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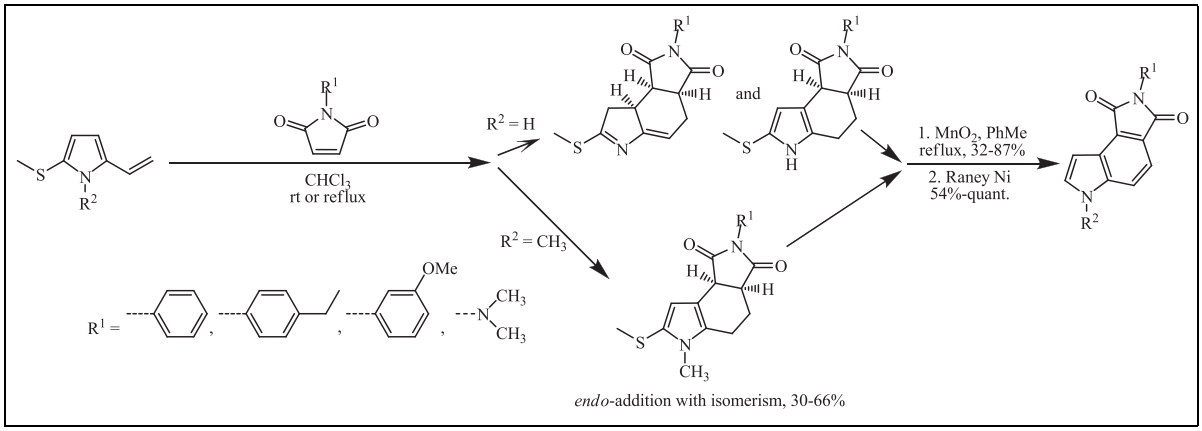
Additional Supporting Information may be found in the online version of this article.
Received May 13, 2011
DOI 10.1002/jhet.1571
Published online 24 June 2013 in Wiley Online Library (wileyonlinelibrary.com).



Diels–Alder reactions of 5-methylthio-2-vinyl-1*H*-pyrroles with maleimides followed by isomerization gave tetrahydroindoles in moderate to good yield. Aromatization using activated MnO_2 in refluxing toluene gave the corresponding 2-methylthioindoles in good yields, and demethylthioation using Raney nickel gave the 2-H indoles in excellent yields. The protection of the adducts produced aromatization in improved yield, demonstrating the effectiveness of the methylthio group as a protecting group for pyrroles; however, 5-methylthio-2-vinylpyrrole was shown to perform with slightly less efficiency than 2-vinylpyrrole in Diels–Alder reactions, indicating the protective group was more deactivating than desired. This route toward indoles offers high convergency and conveniently available starting materials that are easily purified. Bis-methylthioated vinylpyrroles were shown to have potential as highly activated Diels–Alder dienes.

J. Heterocyclic Chem., **50**, 795 (2013).

INTRODUCTION

The ubiquity of indole among biologically active compounds, synthetic [1] and natural [2], has generated continuing interest in useful ways to generate this structure [3]. We have reported that tetrahydroindoles are available via 2-vinylpyrroles derived from acid-catalyzed condensation of pyrrole with cyclic ketones, followed by *in situ* trapping by various maleimides in Diels–Alder reactions [4,5]. We have reported that indoles are available from oxidation of tetrahydroindoles synthesized by Diels–Alder reactions of both *N*-H and *N*-methyl-2-vinylpyrroles [6], and of *N*-*p*-toluenesulfonyl-3-vinylpyrroles[7], with *N*-substituted maleimides. In comparing the efficiency of the Diels–Alder reactions of *N*-H-2-vinylpyrroles and *N*-tosyl-3-vinylpyrrole, we were inspired by the apparent increase in efficiency caused by the use of the *N*-tosyl group, which was later able to be removed. Seeking to expand the usefulness of the technique, we chose to study the use of electron-donating protective groups on the 2-vinylpyrrole diene. Addition of the protective group was aimed to prevent unwanted side reactions while maintaining or increasing reactivity at the vinyl group. The α-position of pyrrole is the most reactive; therefore, we were interested in blocking that location. To enhance the efficiency of the normal electron-demand [4 + 2] cycloaddition, we sought a removable electron-donating functionality that would increase the electron density of the diene through conjugation. We were also interested in placing removable electron-donating groups on the vinyl group itself for temporary enhancement of reactivity. We anticipated that an increase in the reactivity of the diene would broaden the library of indoles conceivably achievable via this method by allowing the use of less electron-deficient dienophiles.

Because of the high reactivity of the pyrrole system, several types of removable groups at the α-position have been used with pyrrole to prevent unwanted reactions [8]. Often used in the setting of porphyrin synthesis [9], most of the methods developed involve electron-withdrawing protecting groups because of a desire to attenuate the reactivity of the pyrrole [10]. These include carboxylate [11] and aldehyde groups [8], which are commonly removed, with aldehydes being oxidized first, by using high temperatures

with strong base or acid, causing saponification followed by decarboxylation. Other electron-withdrawing protective groups used are the more mildly cleavable sulfinyl and sulfonyl groups [12], using Raney nickel or radical-induced reductive desulfonylation with Bu_3SnH/AIBN [13], and the 2,4-dinitrobenzenesulfinyl group, which can be removed by oxidation and then treatment with phenylthiol [12]. Because these protecting groups would decrease the electron density of 2-vinylpyrrole and would therefore likely cause an undesirable decrease in Diels–Alder reactivity, they did not suit our purposes.

Comparatively few examples exist of electron-donating functionalities being used to α-protect pyrrole. The only example, to the best of our knowledge, is the alkylthio group, recently reported by Lindsey and coworkers [14,15]. The alkylthio group has the advantage of being easily removed using Raney nickel, and a variety of 5-alkylthiopyrroles are readily available from the corresponding 5-thiocyanatopyrrole. After protection, further functionalization of pyrrole to the aldehyde via electrophilic aromatic substitution may be enhanced because of the electron-releasing characteristics of the thio-functionality [16]. It was hoped that adequate electron donation would be provided to enhance or maintain Diels–Alder reactivity, without deactivation of the aldehyde toward Wittig methylenation, necessary for formation of the vinyl functionality.

Several examples exist demonstrating the use of removable groups to enhance the efficiency of Diels–Alder reactions. Removable hydrophilic 2-pyridyldimethylsilyl groups on a diene were shown to enhance water solubility as a means of increasing the efficiency of the Diels–Alder reaction [17]. Furan has been shown to have increased reactivity as a Diels–Alder diene when substituted at the 2-position with methylthio [18,19] and phenylthio [19] groups, which were not removed later. To the best of our knowledge, there are no other prior studies that examine the use of removable electron-donating groups in conjugation with the diene as a means to enhance Diels–Alder reactivity.

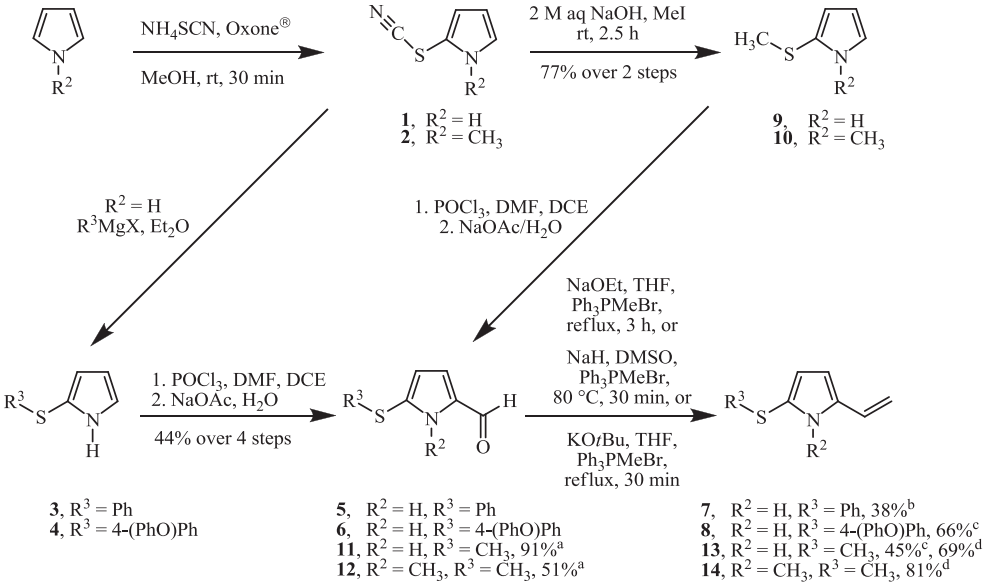
By placing removable electron-donating functionalities on the vinyl group in combination with α-protection, a bis-alkylthio-substituted hyper electron-rich system was envisioned, which later could be dideprotected in a single step. Diels–Alder reactions of sulfonyl-substituted [20,21], sulfinyl-substituted [22], and sulfanyl-substituted [21,23] dienes are known, although none of the examples found involved removal of the sulfur group after the Diels–Alder reaction. Murase *et al*. [24] showed that 3-(1-(methylthio)vinyl)indoles and 3-(1-(benzylthio)vinyl) indoles underwent [4 + 2] cycloadditions with dimethyl acetylenedicarboxylate (DMAD) in 67 and 70% yields, respectively. In the only example found of Diels–Alder reactions of vinylpyrroles having an alkylthio-substituted vinyl group, Murase *et al.* [25] showed that the corresponding 3-(1-benzylthio)vinylpyrrole gave the Diels–Alder adduct with DMAD in 31% yield; surprisingly, the yields we achieved in our work with Diels–Alder reactions of the comparatively deactivated *N*-toluenesulfonyl-3-vinylpyrrole with maleimides were much higher [7]. The poor yields in the pyrrole case of Murase *et al.* could have been caused by predominance of *s-trans* geometry in the diene system because of steric repulsion from the benzylthio functionality; indeed, the authors suggest this is the reason only trace products were found when trying the analogous experiment with DMAD and 2-(1-benzylthio)vinyl-*N*-methylpyrrole. However, this does not explain adequately the 70% yield achieved in the indole work of Murase *et al*., as steric interactions between indole and its 3-(1-benzylthio)vinyl group would be, if anything, greater than those between pyrrole and its 3-(1-benzylthio)vinyl group. We postulated that undesired reactions of the pyrrole at the reactive α-unsubstituted site, which are not possible in the indole case, are more likely to be blamed for the differences in yield. This is a hypothesis we hoped to verify by examining the reactivity of a pyrrole with α-protecting groups in combination with 1-alkylthio-substituted vinyl groups.

RESULTS AND DISCUSSION

Synthesis of starting materials and Diels–Alder reactions

Mono-alkylthioation. Initially, it was hoped that the 5-protective group employed would enhance crystallinity in the 2-vinylpyrrole at room temperature, potentially allowing the benefit of facile purification via recrystallization, as vinylpyrroles are typically unstable on silica gel. With this in mind, 5-phenylthio- and 5-(4-phenoxyphenylthio)-2-vinylpyrroles **7** [26] and **8** were chosen first (Scheme 1). Although Lindsey *et al*. [14] demonstrated that 5-phenylthiopyrrole **3** is deactivated toward deuterium exchange relative to pyrrole itself, it was hoped that any lessening of reactivity would be slight and would be outweighed by ease of purification. Pyrrole was treated with ammonium thiocyanate to give thiocyanatopyrrole **1** [27], which was immediately subjected to a Grignard reaction giving, after time-consuming workups, **3** and **4** [26]. The crude Grignard products were then used in a Vilsmeier–Haack reaction, giving, after flash chromatography, aldehydes **5** and **6** in 44% yield over four steps [28,29]. A Wittig reaction using sodium ethoxide in THF [30], or Corey's modification [31], followed by flash chromatography, gave 5-arylthio-2-vinylpyrroles **7** and **8** in 38 and 66% yields, respectively. Unfortunately, all attempts at crystallizing these pyrroles in a freezer failed; thus, they are probably liquids at room temperature. During chromatography on silica gel, several closely eluting impurities were not fully removed and some decomposition occurred; therefore, the decision was made not to bring vinylpyrroles **7** and

Scheme 1. Synthesis of 5-phenylthio, 5-(4-phenoxyphenyl)thio, and 5-methylthio-2-vinylpyrroles **7**, **8**, **13**, and **14**.



