*p*-tolylthio)butane-1,4-dione **6** (100 mg, 0.257 mmol), ammonium formate (41 mg, 0.643 mmol) and acetic acid (2 mL). The tube was then sealed with a screw-type cap and the resulting reaction mixture was placed in an oil bath at 120 °C with stirring. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was cooled to r.t. and extracted with EtOAc (3 × 15 mL). The extract was then washed with aqueous brine solution. After drying over Na_2SO_4 and evaporation, the crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford **3da** (82 mg, 86%).

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Supporting Information

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References

(1) (a) Young, I. S.; Thornton, P. D.; Thompson, A. *Nat. Prod. Rep.* **2010**, *27*, 1801. (b) Fan, H.; Peng, J.; Hamann, M. T.; Hu, J. F. *Chem. Rev.* **2008**, *108*, 264. (c) Walsh, C. T.; Garneau-Tsodikova, S.; Howard-Jones, A. R. *Nat. Prod. Rep.* **2006**, *23*, 517. (d) Bhardwaj, V.; Gumber, D.; Abbot, V.; Dhiman, S.; Sharma, P. *RSC Adv.* **2015**, *5*, 15233.

(2) (a) Biava, M.; Porretta, G. C.; Deidda, D.; Pompei, R.; Tafic, A.; Manettic, F. *Bioorg. Med. Chem.* **2004**, *12*, 1453. (b) Teixeira, C.; Barbault, F.; Rebehmed, J.; Liu, K.; Xie, L.; Lu, H.; Jiang, S.; Fan, B.; Maurel, F. *Bioorg. Med. Chem.* **2008**, *16*, 3039. (c) Hughes, C. C.; Prieto-Davo, A.; Jensen, P. R.; Fenical, W. *Org. Lett.* **2008**, *10*, 629. (d) Sun, X.; Qiu, J.; Strong, S. A.; Green, L. S.; Wasley, J. W. F.; Blonder, J. P.; Colagiovanni, D. B.; Mutka, S. C.; Stout, A. M.; Richards, J. P.; Rosenthal, G. J. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5849. (e) Yang, T.; Ng, W. H.; Chen, H.; Chomchopbun, K.; Huynh, T. H.; Go, M. L.; Kon, O. L. *ACS Med. Chem. Lett.* **2016**, *7*, 807. (f) Ching, K. C.; Kam, Y. W.; Merits, A.; Ng, L. F.; Chai, C. L. *J. Med. Chem.* **2015**, *58*, 9196.

(3) (a) Zhu, Y.; Xu, L.; Zhang, J.; Hu, X.; Liu, Y.; Yin, H.; Lv, T.; Zhang, H.; Liu, L.; An, H.; Liu, H.; Xu, J.; Lin, Z. *Cancer Sci.* **2013**, *104*, 1052. (b) Sartori, A.; Portioli, E.; Battistini, L.; Calorini, L.; Pupi, A.; Vacondio, F.; Arosio, D.; Bianchini, F.; Zanardi, F. *J. Med. Chem.* **2017**, *60*, 248.

(4) (a) McCrindle, B. W.; Ose, L.; Marais, A. D. *J. Pediatr.* **2003**, *143*, 74. (b) Chen, X.; Xiong, F.; Chen, W.; He, Q.; Chen, F. *J. Org. Chem.* **2014**, *79*, 2723. (c) Dias, L. C.; Vieira, A. S.; Barreiro, E. J. *Org. Biomol. Chem.* **2016**, *14*, 2291. (d) Estévez, V.; Villacampa, M.; Menéndez, J. C. *Org. Chem. Front.* **2014**, *1*, 458. (e) Park, W. K. C.; Kennedy, R. M.; Larsen, S. D.; Miller, S.; Roth, B. D.; Song, Y.; Steinbaugh, B. A.; Sun, K.; Tait, B. D.; Kowala, M. C.; Trivedi, B. K.; Auerbach, B.; Askew, V.; Dillon, L.; Hanselman, J. C.; Lin, Z.; Lu, G. H.; Robertson, A.; Sekerke, C. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1151.

(5) (a) Hantzsch, A. *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 1474. (b) Knorr, L. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 1635. (c) Paal, C. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 367.