[a] Yield over 2 steps [b] NaOEt, THF method used [c] NaH/DMSO method used [d] KO*t*Bu/THF method used

8 to analytical purity until their reactivity as Diels–Alder dienes could be determined.

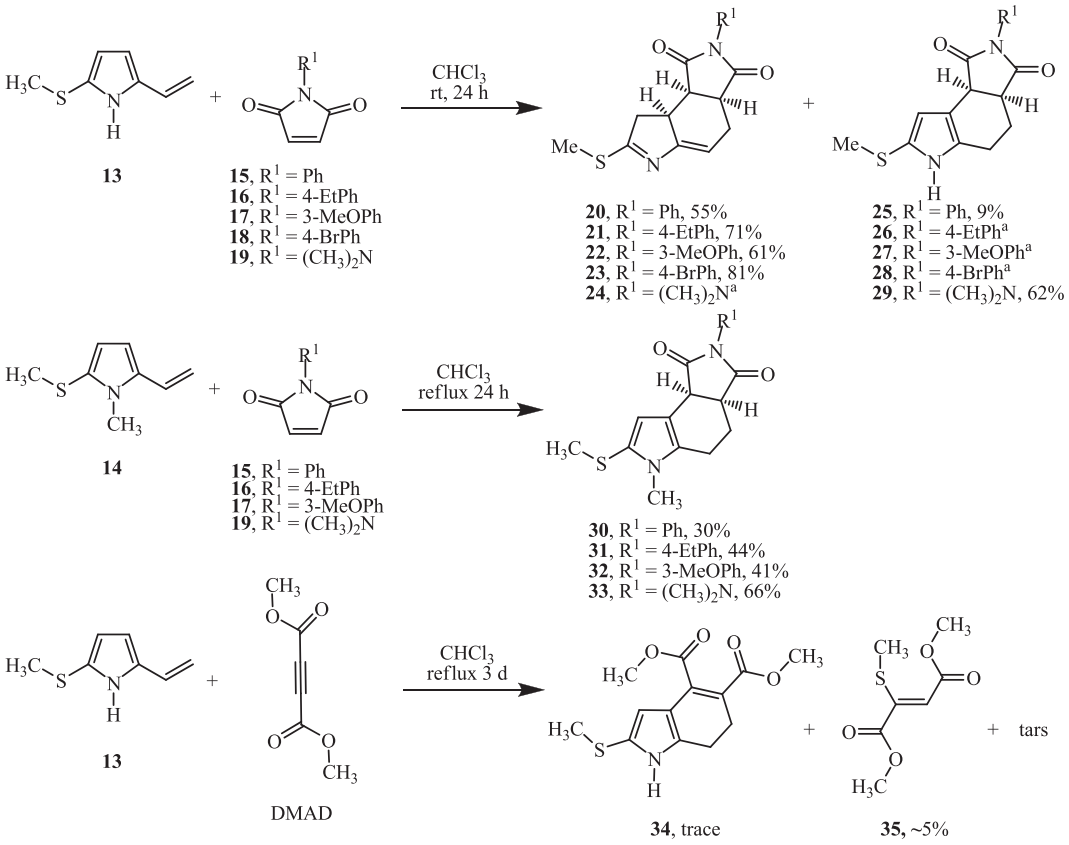
Vinylpyrroles **7** and **8** (1.1 equiv) were stirred with 4-ethylphenylmaleimide **16** in chloroform for several days, but with TLC, no reaction was observed to occur. The vinylpyrrole was used in excess because our past experience with vinylpyrroles indicated any adduct formed would be eluted during chromatography very near to the maleimide [6,7]. The reaction mixtures were refluxed for five days, but still, no new TLC spots appeared; ^{1}H NMR confirmed that only starting materials were present in the reaction mixture. The same results were observed when DMAD was employed as the dienophile.

Arylthio substituents were apparently too electron-withdrawing to maintain reactivity of the diene. The methylthio group was tried next, with some degree of confidence, because studies by Lindsey *et al*. [14] have demonstrated that 5-alkylthio substituents activate pyrrole toward deuterium exchange at the 2-position 1.4-fold to fourfold, but the 3-position was deactivated fivefold to sevenfold, and the 4-position was strongly activated eightfold to 25-fold, as compared with *N*-H-pyrrole. 5-Thiocyanatopyrrole **1** was treated successively with 2 M sodium hydroxide and methyl iodide for 2.5 h, giving 5-methylthiopyrrole **9** in 77% yield over two steps from pyrrole; a small amount of *N*-methyl-5-methylthiopyrrole **10** was also generated (about 5% by mass, as determined by ^{1}H NMR) [32]. The crude **9** was then subjected to a Vilsmeier–Haack reaction [28,29], giving aldehyde **11** in 91% yield, which was conveniently vacuum-distilled for purification; any *N*-methyl-5-methylthio-2-pyrrolecarboxaldehyde **12** that codistilled was easily removed by trituration with hexanes. Lastly, a Wittig reaction was performed on **11** by using potassium *tert*-butoxide in THF [6], which, following vacuum distillation, gave the desired 5-methylthio-2-vinylpyrrole **13** in 69% yield.

Methylthio-protected vinylpyrrole **13** (1.1 equiv) was stirred with 4-ethylphenylmaleimide **16** in chloroform for 24 h, at which point TLC indicated that one new product had been formed and the limiting reagent **16** had been completely consumed (Scheme 2). At first, the ^{1}H NMR of rearranged Diels–Alder adduct **21** was baffling, as there was no *N*-H peak. An extra peak in the carbonyl region of the ^{13}C NMR indicated the distinctive thio–imine functionality of the rearranged adduct [33]; COSY and NOE experiments also verified the structure, with no *exo*-addition product being detectable by NMR.

The *N*-methylvinylpyrrole **14** was synthesized in comparable yield by using the same procedure outlined in Scheme 1 for *N*-H diene **13**, with vacuum distillation being used to purify both aldehyde **12** and vinylpyrrole **14**. In Diels–Alder reactions with vinylpyrrole **13**, the dienophiles *N*-phenyl, *N*-(4-ethylphenyl), *N*-(3-methoxyphenyl), and *N*-(4-bromophenyl)maleimides **15–18** were used, giving rearranged adducts **20–23** in 55, 71, 61, and 81% yields, respectively. Small amounts of adducts **25–28**, which had rearranged to the aromatic pyrrole structure, were detected in all four cases, but because of the small amounts formed, only **25** (9% yield) was isolated and fully characterized. Conversely, Diels–Alder reactions

Scheme 2. Diels–Alder reactions of 5-methylthio-2-vinylpyrroles **13** and **14**.



[a]compounds **24, 26**, **27,** and **28** were detected by TLC but were neither isolated nor further characterized

with *N*-(dimethylamino) **19** formed **24** (<5% yield) and the major adduct rearranged to the aromatic pyrrole structure **29**. The more basic *N*,*N*-dimethylaminomaleimide **19** may be able to facilitate the rearrangement to the aromatic adduct **29** [6] by more easily enabling a 1,3-proton shift than maleimides **15–18**. However, combining adduct **22** with triethylamine in chloroform for about a week produced only minimal rearrangement to the aromatic adduct **27**; thus, we were unable to verify this theory. In another explanation, the loss of steric bulk due to the lack of *N*-phenylmaleimide groups in the adducts **29** and **24** may cause a difference in structure that makes the aromatic adduct **29** more stable than unrearranged adduct **24**. It was decided not to pursue further Diels–Alder reactions with *N*-(4-bromophenyl)maleimide **18** because of difficulties with purification of adduct **23** and because of difficulty experienced in the characterization of 4-bromophenyl compounds in our past work with 2-vinylpyrroles [6]. For *N*-methyl-2-vinylpyrrole **14**, Diels–Alder reactions with maleimides **15–17** and **19** gave adducts **30–33** in 30, 44, 41, and 66% yields, respectively. These yields are lower than those observed in our previous work with 2-vinylpyrroles [6], which had 73 and 92% average yields, respectively, with *N*-H- and *N*-methyl- 2-vinylpyrroles in Diels–Alder reactions run in chloroform.

The results demonstrate that the methylthio group deactivates the vinylpyrrole toward [4 + 2] cycloaddition chemistry; thus, the inductive effect of the sulfur overcomes the effect of its p-electron or d-electron donation to the diene. It is notable that no "double-addition" Michael-type products were detected, such as were seen in our work with unsubstituted 2-vinylpyrroles [6]; just as the methylthio group decreases the electron density of the diene, it also likely makes the adduct a worse Michael component by decreasing its nucleophilicity because of the inductive effect of sulfur. Additionally, rearrangement to the thio–imine may occur too quickly for a Michael addition to occur with the rearranged adduct. The activation energy for formation of Michael addition products from conjugated thio–imines **20–23**, which were stable enough to be easily isolated, is probably higher than that from the adducts with C5–C5a unrearranged double-bonds formed in our work with unsubstituted 2-vinylpyrroles, which we were not able to isolate in that work; rather, we isolated the rearranged aromatic-type isomers of the adducts, with structures similar to those of minor products **25–28**[6]. Further evidence of the stability

of **20–23** was the observation that minor product **25** slowly converted to **20** over several weeks at room temperature, whereas the rearranged adducts isolated in our unsubstituted 2-vinylpyrrole work were not observed to isomerize [6].

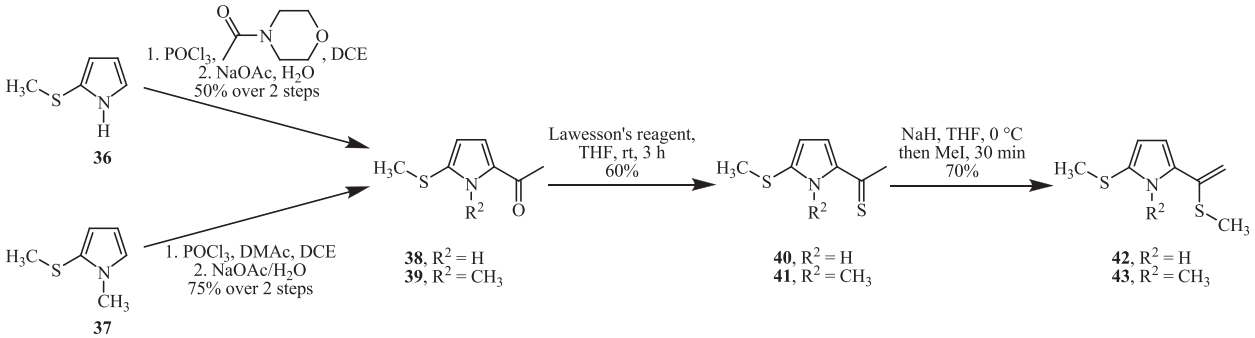
The Diels–Alder reaction of vinylpyrrole **13** with DMAD was also attempted (Scheme 2). The DMAD was added slowly to the vinylpyrrole at 0°C, but black tars formed rapidly, likely indicating a polymerization reaction. After flash chromatography with ethyl acetate/hexanes, only ~10% mass recovery occurred, with most of the material remaining at the top of the column, producing further evidence that the main reaction was not the desired Diels–Alder reaction. The mass peak corresponding to the expected adduct **34** was detected using HRMS, but the adduct was not generated in sufficient quantity to isolate and characterize. Rather, the major product isolated was dimethyl 2-methylthiomaleate **35**[34], corresponding to the result of a Michael addition of the methylthio group to DMAD, with demethylthioation of the vinylpyrrole. The soft electrophilic characteristics of DMAD may make a Michael addition from sulfur, a soft nucleophile, preferred over a Diels–Alder reaction [35], although extensive variation of the reaction conditions was not attempted.

Bis-methylthioation. To synthesize bis-methylthioated vinylpyrroles **42** and **43**, 2-methylthiopyrroles **36** and **37** [27] were first acetylated using a Vilsmeier–Haack reaction, giving 2-acetyl-5-methylthiopyrroles **38** and **39** (Scheme 3) [13,36]; Muchowski *et al*. [29] have demonstrated that the 5-methylthio group has a directing effect to give acylation exclusively at the 2-position. Although *N*-H-acetylpyrrole **38** was a crystalline solid that could be recrystallized for facile purification, *N*-methylacetylpyrrole **39** was a liquid that on TLC showed several closely spotting impurities; two fractional vacuum distillations gave **39** in a purity of approximately 7:1 by mass. 2-Acetyl-5-methylthiopyrroles **38** and **39** were then treated with Lawesson's reagent [37], giving *N*-H- and *N*-methyl- 2-acetyl-5-methylthiopyrroles **40** and **41** [24,25].

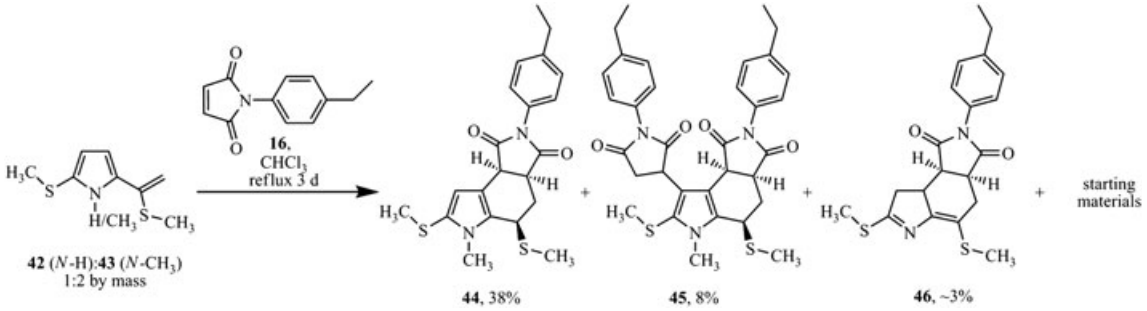
The thioacetylpyrroles **40** and **41** were then treated at 0°C with sodium hydride (1.5 equiv) for 10 min followed by the addition of methyl iodide (1.5 equiv) and stirring for 30 min at 0°C, giving the 5-methylthio-2-(1-(methylthio)vinyl)pyrroles **42** and **43** [24,25]. From TLC analysis, it was seen that *N*-H-thioacetylpyrrole **40** gave a single product in the first 15 min, which then began to convert into another product with a higher R_f value. Comparison of TLCs and ^{1}H NMR analysis of the products revealed that the *N*-H-vinylpyrrole **42** was being transformed into the *N*-methylvinylpyrrole **43** in the presence of sodium hydride and methyl iodide. The ratio of *N*-methyl to *N*-H product depended on the time allowed before the reaction was quenched with aqueous ammonium chloride and was generally at least 1:1 by mass. For the reaction to run long enough for complete conversion of the starting *N*-H-thioacetylpyrrole **40** to the corresponding vinylpyrroles, a larger amount of *N*-methylvinylpyrrole was produced, with a ratio of **42** and **43** being approximately 1:2 by mass. Perhaps the use of lower temperatures could help avoid this problem in the future. When flash chromatography of the mixture of **42** and **43** was attempted on silica gel by using ethyl acetate/hexanes, significant degradation of the vinylpyrroles was observed. However, when generated from *N*-methyl-thioacetylpyrrole **41**, vinylpyrrole **43** had impurities caused by the use of impure **41**. These impurities did not allow formation of the pure vinylpyrroles that were desired for ease of analysis of the subsequent Diels–Alder reactions. Therefore, the mixture of bis-methylthioated vinylpyrroles **42** and **43** formed from *N*-H-thioacetylpyrrole **40** was used as the starting material.

The approximately 1:2 mixture of bis-methylthioated *N*-H and *N*-methylvinylpyrroles **42** and **43** was allowed to react with 1-(4-ethylphenyl)maleimide **16** (0.8 equiv) in chloroform at room temperature (Scheme 4). The vinylpyrrole was used in excess to simplify purification because previous experience has shown that the Diels–Alder adduct is generally eluted during column chromatography very near to the maleimide starting material. After 3 days, all the *N*-H-vinylpyrrole **42** was consumed, but both *N*-methylvinylpyrrole **43** and maleimide **16** remained. The reaction was refluxed, and after 5 h, little change was observed by TLC

Scheme 3. Synthesis of bis-methylthioated vinylpyrroles **42** and **43**.



Scheme 4. Diels–Alder reactions of bis-methylthioated vinylpyrroles **42** and **43**.



analysis; therefore, in a desire to prevent destruction or rearrangement of the products that were anticipated to have formed, the reaction was stopped at that time, with some *N*-methylvinylpyrrole **43** and maleimide **16** still remaining in the reaction mixture.

The crude reaction mixture was subjected to chromatography and, as expected, the remaining *N*-methylvinylpyrrole **43** suffered degradation, and several other new TLC spots formed. Along with the maleimide **16**, three new products were isolated, all of which were formed during the Diels–Alder reaction. The major product isolated was the expected rearranged adduct **44** from *N*-methylvinylpyrrole **43**. Additionally, a double-addition type product **45** was isolated, likely formed by a Michael addition between the adduct from *N*-methylvinylpyrrole **43** and another molecule of maleimide **16**. Although in our prior work with unsubstituted 2-vinylpyrroles, double-addition products were formed from a Michael addition at the 5-position of the adducts, this is the first example of a Michael addition from an adduct at the β-pyrrole position. There appears to be no precedent for this type of double-addition product in the literature. These types of products may not have formed in our earlier work, or elsewhere in the present work, because the activation energy required to form **45** could be lowered by resonance stabilization of the thio–imine functionality with the 5-methylthio group in the Michael addition intermediate (Fig. 1). A third new product, compound **46**, was isolated but did not seem to be stable and was not able to be purified enough to be fully characterized. However, in consideration of ^{1}H and ^{13}C NMR, TLC (prior to decomposition, a single spot in 1:1 ethyl acetate/hexanes, $R_f \approx 0.42$), and HRMS data ($M + Na^+$ calculated 409.1016, found 409.1026), it is likely that product **46** was a rearranged adduct formed from the *N*-H-vinylpyrrole **42**. The isolated vinylpyrrole **43** in combination with the uncharacterized degradation products resulting from chromatography of **43** approximately completed the mass balance for this reaction.

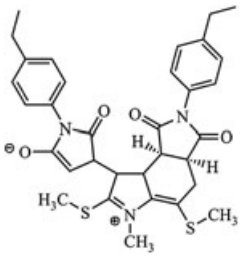
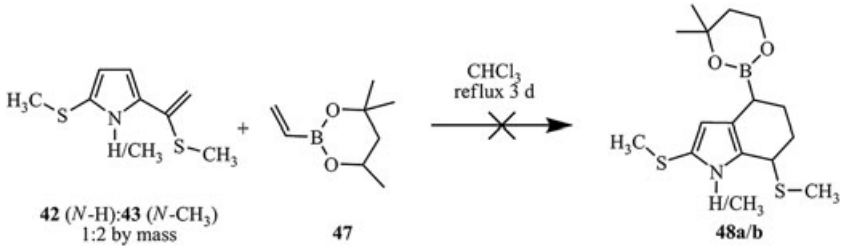


Figure 1. A possible stabilized intermediate toward double-addition product **45**.

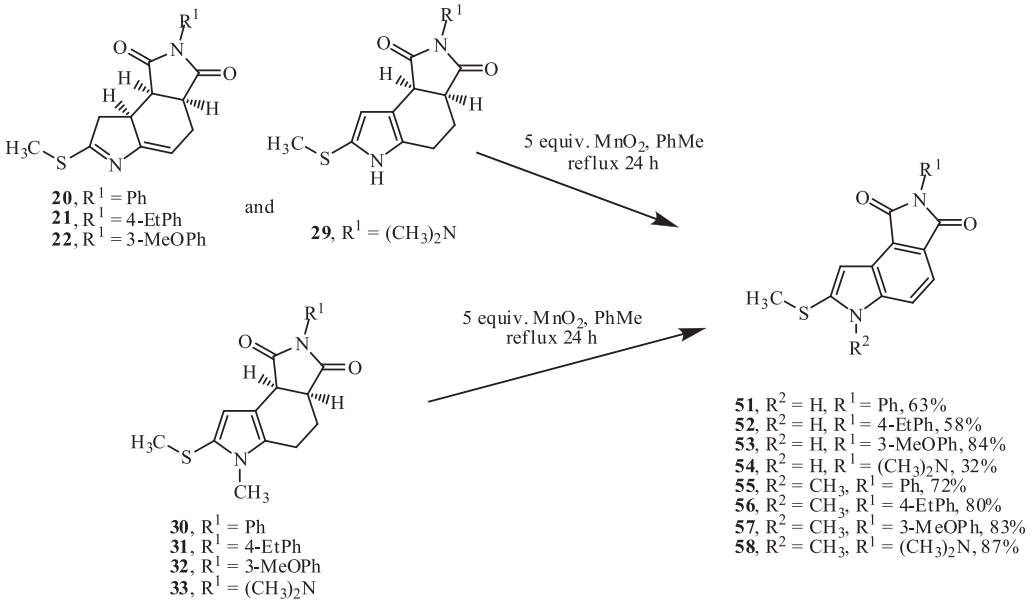
The mixture of bis-methylthioated *N*-methyl and *N*-H-vinylpyrroles **42** and **43** was allowed to react with vinylboronic acid 2-methyl-2,4-pentanediol ester **47** (0.8 equiv) in chloroform at room temperature in hope that the reaction would give an adduct that could be easily used as a Suzuki coupling partner (Scheme 5) [38]. After 3 days at room temperature, no reaction was observed by TLC, so the mixture was refluxed. After 5 days, no reaction was detected by TLC and an ^{1}H NMR of the crude reaction showed no sign of the desired Diels–Alder products **48a** and **48b**.

Aromatization of Diels–Alder adducts. Tetrahydroindoles **20–22**, **29**, and **30–33** were aromatized using activated MnO_2 (5 equiv) in refluxing toluene for 3 h, giving indoles **52–58** in 32–87% yields (Scheme 6). The activated MnO_2 was generated from manganese(II) sulfate and potassium permanganate [39], which was also used in our prior work with 2- and 3-vinypyrroles [6,7]. The average yield from these dehydrogenations was 69%, slightly less than the 74% average yield of aromatizations in our 3-vinylpyrrole work and higher than the 54% average achieved in aromatizing the adducts in our prior work with 2-vinylpyrroles. This indicates that the methylthio group may provide some degree of stability to the tetrahydroindoles, which possessed conjugated thio–imine functionality or a methylated heterocyclic nitrogen, during the aromatization process. Tetrahydroindole **29** lacked the stabilization that the conjugated thio–imines **20–22** possessed, potentially contributing to the high degree of degradation observed when it was allowed to reflux with activated MnO_2 in toluene, resulting in a lower yield (32%) than in the aromatization of **20–22** (63–84% yields).