(6) (a) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084. (b) Zhou, C.; Ma, D. *Chem. Commun.* **2014**, *50*, 3085. (c) Trost, B. M.; Lumb, J.-P.; Azzarelli, J. M. *J. Am. Chem. Soc.* **2011**, *133*, 740. (d) Borra, S.; Chandrasekhar, D.; Newar, U. D.; Maurya, R. A. *J. Org. Chem.* **2019**, *84*, 1042. (e) Zhang, M.; Fang, X.; Neumann, H.; Beller, M. *J. Am. Chem. Soc.* **2013**, *135*, 11384. (f) Jiang, Y.; Chan, W. C.; Park, C.-M. *J. Am. Chem. Soc.* **2012**, *134*, 4104. (g) Daw, P.; Ben-David, Y.; Milstein, D. *J. Am. Chem. Soc.* **2018**, *140*, 11931. (h) Li, B.; Wang, N.; Liang, Y.; Xu, S.; Wang, B. *Org. Lett.* **2013**, *15*, 136. (i) Wang, L.; Ackermann, L. *Org. Lett.* **2013**, *15*, 176. (j) Michlik, S.; Kempe, R. *Nat. Chem.* **2013**, *5*, 141. (k) Rakshit, S.; Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9585.

(7) (a) Estevez, V.; Villacampa, M.; Menéndez, J. C. *Chem. Soc. Rev.* **2010**, *39*, 4402. (b) Estévez, V.; Villacampa, M.; Menéndez, J. C. *Chem. Soc. Rev.* **2014**, *43*, 4633. (c) Dhinakaran, I.; Padmini, V.; Bhuvanesh, N. *ACS Comb. Sci.* **2016**, *18*, 236. (d) Xu, H.; Liu, H.-W.; Chen, K.; Wang, G.-W. *J. Org. Chem.* **2018**, *83*, 6035. (e) Balme, G. *Angew. Chem. Int. Ed.* **2004**, *43*, 6238. (f) Hong, D.; Zhu, Y.-X.; Li, Y.; Lin, X.-F.; Lu, P.; Wang, Y.-G. *Org. Lett.* **2011**, *13*, 4668. (g) Wu, X. D.; Li, K.; Wang, S. S.; Liu, C.; Lei, A. W. *Org. Lett.* **2016**, *18*, 56. (h) Fleige, M.; Glorius, F. *Chem. Eur. J.* **2017**, *23*, 10773.

(8) (a) Boger, D. L.; Boyce, C. W.; Labroli, M. A.; Sehon, C. A.; Jin, Q. *J. Am. Chem. Soc.* **1999**, *121*, 54. (b) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *Tetrahedron Lett.* **2005**, *46*, 2563. (c) Cyr, D. J. St.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2007**, *129*, 12366. (d) Morin, M. S. T.; Cyr, D. J. St.; Arndtsen, B. A. *Org. Lett.* **2010**, *12*, 4916. (e) Lourdusamy, E.; Yao, L.; Park, C.-M. *Angew. Chem. Int. Ed.* **2010**, *49*, 7963.

(9) (a) Antonchick, A. P.; Samanta, R.; Kulikov, K.; Lategahn, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 8605. (b) Takeda, Y.; Kajihara, R.; Kobayashi, N.; Noguchi, K.; Saito, A. *Org. Lett.* **2017**, *19*, 6744. (c) Tang, S.; Liu, K.; Long, Y.; Gao, X.; Gao, M.; Lei, A. *Org. Lett.* **2015**, *17*, 2404. (d) Gao, Q.; Liu, Z.; Wang, Y.; Wu, X.; Zhang, J.; Wu, A. *Adv. Synth. Catal.* **2018**, *360*, 1364.

(10) (a) Jalani, H. B.; Mali, J. R.; Park, H.; Lee, J. K.; Lee, K.; Lee, K.; Choi, Y. *Adv. Synth. Catal.* **2018**, *360*, 4073. (b) Reddy, N. N. K.; Rawat, D.; Adimurthy, S. *J. Org. Chem.* **2018**, *83*, 9412. (c) Wang, Y.; Jiang, C.-M.; Li, H.-L.; He, F.-S.; Luo, X.; Deng, W.-P. *J. Org. Chem.* **2016**, *81*, 8653. (d) Wu, X.; Zhao, P.; Geng, X.; Wang, C.; Wu, Y. D.; Wu, A. X. *Org. Lett.* **2018**, *20*, 688.