Scheme 5. Attempted Diels–Alder reaction between vinylboronate **47** and vinylpyrroles **42** and **43**.



Scheme 6. Aromatization of Diels–Alder adducts.



Deprotection of indoles. To cleave carbon–sulfur bonds, a variety of organometallic or metallic reagents may be used, of which Raney nickel is employed most frequently [14,40]. Methylthioated indoles **51–58** were deprotected using excess Raney nickel in acetone over 2 h at room temperature, giving indoles **59–66** in 54–100% yields (Scheme 7).

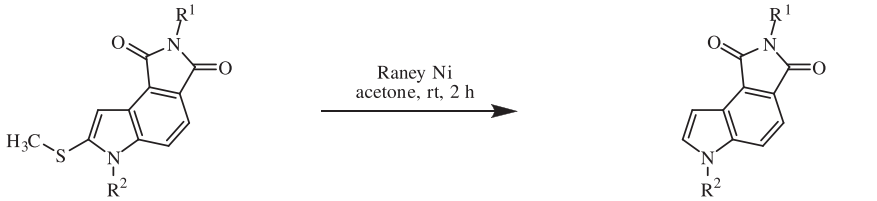
CONCLUSION

Diels–Alder reactions of 5-methylthio-2-vinyl-1*H*-pyrroles with maleimides followed by isomerization gave tetrahydroindoles in moderate to good yield. Aromatization using activated MnO_2 in refluxing toluene gave the corresponding 2-methylthioindoles in good yields, and demethylthioation using Raney nickel gave the 2-H indoles in excellent yields. The protection of the adducts resulted in aromatization in improved yields, demonstrating the effectiveness of the methylthio group as a protecting group for pyrroles; however, 5-methylthio-2-vinylpyrrole was shown to perform with slightly less efficiency than 2-vinylpyrrole in Diels–Alder reactions, indicating the protective group to be more deactivating than desired. This route toward indoles offers high convergency and conveniently available starting materials that are easily purified. Bis-methylthioated vinylpyrroles were shown to have potential as highly activated Diels–Alder dienes, but either steric bulk or a thermodynamic preference for the *s-trans* configuration of the diene prevented the increase in efficiency that was desired.

EXPERIMENTAL

General. Solvents and reagents were purchased and used as received. Flash chromatography was performed using 230–450 mesh silica gel. MPLC refers to medium pressure liquid chromatography, performed using 325–635 mesh silica gel. Ethyl acetate/hexanes were used as eluent unless otherwise indicated. TLC analyses were performed on plastic-backed plates precoated with 0.2 mm silica with F_{254} indicator. Infrared spectra were recorded on a 4000 FT-IR spectrometer; only the most intense and/or diagnostic peaks are reported.

Scheme 7. Deprotection of indoles **51–58**.



51, R^2 = H, R^1 = Ph
52, R^2 = H, R^1 = 4-EtPh
53, R^2 = H, R^1 = 3-MeOPh
54, R^2 = H, R^1 = $(CH_3)_2N$
55, R^2 = CH_3, R^1 = Ph
56, R^2 = CH_3, R^1 = 4-EtPh
57, R^2 = CH_3, R^1 = 3-MeOPh
58, R^2 = CH_3, R^1 = $(CH_3)_2N$

59, R^2 = H, R^1 = Ph, 68%
60, R^2 = H, R^1 = 4-EtPh, 78%
61, R^2 = H, R^1 = 3-MeOPh, 100%
62, R^2 = H, R^1 = $(CH_3)_2N$, 54%
63, R^2 = CH_3, R^1 = Ph, 95%
64, R^2 = CH_3, R^1 = 4-EtPh, 88%
65, R^2 = CH_3, R^1 = 3-MeOPh, 87%
66, R^2 = CH_3, R^1 = $(CH_3)_2N$, 92%

High-resolution mass spectra were recorded with a time-of-flight instrument using electrospray ionization with PEG as an internal calibrant. For NMR spectra, chemical shifts (δ) were referenced to the solvent. ^{13}C NMR spectra were proton-decoupled. Melting points were uncalibrated. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. Petroleum ether refers to the 35–60°C boiling point fraction.

2-Thiocyanato-1H-pyrrole (1) [27]. In a 1-L round-bottom flask, Oxone® (184.434 g, 0.3 mol) was added to a mixture of ammonium thiocyanate (22.836 g, 0.3 mol) and pyrrole (13.89 mL, 13.418 g, 0.2 mol) in methanol (150 mL). The thick mixture was stirred vigorously at RT for 30 min. The round-bottom flask was immersed in an ice bath, with vigorous stirring and ice was added slowly until heat was no longer evolved, and then water was added (100 mL). The mixture was vacuum-filtered on a fritted glass funnel, the filter cake was washed with dichloromethane (3 × 25 mL), the washings and filtrate were placed in a separatory funnel, and the organic layer was removed. The water layer was extracted with dichloromethane (5 × 25 mL), the combined organics were washed with brine and dried over anhydrous sodium sulfate, and the solvents were removed using a rotating evaporator, giving **1** as a dark-colored burnt-rubber-smelling liquid, used immediately as is in the next step. *Caution*: If 2-thiocyanatopyrrole **1** is allowed to contact the skin, even in small amounts, dark red splotches appear beneath the skin over the next 24 h and, although painless, they do not disappear for up to a month [41].

2-Methylthio-1H-pyrrole (9) [32]. Methyl iodide (37.43 mL, 85.16 g, 0.6 mol) was added to the freshly prepared 2-thiocyanatopyrrole **1**. Carefully, by using an ice bath to maintain temperature at RT, 2 N NaOH (0.30 L, 0.60 mol) was added, and the mixture was stirred at RT for 2.5 h. The mixture was acidified to neutrality using 1 N HCl and extracted with dichloromethane (3 × 75 mL). The dichloromethane was washed with water (50 mL) and brine (50 mL) and dried over sodium sulfate, and the solvent was evaporated using a rotating evaporator, giving **9** (34.52 g, 76% over two steps) as a dark-colored slightly viscous liquid. ^1H NMR data matched those found in the literature [42]. The material was used in the next step without further purification.

1-Methyl-2-methylthio-1H-pyrrole (10) [27,32]. In each of two 1-L round-bottom flasks, Oxone® (184.43 g, 0.300 mol) was added to a mixture of ammonium thiocyanate (22.83 g, 0.300 mol) and 1-methylpyrrole (17.8 mL, 16.223 g, 0.2 mol) in methanol (150 mL). The thick mixture was stirred vigorously at RT for 12 h, preferably using a mechanical stirrer. The round-bottom flask was immersed in an ice bath, with continued vigorous stirring, and ice was added slowly until heat was no longer evolved, and then water was added (100 mL). The mixture was vacuum-filtered on a fritted glass funnel, the filter cake was washed with dichloromethane (5 × 25 mL), the washings and filtrate were placed in a separatory funnel, and the organic layer was removed. The water layer was extracted with dichloromethane (3 × 50 mL), the combined organics were washed with brine and dried over anhydrous sodium sulfate, the solvents were removed using a rotating evaporator, and the crude products from each of the two reactions were combined, giving crude 1-methyl-2-thiocyanato-1*H*-pyrrole **2** as a dark-colored foul-smelling liquid, used immediately as is in the next step [43]. Methyl iodide (74.86 mL, 170.33 g, 1.2 mol) was added to the freshly prepared 2-thiocyanatopyrrole **2**. By using an ice bath to maintain temperature at RT, 2 N NaOH (0.60 L, 1.2 mol) was added carefully, and the mixture was stirred at RT for 2.5 h. The mixture was acidified to neutrality using 1 N HCl and extracted with dichloromethane (3 × 150 mL). The dichloromethane was washed with water (100 mL) and brine (100 mL) and dried over sodium sulfate, and the solvent was removed using a rotating evaporator, giving **10** (38.33 g, 75% over two steps) as a dark-colored slightly viscous liquid. The ^1H NMR data matched those found in the literature [43,44]. The material was used without further purification in the next step.

5-Methylthio-1H-pyrrole-2-carboxaldehyde (11) [45]. The literature procedure [28] was used, with pyrrole **9** (34.5 g, 0.305 mol), followed by vacuum distillation at about 40–60°C/0.15 mm Hg. It was difficult to record an accurate boiling point during distillation because the compound crystallized on the thermometer and needed to be melted with a heat gun. The distillate was triturated with hexanes (5 × 30 mL) to remove any codistilled 5-methylthio-*N*-methyl-1*H*-pyrrole-2-carboxaldehyde **12**. The solid was recrystallized from dichloromethane/petroleum ether, giving **11** (39.16 g, 91%) as white crystals: mp 101.5–102.5°C; ^1H NMR (300 MHz, $CDCl_3$, δ) 9.50 (bs, 1H, 1-H), 9.41 (s, 1H, formyl-H), 6.96 (dd, J = 3.8, 2.6 Hz, 1H, 3-H), 6.31 (dd, J = 3.6, 2.4 Hz, 1H, 4-H), 2.52 (s, 3H, SCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 178.5, 137.1, 134.3, 123.9, 113.4, 18.4.

1-Methyl-5-methylthio-1H-pyrrole-2-carboxaldehyde (12). The literature procedure [28] was used, with pyrrole **10** (50.88 g, 0.40 mol), followed by vacuum distillation at 59°C/0.02 mm Hg, giving **12** (24.09 g, 51%) as white crystals: mp 24–25°C; the ^{1}H NMR data matched those found in the literature [44].

2-Methylthio-5-vinyl-1H-pyrrole (13). Potassium *t*-butoxide (14.000 g, 0.125 mol) was added slowly to methyltriphenylphosphonium bromide (33.581 g, 0.094 mol) in THF (100 mL) at 0°C. The bright yellow color characteristic of the ylide was observed immediately. The mixture was stirred at RT under nitrogen for 30 min and then cooled to 0°C. A solution of aldehyde **11** (8.75 g, 0.062 mol) in THF (20 mL) was added over 5 min, with stirring, and the mixture was refluxed for 30 min until TLC analysis indicated the reaction was complete. The mixture was allowed to cool to RT and filtered using a fritted glass funnel, and the solids on the frit were washed with diethyl ether (4 × 25 mL). The filtrate was washed with saturated $NaHSO_3$ (50 mL), saturated Na_2CO_3 (50 mL), and brine (50 mL) and dried over anhydrous Na_2SO_4. The solvents were removed using a rotating evaporator, and the residue was vacuum-distilled at 39.0°C/0.02 mm Hg, giving **13** as a colorless liquid (5.99 g, 69%): ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.47 (bs, 1H, 1-H), 6.53 (dd, *J* = 18.0, 11.4 Hz, 1H, 1′-H), 6.36 (dd, *J* = 3.6, 2.4, 1H, pyrrole-β-H), 6.24 (dd, *J* = 3.0, 3.0 Hz, 1H, pyrrole-β-H), 5.34 (d, *J* = 18.0 Hz, 1H, 2′-H *cis* to pyrrole), 5.07 (d, *J* = 11.1 Hz, 1H, 2′-H *trans* to pyrrole), 2.40 (s, 3H, SCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 133.7, 127.5, 123.4, 116.7, 110.7, 109.8, 22.3; IR (CH_2Cl_2 thin film, cm^{-1}) 3445(bs), 3053(s), 2987(w), 2925(w), 1633(m), 1538(w), 1453 (m), 1424(m), 1374(w), 1314(w), 1266(s), 1135(m), 1036(m), 982(m), 893(m), 781(s), 739(s), 705(s), 638(m). *Anal.* Calcd for C_7H_9NS: C, 60.39; H, 6.52; N, 10.06. Found: C, 60.13; H, 6.32; N, 9.84.

1-Methyl-2-methylthio-5-vinyl-1H-pyrrole (14). The procedure for **13** was used using aldehyde **12** (14.37 g, 92.6 mmol). The residue was distilled at 57.0°C/0.02 mm Hg, giving **14** as a colorless liquid (11.46 g, 81%): ^{1}H NMR (300 MHz, $CDCl_3$, δ) 6.63 (dd, *J* = 17.4, 11.1, 1H, 1′-H), 6.39–6.41 (m, 2H, pyrrole-β-H), 5.57 (d, *J* = 17.4 Hz, 1H, 2′-H *cis* to pyrrole), 5.15 (d, *J* = 11.4 Hz, 1H, 2′-H *trans* to pyrrole), 3.72 (s, 3H, NCH_3), 2.29 (s, 3H, SCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 135.6, 126.7, 125.2, 116.6, 112.9, 106.8, 31.4, 20.0; IR (CH_2Cl_2 thin film, cm^{-1}) 3092(w), 3049(m), 2984(m), 2943(m), 2921(s), 2849(w), 2305(w), 1803(w), 1692(w), 1622(m), 1461(w), 1435 (s), 1408(m), 1388(w), 1306(m), 1265(s), 1200(w), 1151(w), 1092 (w), 1038(w), 1018(w), 978(m), 968(m), 897(m), 766(s), 742(s), 705(s), 630(m). *Anal.* Calcd for $C_8H_{11}NS$: C, 62.70; H, 7.24; N, 9.14. Found: C, 62.81; H, 6.99; N, 8.86.

General method for Diels–Alder reactions. A mixture of vinylpyrrole (1.1 equiv) and dienophile (1.0 equiv) in chloroform (20 mL) was stirred at RT for 24 h and, if TLC analysis indicated insignificant consumption of the dienophile, was refluxed for 24 h, at which point the TLC analysis indicated completion of the reaction. The solvent was removed using a rotating evaporator. The crude adduct was purified by MPLC using ethyl acetate/hexanes as eluent followed by recrystallization from dichloromethane/petroleum ether, giving the desired product in moderate to good yields.

7-Methylthio-2-phenyl-4,8,8aα,8bα-tetrahydro-2H,3aαH-pyrrolo[3,4-e]indole-1,3-dione(20). The general method was used with vinylpyrrole **13** (2.78 g, 20.0 mmol) and maleimide **15** (3.16 g, 18.3 mmol) at RT for 24 h, giving **25** and **20** (3.117 g, 55%) as a brown powder: mp 139–141°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.33–7.46 (m, 3H, Ph), 7.14–7.19 (m, 2H, Ph), 5.80 (ddd, *J* = 7.5, 3.5, 2.3 Hz, 1H, 5-H), 3.81 (dd, *J* = 17.1, 3.9 Hz, 1H, 8-H), 3.46 (dd, *J* = 8.9, 7.1 Hz, 1H, 8bα-H), 3.29 (ddd, *J* = 8.8, 7.1, 1.6 Hz, 1H, 3aα-H), 3.06 (ddddd, *J* = 9.6, 7.1, 3.9, 2.3, 2.3 Hz, 1H, 8aα-H), 2.98 (ddd, *J* = 15.5, 7.7, 1.7 Hz, 1H, 4β-H), 2.98 (dd, *J* = 17.4, 9.6 Hz, 1H, 8-H), 2.50 (s, 3H, SCH_3), 2.35 (dddd, *J* = 15.3, 6.9, 3.6, 2.3 Hz, 1H, 4α-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 182.6, 179.3, 177.4, 159.8, 132.4, 129.8, 129.4, 127.2, 107.3, 41.9, 41.1, 40.2, 37.6, 26.0, 14.6; IR (KBr, cm^{-1}) 3100 (w), 3050(w), 2960(m), 2943(m), 2926(m), 2890(m), 2842(m), 1774(m), 1703(s), 1594(w), 1533(m), 1498(m), 1450(w), 1422 (m), 1391(s), 1340(m), 1314(w), 1287(m), 1204(s), 1095(m), 1074(m), 1023(w), 996(w), 953(w), 863(w), 840(w), 815(w), 800 (w), 780(w), 754(m), 695(w); HRMS *m/z* ($M + Na^+$) calcd 335.0825, found 335.0826. *Anal.* Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.51; H, 5.37; N, 8.77.

2-(4-Ethylphenyl)-7-methylthio-4,8,8aα,8bα-tetrahydro-2H,3aαH-pyrrolo[3,4-e]indole-1,3-dione (21). The general method was used with vinylpyrrole **13** (2.68 g, 19.3 mmol) and maleimide **16** (3.53 g, 17.5 mmol) at RT for 24 h, giving **21** (4.230 g, 71%) as a cream-colored powder: mp 140–142°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.27 (d, *J* = 7.8 Hz, 2H, Ph), 7.09 (d, *J* = 8.4 Hz, 2H, Ph), 5.81 (ddd, *J* = 7.5, 3.6, 2.7 Hz, 1H, 5-H), 3.83 (dd, *J* = 17.3, 4.4 Hz, 1H, 8-H), 3.47 (dd, *J* = 8.9, 7.4 Hz, 1H, 8bα-H), 3.29 (ddd, *J* = 8.7, 7.1, 1.7 Hz, 1H, 3aα-H), 3.08 (ddddd, *J* = 9.7, 7.4, 4.6, 2.6, 2.0 Hz, 1H, 8aα-H), 3.00 (ddd, *J* = 15.5, 7.5, 1.8 Hz, 1H, 4β-H), 2.99 (dd, *J* = 17.4, 9.9 Hz, 1H, 8-H), 2.67 (q, *J* = 7.7 Hz, 2H, CH_2CH_3), 2.52 (s, 3H, SCH_3), 2.36 (dddd, *J* = 15.5, 6.7, 3.5, 2.2 Hz, 1H, 4α-H), 1.24 (t, *J* = 7.7 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 181.9, 178.8, 176.8, 159.2, 145.0, 129.3, 128.7, 126.4, 106.7, 41.3, 40.5, 39.6, 37.1, 28.7, 25.4, 15.5, 14.0; IR (KBr, cm^{-1}) 3053(m), 2967(s), 2927(s), 2848(m), 2595(w), 1771(w), 1702 (s), 1528(s), 1514(s), 1459(w), 1397(s), 1337(m), 1313(m), 1283(m), 1251(w), 1205(s), 1092(m), 1077(m), 1052(w), 1020 (w), 996(w), 958(w), 897(w), 862(w), 839(m), 799(m), 657(w); HRMS *m/z* ($M + Na^+$) calcd 363.1138, found 363.1136. *Anal.* Calcd for $C_{19}H_{20}N_2O_2S$: C, 67.03; H, 5.92; N, 8.23. Found: C, 66.99; H, 6.00; N, 8.18.

2-(3-Methoxyphenyl)-7-methylthio-4,8,8aα,8bα-tetrahydro-2H,3aαH-pyrrolo[3,4-e]indole-1,3-dione (22). The general method was used with vinylpyrrole **13** (2.023 g, 14.5 mmol) and maleimide **17** (2.684 g, 13.2 mmol) at RT for 24 h, giving **22** (2.744 g, 61%) as an orange powder: mp 151–152°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.34 (dd, *J* = 8.3, 8.3 Hz, 1H, 5′-H), 6.92 (ddd, *J* = 8.4, 2.7, 0.9 Hz, 1H, 4′-H), 6.77 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H, 6′-H), 6.71 (dd, *J* = 2.1, 2.1 Hz, 1H, 2′-H), 5.81 (ddd, *J* = 7.5, 3.6, 2.7 Hz, 1H, 5-H), 3.82 (dd, *J* = 17.1, 4.2 Hz, 1H, 8-H), 3.80 (s, 3H, OCH_3), 3.47 (dd, *J* = 8.9, 7.4 Hz, 1H, 8bα-H), 3.29 (ddd, *J* = 8.8, 7.1, 1.6 Hz, 1H, 3aα-H), 3.08 (ddddd, *J* = 10.4, 7.4, 4.2, 2.7, 2.1 Hz, 1H, 8aα-H), 3.00 (ddd, *J* = 15.6, 7.5, 1.5 Hz, 1H, 4β-H), 2.99 (dd, *J* = 17.0, 10.4 Hz, 1H, 8-H), 2.52 (s, 3H, SCH_3), 2.36 (dddd, *J* = 15.6, 7.0, 3.5, 2.1Hz, 1H, 4α-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 182.0, 178.6, 176.6, 160.1, 159.2, 132.8, 129.9, 118.9, 114.6, 112.5, 106.7, 55.5, 41.3, 40.5, 39.6, 37.1, 25.4, 14.0; IR (KBr, cm^{-1}) 3068(m), 3003(m), 2957(s), 2923(s), 2834(m), 2571(w), 1775 (w), 1703(s), 1607(m), 1590(m), 1522(m), 1490(m), 1457(m), 1427(m), 1383(s), 1337(m), 1313(m), 1286(s), 1255(s), 1227 (m), 1190(s), 1166(s), 1135(m), 1094(m), 1083(m), 1048(m),

1023(w), 960(w), 865(w), 843(w), 810(m), 783(w), 690(m); HRMS *m/z* ($M+Na^+$) calcd 365.0931, found 365.0919. *Anal*. Calcd for $C_{18}H_{18}N_2O_3S$: C, 63.14; H, 5.30; N, 8.18. Found: C, 62.82; H, 5.18; N, 7.98.

2-(4-Bromophenyl)-7-methylthio-4,8,8aα,8bα-tetrahydro-2H,3aαH-pyrrolo[3,4-e]indole-1,3-dione(23). The general method was used with vinylpyrrole **13** (1.54 g, 11 mmol) and maleimide **18** (2.5 g, 10 mmol) at RT for 24 h, giving **23** (3.54 g, 81%) as cream-colored crystals: mp 188–190°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 7.66 (d, J = 8.4 Hz, 2H, Ph), 7.06 (d, J = 8.7 Hz, 2H, Ph), 5.62 (ddd, J = 6.9, 3.4, 3.3 Hz, 1H, 5-H), 3.54 (dd, J = 8.7, 7.0 Hz, 1H, 8bα-H), 3.52 (dd, J = 16.2, 4.2 Hz, 1H, 8-H), 3.31 (ddd, J = 8.2, 7.2, 1.5 Hz, 1H, 3aα-H), 3.07 (ddddd, J = 9.9, 7.0, 4.2, 3.4, 2.5 Hz, 1H, 8aα-H), 2.99 (dd, J = 16.9, 9.9 Hz, 1H, 8-H), 2.65 (ddd, J = 15.6, 7.2, 1.5 Hz, 1H, 4β-H) 2.42 (s, 3H, SCH_3), 2.29 (dddd, J = 15.6, 7.2, 3.3, 1.5 Hz, 1H, 4α-H); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 181.9, 179.8, 178.1, 160.6, 133.1, 132.4, 130.0, 122.4, 107.1, 42.3, 41.4, 40.2, 37.6, 26.0, 14.6.