(11) (a) Prabagar, B.; Mallick, R. K.; Prasad, R.; Gandon, V.; Sahoo, A. K. *Angew. Chem. Int. Ed.* **2019**, *58*, 2365. (b) Dutta, S.; Mallick, R. K.; Prasad, R.; Gandon, V.; Sahoo, A. K. *Angew. Chem. Int. Ed.* **2019**, *58*, 2289. (c) Yin, G.; Wang, Z.; Chen, A.; Gao, M.; Wu, A.; Pan, Y. *J. Org. Chem.* **2008**, *73*, 3377.

(12) (a) Shibuya, K.; Kawamine, K.; Ozaki, C.; Ohgiya, T.; Edano, T.; Yoshinaka, Y.; Tsunenari, Y. *J. Med. Chem.* **2018**, *61*, 10635. (b) Mahadevegowda, S. H.; Hou, S.; Ma, J.; Keogh, D.; Zhang, J.; Mallick, A.; Liu, X.-W.; Duan, H.; Chan-Park, M. B. *Biomater. Sci.* **2018**, *6*, 1339. (c) Jackson, P. A.; Widen, J. C.; Harki, D. A.; Brummond, K. M. *J. Med. Chem.* **2017**, *60*, 839. (d) Rajeshkumar, V.; Neelamegam, C.; Anandan, S. *Org. Biomol. Chem.* **2019**, *17*, 982. (e) Kalia, D.; Pawar, S. P.; Thopate, J. S. *Angew. Chem. Int. Ed.* **2017**, *56*, 1885.

(13) (a) Gensch, T.; Klauck, F. J. R.; Glorius, F. *Angew. Chem. Int. Ed.* **2016**, *55*, 11287. (b) Vasquez-Cespedes, S.; Ferry, A.; Candish, L.; Glorius, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 5772. (c) Song, Z.; Antonchick, A. P. *Org. Biomol. Chem.* **2016**, *14*, 4804. (d) Mandal, A.; Sahoo, H.; Baidya, M. *Org. Lett.* **2016**, *18*, 3202. (e) Meller, T.; Ackermann, L. *Chem. Eur. J.* **2016**, *22*, 14151.

(14) (a) Yang, F.-L.; Tian, S.-K. *Angew. Chem. Int. Ed.* **2013**, *52*, 4929. (b) Kang, X.; Yan, R.; Yu, G.; Pang, X.; Liu, X.; Li, X.; Xiang, L.; Huang, G. *J. Org. Chem.* **2014**, *79*, 10605. (c) Zhao, W.; Xie, P.; Bian, Z.; Zhou, A.; Ge, H.; Zhang, M.; Ding, Y.; Zheng, L. *J. Org. Chem.* **2015**, *80*, 9167. (d) Sun, J.; Qiu, J.-K.; Zhu, Y.-L.; Guo, C.; Hao, W.-J.; Jiang, B.; Tu, S.-. J. *J. Org. Chem.* **2015**, *80*, 8217. (e) Zhao, X.; Zhang, L.; Lu, X.; Li, T.; Lu, K. *J. Org. Chem.* **2015**, *80*, 2918.

(15) CCDC 1895966 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

(16) (a) Herrera, A.; Alvarez, R. M.; Ramiro, P.; Molero, D.; Almy, J. *J. Org. Chem.* **2006**, *71*, 3026. (b) Griffin, R. J.; Henderson, A.; Curtin, N. J.; Echalier, A.; Endicott, J. A.; Hardcastle, I. R.; Newell, D. R.; Noble, M. E. M.; Wang, L. Z.; Golding, B. T. *J. Am. Chem. Soc.* **2006**, *128*, 6012.

(17) The intermediate compound **6** was completely characterized by ^{1}H and ^{13}C NMR spectroscopy and HRMS. For details, see the Supporting Information.

(18) (a) Chauhan, P.; Mahajan, S.; Enders, D. *Chem. Rev.* **2014**, *114*, 8807. (b) Hoyle, C. E.; Bowman, C. N. *Angew. Chem. Int. Ed.* **2010**, *49*, 1540. (c) Khalili, B.; Jajarmi, P.; Eftekhari-Sis, B.; Hashemi, M. M. *J. Org. Chem.* **2008**, *73*, 2090.