7-Methylthio-2-phenyl-3aα,4,5,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione(25). The procedure for compound **20** was used and then isolated by MPLC, and followed with recrystallization from methylene chloride/petroleum ether, giving **25** (513 mg, 9%) as a cream-colored powder: mp 166–168°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.99 (bs, 1H, 6-H), 7.31–7.46 (m, 3H, Ph), 7.22–7.27 (m, 2H, Ph), 6.50 (d, J = 2.7 Hz, 1H, 8-H), 4.07 (d, J = 8.1 Hz, 1H, 8bα-H), 3.41 (ddd, J = 8.0, 5.0, 5.0 Hz, 1H, 3aα-H), 2.56–2.63 (m, 2H, 5-H), 2.48 (dddd, J = 13.5, 4.6, 4.6, 4.6 Hz, 1H, 4β-H), 2.33 (s, 3H, SCH_3), 2.02 (dddd, J = 13.0, 7.8, 7.8, 5.3 Hz, 1H, 4α-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 178.6, 177.5, 132.6, 130.1, 129.7, 129.1, 126.9, 121.8, 114.8, 112.4, 40.9, 40.7, 22.4, 22.4, 20.1; IR (KBr, cm^{-1}) 3350(bs), 3050(w), 2921(m), 2851(m), 1776(w), 1709(s), 1595(w), 1498(m), 1453(w), 1436(w), 1382(s), 1309(w), 1290(w), 1258(w), 1236(w), 1185(m), 1152(m), 1086(m), 1040 (w), 1010(w), 995(w), 970(w), 910(w), 873(w), 823(w), 806(w), 789(w), 740(m), 693(m); HRMS *m/z* ($M+Na^+$) calcd 335.0825, found 335.0824. *Anal*. Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97, for $C_{17}H_{16}N_2O_2S{\cdot}0.33H_20$: C, 64.15; H, 5.27; N, 8.80. Found: C, 64.15; H, 5.33; N, 8.50.

2-Dimethylamino-7-methylthio-3aα,4,5,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (29). The general method was used with vinylpyrrole **13** (1.76 g, 12 mmol) and maleimide **19** (1.61 g, 11 mmol) with reflux for 24 h, giving **29** (2.08 g, 62%) as a peach-colored glass: mp 104–106°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.20 (bs, 1H, 6-H), 6.40 (d, J = 2.7 Hz, 1H, 8-H), 3.80 (d, J = 8.1 Hz, 1H, 8bα-H), 3.12 (ddd, J = 7.8, 5.4, 5.4 Hz, 1H, 3aα-H), 2.81 (s, 6-H, NCH_3), 2.20–2.55 (m, 2H, 5-H), 2.29 (s, 3-H, SCH_3), 2.26 (dddd, J = 13.8, 8.7, 5.7, 5.4 Hz, 1H, 4β-H), 1.95 (dddd, J = 13.8, 5.4, 5.4, 5.4 Hz, 1H 4α-H); ^{13}C NMR (300 MHz, $CDCl_3$, δ) 178.0, 176.9, 130.0, 121.6, 114.6, 111.9, 44.6, 39.2, 39.0, 22.7, 22.3, 20.2; IR (CH_2Cl_2 thin film, cm^{-1}) 3314(w), 2975(m), 2937(m), 1717(s), 1709(s), 1559(s), 1360 (m), 1196(m), 1140(m), 1083(m), 1017(m0, 800(m), 732(m); HRMS *m/z* ($M+Na^+$) calcd 302.0934, found 302.0941. *Anal*. Calcd for $C_{14}H_{19}N_3O_2S$: C, 55.89; H, 6.13; N, 15.04. Found: C, 55.82; H, 6.05; N, 14.82.

6-Methyl-7-methylthio-2-phenyl-3aα,4,5,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (30). The general method was used with vinylpyrrole **14** (2.069 g, 13.05 mmol) and maleimide **15** (2.054 g, 11.86 mmol) with reflux for 24 h, giving **30** (1.153 g, 30%) as cream-colored crystals: mp 130–131°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.31–7.45 (m, 3H, Ph), 7.22–7.27 (m, 2H, Ph), 6.54 (s, 1H, 8-H), 4.07 (ddd, J = 8.1, 1.3, 1.3 Hz, 1H, 8bα-H), 3.55 (s, 3H, NCH_3), 3.41 (ddd, J = 8.0, 4.9, 4.9 Hz, 1H, 3aα-H), 2.49–2.63 (m, 3H, 5-H, 4β-H), 2.60 (s, 3H, SCH_3), 2.04 (dddd, J = 13.3, 9.9, 5.9, 5.1 Hz, 1H, 4α-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 178.6, 177.5, 132.7, 131.6, 129.7, 129.0, 126.9, 124.1, 114.8, 111.1, 41.1, 40.8, 30.8, 22.2, 21.9, 19.7; IR (KBr, cm^{-1}) 3061(w), 2980(w), 2952(m), 2918(m), 2845(m), 1774(m), 1711(s), 1595(m), 1496(m), 1448(m), 1389(s), 1346(m), 1289(m), 1210(s), 1187(s), 1155(s), 1138(m), 1098(m), 1071(w), 1051(w), 1028(w), 964(m), 911(w), 890(m), 873(m), 830 (m), 795(m), 780(m), 750(s), 698(m); HRMS m/z ($M+Na^+$) calcd 349.0982, found 349.0989. *Anal*. Calcd for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.56; N, 8.58. Found: C, 66.25; H, 5.76; N, 8.40.

2-(4-Ethylphenyl)-6-methyl-7-methylthio-3aα,4,5,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (31). The general method was used with vinylpyrrole **14** (2.069 g, 13.05 mmol) and maleimide **16** (2.386 g, 11.86 mmol) with reflux for 24 h, giving **31** (1.827 g, 44%) as cream-colored crystals: mp 185–186°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.25 (d, J = 9.3 Hz, 2H, Ph), 7.14 (d, J = 8.8 Hz, 2H, Ph), 6.53 (s, 1H, 8-H), 4.06 (ddd, J = 7.8, 1.2, 1.2 Hz, 1H, 8bα-H), 3.55 (s, 3H, NCH_3), 3.40 (ddd, J = 8.0, 4.9, 4.9 Hz, 1H, 3aα-H), 2.65 (q, J = 7.6 Hz, 2H, CH_2CH_3), 2.52–2.66 (m, 2H, 5-H), 2.52 (dddd, J = 13.8, 4.7, 4.7, 4.7 Hz, 1H, 4β-H), 2.25 (s, 3H, SCH_3), 2.04 (dddd, J = 13.3, 9.8, 6.0, 5.2 Hz, 1H, 4α-H), 1.22 (t, J = 7.5 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 178.8, 177.6, 145.2, 131.6, 130.2, 129.2, 126.8, 124.0, 114.8, 111.2, 41.1, 40.8, 30.8, 29.3, 22.2, 21.9, 19.7, 16.2; IR (KBr, cm^{-1}) 3090(w), 3040(w), 2930(s), 2927(s), 2894(m), 2868 (m), 2845(m), 1776(w), 1706(s), 1607(w), 1513(m), 1444(m), 1392(s), 1345(m), 1289(m), 1256(w), 1232(w), 1207(m), 1175(s), 1137(m), 1105(w), 1055(w), 1023(w), 998(w), 963(m), 952(w), 909(w), 874(w), 839(w), 820(m), 797(m), 770(w), 730(w), 695 (m); HRMS *m/z* ($M+Na^+$) calcd 377.1292, found 377.1293. *Anal*. Calcd for $C_{20}H_{22}N_2O_2S$: C, 67.77; H, 6.26; N, 7.90. Found: C, 67.55; H, 6.00; N, 7.60.

2-(3-Methoxyphenyl)-6-methyl-7-methylthio-3aα,4,5,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (32). The general method was used with vinylpyrrole **14** (2.069 g, 13.05 mmol) and maleimide **17** (2.410 g, 11.86 mmol) with reflux for 24 h, giving **32** (1.729 g, 41%) as cream-colored crystals: mp 161–162°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.32 (dd, J = 8.3, 8.3 Hz, 1H, 5′-H), 6.78–6.91 (m, 3H, 2′-H, 4′-H, 6′-H), 6.54 (s, 1H, 8-H), 4.06 (d, J = 8.1 Hz, 1H, 8bα-H), 3.78 (s, 3H, OCH_3), 3.55 (s, 3H, NCH_3), 3.40 (ddd, J = 8.1, 5.0, 5.0 Hz, 1H, 3aα-H), 2.46-2.68 (m, 3H, 5-H, 4β-H), 2.25 (s, 3H, SCH_3), 2.04 (dddd, J = 14.4, 9.5, 5.3, 4.8 Hz, 1H, 4α-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 178.6, 177.4, 160.6, 133.7, 131.6, 130.4, 124.1, 119.2, 114.9, 114.8, 112.8, 111.1, 56.1, 41.1, 40.8, 30.8, 22.2, 21.9, 19.7; IR (KBr, cm^{-1}) 3103(m), 3060(w), 3034(w), 2996 (m), 2977(m), 2944(s), 2928(s), 2914(s), 2849(m), 2839(m), 1781(w), 1708(s), 1606(m), 1591(m), 1567(w), 1493(m), 1443(m), 1390(s), 1368(m), 1348(w), 1332(w), 1316(w), 1292(s), 1252(m), 1230(m), 1208(m), 1176(s), 1137(m), 1095(w), 1039(m), 1008(w), 968(w), 953(w), 903(w), 889(w), 859(w), 835(w), 808(w), 795(m), 754(w), 734(w), 695(m), 653(w); HRMS *m/z* ($M+Na^+$) calcd 379.1088, found 379.1087. *Anal*. Calcd for $C_{19}H_{20}N_2O_3S$: C, 64.02; H, 5.66; N, 7.86. Found: C, 63.89; H, 5.62; N, 7.63.

2-Dimethylamino-6-methyl-7-methylthio-3aα,4,5,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (33). The general method was used with vinylpyrrole **14** (5.84 g, 0.038 mol) and maleimide **19** (3.56 g, 0.025 mol) with reflux for 24 h, giving **33**

(3.98 g, 66%) as colorless crystals: mp 133–134°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 6.50 (s, 1H, 8-H), 3.81 (d, J = 7.8 Hz, 1H, 8bα-H), 3.52 (s, 3H, NCH_3), 3.13 (ddd, J = 7.9, 5.3, 5.1 Hz, 1H, 3aα-H), 2.83 (s, 6H, $N(CH_3)_2$), 2.42–2.62 (m, 2H, 5-H), 2.30 (dddd, J = 13.5, 5.2, 5.2, 5.1 Hz, 1H, 4β-H), 2.23 (s, 3H, SCH_3), 1.99 (dddd, J = 14.0, 8.7, 5.5, 5.5 Hz, 1H, 4α-H) ^{13}C NMR (300 MHz, $CDCl_3$, δ) 178.0, 176.9, 131.5, 124.0, 114.7, 110.7, 44.6, 39.3, 39.1, 30.8, 22.6, 21.8, 19.8; IR (KBr, cm^{-1}) 2940 (w), 1776(m), 1706(s), 1654(m), 1560(w), 1442(m), 1369(m), 1346(w), 1292(w), 1187(m), 1148(m), 1107(w), 1033(w), 968 (w), 906(w), 875(w), 823(w), 802(w), 768(w), 630(w); HRMS *m/z* ($M + Na^+$) calcd 316.1091, found 316.1093. *Anal*. Calcd for $C_{14}H_{19}N_3O_2S$: C, 57.31; H, 6.53; N, 14.32. Found: C, 57.11; H, 6.38; N, 14.12.

2-Methylthio-5-thioacetyl-1H-pyrrole (40) [24,25]. 2-Methylthio-5-acetylpyrrole **38** [13,36] (8.657 g, 55.773 mmol) was dissolved in THF (250 mL). Lawesson's reagent (27.07 g, 66.928 mmol) was added, and the mixture was stirred at RT for 3 h, at which time TLC indicated complete consumption of the starting material. The solvent was removed using a rotating evaporator, and the crude product was flash chromatographed on a short silica gel column by using 1:2 ethyl acetate : hexanes. The solvent was removed using a rotating evaporator, giving **40** (7.735 g, 81%) as brown plates: mp 75–76°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 9.50 (bs, 1H, 1-H), 6.94 (dd, J = 3.9, 2.4 Hz, 1H, 3-H), 6.27 (dd, J = 4.2, 2.7 Hz, 1H, 4-H), 2.84 (s, 3H, thioacetyl), 2.52 (s, 3H, thioacetyl); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 143.2, 140.8, 116.0, 114.0, 34.1, 17.7; IR (KBr, cm^{-1}) 3291 (bs), 2977(m), 1709(w), 1524(m), 1459(m), 1432(m), 1379(s), 1341(m), 1319(m), 1227(m), 1190(m), 1142(m), 1078(w), 1059 (m), 990(w), 970(w), 969(w), 931(w), 865(w), 832(s), 760(s). *Anal*. Calcd for $C_7H_9N_1S_2$: C, 49.09; H, 5.30; N, 8.18. Found: C, 48.98; H, 5.46; N, 7.99.

1-Methyl-2-methylthio-5-thioacetyl-1H-pyrrole (41) [24,25]. Crude *N*-methyl-2-methylthio-5-acetylpyrrole **39** [13,36] (9.15 g, 54.064 mmol, included approximately 13% 2- and 3-acetyl-*N*-methylpyrrole by mass) was dissolved in THF (250 mL). Lawesson's reagent (26.24 g, 64.877 mmol) was added, and the mixture was stirred at RT for 3 h, at which time TLC indicated complete consumption of the starting materials. The solvent was removed using a rotating evaporator, and the crude product was flash chromatographed on a short silica gel column by using 1:2 ethyl acetate : hexanes. The solvent was removed using a rotating evaporator, giving **41** (5.207 g, 52%) as a dark-colored foul-smelling liquid that included approximately 15% impurities by mass: ^{1}H NMR (300 MHz, $CDCl_3$, δ, only peaks from **41** reported) 7.17 (d, J = 4.5 Hz, 1H, 3-H), 6.17 (d, J = 4.8 Hz, 1H, 4-H), 4.07 (s, 3H, 1-CH_3), 2.95 (s, 3H, thioacetyl), 2.48 (s, 3H, SCH_3); HRMS *m/z* ($M + H^+$) calcd 186.0412, found 186.0402.

2-(4-Ethylphenyl)-5β,7-bis(methylthio)-3aα,4,5α,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (44). A mixture of the vinylpyrroles **42** and **43** [2.919 mmol, generated freshly from 2-methylthio-5-thioacetyl-1*H*-pyrrole **40** (500 mg), approximately 1:2 **42** : **43** by mass [24,25]], and the maleimide **16** (1.1 equiv) in chloroform was stirred at RT for 3 d and then refluxed for 5 h. The solvent was removed using a rotating evaporator. The crude adduct was purified by MPLC using ethyl acetate/hexanes as eluent, followed by recrystallization from methylene chloride/petroleum ether, giving **44** (405 mg, 38%) as a white powder: mp 136–137°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.25 (d, J = 8.7 Hz, 2H, Ph), 7.19 (d, J = 8.7 Hz, 2H, Ph), 6.50 (s, 1H, 7-H), 4.13 (d, J = 9.3 Hz, 1H, 8bα-H), 4.07 (dd, J = 3.9, 2.4 Hz, 1H, 5α-H), 3.65 (s, 3H, 6-Me), 3.33 (ddd, J = 9.2, 7.1, 2.0 Hz, 1H, 3aα-H), 3.03 (ddd, J = 14.6, 2.0, 2.0 Hz, 1H, 4β-H), 2.65 (q, J = 7.6 Hz, 2H, CH_2CH_3), 2.27 (s, 3H, MeS), 2.18 (s, 3H, MeS), 2.16 (ddd, J = 14.7, 6.9, 3.9 Hz, 1H, 4α-H), 1.22 (t, J = 7.7 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 179.5, 177.3, 145.2, 130.7, 129.9, 129.2, 127.0, 125.9, 114.6, 112.7, 39.6, 38.4, 38.2, 30.5, 29.3, 26.4, 21.4, 16.13, 16.11; IR (KBr, cm^{-1}) 2965(m), 2916(m), 1775(w), 1705(s), 1514(m), 1444(m), 1432(m), 1395(m), 1347(w), 1309(w), 1296(w), 1258 (w), 1216(m), 1191(m), 1139(w), 1109(w), 960(w), 870(w), 837(w), 817(m), 789(w), 761(w); HRMS *m/z* ($M + Na^+$) calcd 423.1172, found 423.1187. *Anal*. Calcd for $C_{21}H_{24}N_2O_2S_2$: C, 62.97; H, 6.04; N, 6.99. Found: C, 62.77; H, 5.95; N, 6.77.

2-(4-Ethylphenyl)-8-(1-(4-ethylphenyl)-2,5-dioxopyrrolidin-3-yl)-5β,7-bis(methylthio)-3aα,4,5α,8bα-tetrahydro-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (45). By using the procedure for **44** and MPLC to isolate **45** from the crude product, recrystallization from methylene chloride/petroleum ether followed, giving **45** (54 mg, 7%) as white crystals: mp 207–208°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.32 (d, J = 8.7 Hz, 2H, Ph), 7.24–7.27 (m, 4H, Ph), 7.16 (d, J = 8.4 Hz, 2H, Ph), 4.80 (dd, J = 9.8, 6.8 Hz, 1H, 3′-H), 4.26 (d, J = 9.3 Hz, 1H, 8bα-H), 4.10 (dd, J = 3.8, 2.3 Hz, 1H, 5α-H), 3.72 (s, 3H, 6-Me), 3.28 (ddd, J = 9.0, 7.4, 1.5 Hz, 1H, 3aα-H), 3.24 (dd, J = 9.6, 17.7, 9.6 Hz, 1H, 4′-H), 3.05 (dd, J = 18.0, 6.6 Hz, 1H, 4′-H), 3.01 (ddd, J = 14.6, 2.0, 2.0 Hz, 1H, 4β-H), 2.69 (q, J = 7.6 Hz, 2H, CH_2CH_3), 2.66 (q, J = 7.6 Hz, 2H, CH_2CH_3), 2.20 (s, 3H, MeS), 2.19 (s, 3H, MeS), 2.13 (ddd, J = 14.5, 7.1, 3.9 Hz, 1H, 4α-H), 1.26 (t, J = 7.5 Hz, 3H, $-CH_2CH_3$), 1.23 (t, J = 7.5 Hz, 3H, $-CH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 179.4, 179.1, 177.5, 176.8, 145.4, 145.3, 130.80, 130.76, 130.5, 129.4, 129.2, 127.4, 126.9, 39.2, 38.6, 38.5, 38.2, 30.8, 29.33, 29.31, 26.2, 16.2, 16.1; IR (KBr, cm^{-1}) 2960(m), 2923(m), 1776(w), 1709(s), 1514(m), 1457(w), 1419 (w), 1388(m), 1353(w), 1177(s), 986(w), 970(w), 877(w), 829 (m), 753(m), 732(w); HRMS *m/z* ($M + Na^+$) calcd 624.1962, found 624.1984. *Anal*. Calcd for $C_{33}H_{35}N_3O_4S_2$: C, 65.86; H, 5.86; N, 6.98. Found: C, 65.98; H, 6.01; N, 6.84.

General method for dehydrogenation of the Diels–Alder adducts. A mixture of the adduct (1 equiv) and activated MnO_2 [39] (5 equiv) in toluene (20 mL) was stirred under reflux for 24 h at which point TLC analysis indicated complete conversion of the starting materials. The mixture was cooled to RT and vacuum-filtered through a fine glass-fritted funnel. The insoluble manganese salts were washed with several portions of dichloromethane until the washings ran colorless (5 × 20 mL), and the combined organic filtrate and washings were evaporated to dryness using a rotating evaporator.Following evaporation, the crude mixtures were purified by MPLC with ethyl acetate/hexanes as eluent and succeeded by recrystallization from dichloromethane/petroleum ether, giving the desired product in fair to good yield.

7-Methylthio-2-phenyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (51). The general method was used with adduct **20** (3.138 g, 10.05 mmol), giving **51** (1.941 g, 63%) as yellow crystals: mp 282–283°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 12.29 (bs, 1H, 6-H), 7.64 (d, J = 8.1 Hz, 1H, 5-H), 7.54 (d, J = 8.1 Hz, 1H, 4-H), 7.48–7.55 (m, 2H, Ph), 7.37–7.45 (m, 3H, Ph), 6.68 (s, 1H, 7-H), 2.64 (s, 3H, SCH_3); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 169.4, 169.0, 143.6, 143.1, 133.5, 129.9, 128.7, 128.4, 124.8, 124.6, 121.1, 116.4, 116.2, 99.0, 34.6; IR (KBr, cm^{-1}) 3289 (bs), 3095(w), 3060(w), 2980(w), 2995(w), 2930(w), 1749(m),

1703(s), 1598(w), 1494(m), 1468(m), 1420(w), 1386(s), 1367(s), 1324(w), 1283(m), 1219(m), 1151(m), 1093(m), 1018(w), 960(w), 943(w), 844(w), 826(w), 793(w), 766(w), 752(s), 725(w), 686(m), 667(w), 625(m); HRMS *m/z* ($M+Na^+$) calcd 331.0512, found 331.0511. *Anal*. Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.22; H, 3.92; N, 9.08, for $C_{17}H_{12}N_2O_2S{\cdot}0.37H_2O$: C, 64.82; H, 4.08; N, 8.89. Found: C, 64.83; H, 3.80; N, 8.76.

2-(4-Ethylphenyl)-7-methylthio-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (52). The general method was used with adduct **21** (5.263 g, 15.46 mmol), giving **52** (3.016 g, 58%) as yellow crystals: mp 280–282°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 12.30 (bs, 1H, 6-H), 7.67 (dd, *J* = 8.3, 0.8 Hz, 1H, 5-H), 7.56 (d, *J* = 8.1 Hz, 1H, 4-H), 7.36 (d, *J* = 8.7 Hz, 2H, Ph), 7.33 (d, *J* = 8.4 Hz, 2H, Ph), 6.71 (dd, *J* = 1.8, 0.6 Hz, 1H, 8-H), 2.67 (q, *J* = 7.6 Hz, 2H, C*H*$_2$CH$_3$), 2.67 (s, 3H, SCH$_3$), 1.23 (t, *J* = 7.7 Hz, 3H, CH$_2$C*H*$_3$); ^{1}H NMR (300 MHz, Acetone-d_6, δ) 11.28 (bs, 1H, 6-H), 7.76 (dd, *J* = 8.1, 0.9 Hz, 1H, 5-H), 7.61 (d, *J* = 8.4 Hz, 1H, 4-H), 7.44 (d, *J* = 8.7 Hz, 2H, Ph), 7.38 (d, *J* = 8.7 Hz, 2H, Ph), 6.85 (d, *J* = 2.1, 0.9 Hz, 1H, 8-H), 2.74 (q, *J* = 7.6 Hz, 2H, C*H*$_2$CH$_3$), 2.74 (s, 3H, −SCH$_3$), 1.29 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 168.9, 168.5, 143.8, 143.0, 142.5, 130.4, 128.7, 127.8, 124.2, 124.1, 120.6, 115.7, 115.5, 98.4, 28.4, 16.2, 16.0; IR (KBr, cm^{-1}) 3352(bs), 3041(w), 2971(m), 2927(m), 2856(w), 1753(m), 1695(s), 1516(m), 1491(m), 1464(m), 1456(m), 1419(w), 1386(s), 1365(s), 1318(w), 1277(m), 1232(m), 1180(w), 1154(m), 1117(w), 1097(m), 1061(w), 1016(w), 949(w), 810(w), 801(w), 760(m), 750(m); HRMS *m/z* ($M+Na^+$) calcd 359.0825, found 359.0836. *Anal*. Calcd for $C_{19}H_{16}N_2O_2S$: C, 67.84; H, 4.79; N, 8.33. Found: C, 67.60; H, 5.20; N, 8.44.

2-(3-Methoxyphenyl)-7-methylthio-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (53). The general method was used with adduct **22** (2.260 g, 6.60 mmol), giving **53** (1.879 g, 84%) as yellow crystals: mp 232–233°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 12.31 (bs, 1H, 6-H), 7.66 (d, *J* = 8.4 Hz, 1H, 5-H), 7.55 (d, *J* = 8.1 Hz, 1H, 4-H), 7.43 (dd, *J* = 8.1, 8.1 Hz, 1H, 5′-H), 6.98–7.06 (m, 3H, 2′-H, 4′-H, 6′-H), 6.70 (d, *J* = 0.9 Hz, 1H, 8-H), 3.79 (s, 3H, OCH$_3$), 2.67 (s, 3H, SCH$_3$); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 168.7, 168.3, 160.0, 143.0, 142.5, 134.0, 130.0, 124.2, 124.0, 120.5, 120.0, 115.8, 115.5, 113.7, 98.5, 55.8, 16.0; IR (KBr, cm^{-1}) 3316(bs), 2957(w), 2922(w), 1753(m), 1703(s), 1607(m), 1495(m), 1459(m), 1387(m), 1371(m), 1316(w), 1288(w), 1264(m), 1217(m), 1181(w), 1152(w), 1098(m), 1034(w), 1022(w), 977(w), 946(w), 902(w), 852(w), 800(w), 768(m), 715(m), 680(w); HRMS *m/z* ($M+Na^+$) calcd 361.0638, found 361.0643. *Anal*. Calcd for $C_{18}H_{14}N_2O_3S$: C, 63.89; H, 4.17; N, 8.28. Found: C, 63.71; H, 4.12; N, 8.13.

2-Dimethylamino-7-methylthio-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (54). The general method was used with adduct **29** (0.400 g, 1.43 mmol), giving **54** (120 mg, 32%) as an orange solid: mp 259–261°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.55 (bs, 1H, N-H), 7.56 (d, 1H, 6.0 Hz, 4-H), 7.50 (dd, 1H, 6.0, 0.75 Hz, 5-H), 6.87 (dd, 1H, 1.2, 0.7 Hz, 8-H), 3.06 (s, 6H, NCH$_3$), 2.63 (s, 3H, SCH$_3$); ^{13}C NMR (500 MHz, $CDCl_3$, δ) 168.4, 168.3, 141.5, 141.1, 124.0, 122.6, 119.3, 115.5, 114.5, 100.1, 44.9, 16.6, 0.86; IR (KBr, cm^{-1}) 3191(s), 2957(m), 2919 (m), 1779(m), 1734(m), 1718(s), 1701(s), 1656(w), 1652(w), 1555(w), 1440(w), 1363(w), 1202(w), 1142(w), 1083(w), 789(w); HRMS *m/z* ($M+Na^+$) calcd 298.0621, found 298.0617. *Anal.* Calcd for $C_{13}H_{13}N_3O_2S$: C, 56.71; H, 4.76; N, 15.26. Found: C, 56.56; H, 4.97; N, 15.08.

6-Methyl-7-methylthio-2-phenyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (55). The general method was used with adduct **30** (0.314 g, 0.962 mmol), giving **55** (224 mg, 72%) as light-orange crystals: mp 239–240°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 7.87 (dd, *J* = 8.3, 0.75 Hz, 1H, 5-H), 7.61 (d, *J* = 8.4 Hz, 1H, 4-H), 7.38–7.55 (m, 5H, Ph), 6.74 (d, *J* = 0.9 Hz, 1H, 8-H), 3.80 (s, 3H, NCH$_3$), 2.66 (s, 3H, SCH$_3$); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 169.3, 168.9, 146.1, 143.5, 133.4, 130.0, 128.8, 128.4, 124.9, 123.9, 121.2, 116.0, 115.6, 98.7, 31.8, 16.9; IR (KBr, cm^{-1}) 3120(m), 3060(m), 3010(m), 2930(m), 1753(m), 1705(s), 1595(w), 1502(m), 1477(s), 1426(m), 1378(s), 1343(m), 1318(m), 1293(m), 1232(m), 1182(m), 1168(w), 1095(m), 1063(w), 998(w), 958(w), 907(w), 849(w), 820(w), 802(w), 740 (m), 730(m), 692(m), 662(w); HRMS *m/z* ($M+Na^+$) calcd 345.0669, found 345.0679. *Anal*. Calcd for $C_{18}H_{14}N_2O_2S$: C, 67.06; H, 4.38; N, 8.69. Found: C, 66.89; H, 4.37; N, 8.52.

2-(4-Ethylphenyl)-6-methyl-7-methylthio-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (56). The general method was used with adduct **31** (0.320 g, 0.903 mmol), giving **56** (261 mg, 80%) as yellow crystals: mp 200–201°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 7.87 (d, *J* = 8.4 Hz, 1H, 5-H), 7.60 (d, *J* = 8.4 Hz, 1H, 4-H), 7.26–7.41 (m, 4H, Ph), 6.75 (s, 1H, 8-H), 3.80 (s, 3H, NCH$_3$), 2.66 (s, 3H, SCH$_3$), 2.66 (q, *J* = 7.7 Hz, 2H, C*H*$_2$CH$_3$), 1.21 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 169.5, 169.0, 146.0, 144.5, 143.5, 131.0, 129.3, 128.4, 124.9, 123.9, 121.3, 115.9, 115.5, 98.7, 31.7, 29.0, 16.9, 16.8; IR (KBr, cm^{-1}) 3140(w), 3105(w), 3050(w), 2953(m), 2926 (m), 2880(m), 1761(m), 1703(s), 1625(w), 1515(m), 1480(m), 1423(w), 1376(s), 1342(m), 1294(w), 1236(w), 1180(w), 1118(w), 1084(m), 1000(w), 962(w), 855(w), 844(w), 823(w), 750(m), 721(w), 677(w), 665(w); HRMS *m/z* ($M+Na^+$) calcd 373.0982, found 373.0982. *Anal*. Calcd for $C_{20}H_{18}N_2O_2S$: C, 68.55; H, 5.18; N, 7.99. Found: C, 68.31; H, 5.40; N, 7.83.

2-(3-Methoxyphenyl)-6-methyl-7-methylthio-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (57). The general method was used with adduct **32** (0.307 g, 0.861 mmol), giving **57** (251 mg, 83%) as a yellow powder: mp 237–238°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 7.88 (dd, *J* = 8.1, 0.6 Hz, 1H, 5-H), 7.61 (d, *J* = 8.1 Hz, 1H, 4-H), 7.41 (dd, *J* = 8.0 Hz, 1H, 5′-H), 6.97-7.05 (m, 3H, 2′-H, 4′-H, 6′-H), 6.76 (d, *J* = 0.8 Hz, 1H, 8-H), 3.81 (s, 3H, NCH$_3$), 3.77 (s, 3H, OCH$_3$), 2.69 (s, 3H, SCH$_3$); IR (KBr, cm^{-1}) 3100(w), 3030(w), 3005(w), 2960(w), 2940(w), 1752(m), 1710(s), 1607(w), 1591(w), 1491(m), 1478 (m), 1437(w), 1407(w), 1378(s), 1343(m), 1310(w), 1290(m), 1256(s), 1213(m), 1182(m), 1100(m), 1044(m), 995(w), 969 (w), 862(w), 831(w), 750(m), 722(w), 680(w), 620(w); HRMS *m/z* ($M+Na^+$) calcd 375.0775, found 375.0781. *Anal*. Calcd for $C_{19}H_{16}N_2O_3S$: C, 64.76; H, 4.58; N, 7.95, for $C_{19}H_{16}N_2O_3S{\cdot}0.31H_2O$: C, 63.78; H, 4.68; N, 7.83. Found: C, 63.76; H, 4.85; N, 7.67.

2-Dimethylamino-6-methyl-7-methylthio-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (58). The general method was used with adduct **33** (0.159 g, 0.54 mmol), giving **58** (136 mg, 87%) as a yellow powder: mp 167–168°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.51 (d, *J* = 8.1 Hz, 1H, 5-H), 7.40 (d, *J* = 8.4 Hz, 1H, 4-H), 6.74 (s, 1H, 8-H), 3.72 (s, 3H, NCH$_3$), 3.03 (s, 6H, N(CH$_3$)$_2$), 2.58 (s, 3H, SCH$_3$); ^{13}C NMR (300 MHz, $CDCl_3$, δ) 169.3, 169.1, 145.1, 143.3, 123.9, 123,2, 120.0, 115.8, 113.6, 99.4, 45.7, 31.1, 17.3; IR (KBr, cm^{-1}) 2994(m), 2964(m), 2923(m), 2884(m), 1767(s), 1706(m), 1479(s), 1448(s), 1423(m), 1368(s), 1354(s), 1342(s), 1323(w), 1293(m), 1247(w), 1173(m), 1100(s), 1024(s), 994(m), 970(w), 927(w); HRMS *m/z* ($M+Na^+$) calcd 312.0778,

found 312.0782. *Anal*. Calcd for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.23; N, 14.52. Found: C, 58.21; H, 5.40; N, 14.37.

General method for demethylthioation of 2-methylthioindoles. The indole was dissolved in acetone (5 mL), and Raney nickel (300 mg, 5.11 mmol) was added in excess, in several portions, at 30-min intervals over the time of the reaction. The reaction mixture was stirred at RT and monitored by TLC; the starting material was observed to be completely consumed after 2 h. The mixture was filtered, and the filtrate was washed with brine, dried over sodium sulfate, and evaporated to dryness using a rotating evaporator. MPLC with ethyl acetate/hexanes as eluent followed by recrystallization from dichloromethane/petroleum ether was used, giving the desired product in excellent yield.

2-Phenyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (59) [6]. The general method was used with 2-(methylthio)indole **51** (0.066 g, 0.214 mmol)L, giving **59** (38 mg, 68%) as yellow crystals: mp 269–270°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.74 (bs, 1H, 6-H), 7.76 (d, J = 8.4 Hz, 1H, 4-H), 7.72 (dd, J = 8.4, 0.9 Hz, 1H, 5-H), 7.48–7.55 (m, 5H, 7-H, Ph), 7.36–7.48 (m, 1H, Ph), 7.13 (ddd, J = 3.2, 3.2, 1.1 Hz, 1H, 8-H); ^{13}C NMR matched the literature data [6]; IR (KBr, cm^{-1}) 3292(bs), 3105(w), 3080(w), 3010(w), 2970(w), 2910(m), 2870(w), 1768(m), 1702(s), 1627(m), 1595(w), 1496(m), 1468(m), 1443(w), 1385(s), 1370(s), 1344(m), 1270(w), 1230(m), 1156(m), 1113(w), 1094(m), 1069 (w), 1007(w), 956(w), 914(w), 892(w), 827(w), 755(m), 692(w); HRMS *m/z* ($M + Na^+$) calcd 285.0635, found 285.0635. *Anal*. Calcd for $C_{16}H_{10}N_2O_2$: C, 73.27; H, 3.84; N, 10.68. Found: C, 73.28; H, 3.65; N, 10.35.

2-(4-Ethylphenyl)-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (60) [6]. The general method was used with 2-(methylthio)indole **52** (0.068 g, 0.202 mmol), giving **60** (46 mg, 78%) as light-yellow crystals: mp 172–173°C; ^{1}H NMR spectra matched those in the literature [6]; ^{13}C NMR (75 MHz, $CDCl_3$, δ) 169.4, 168.9, 144.1, 140.8, 130.1, 129.7, 128.7, 126.8, 124.8, 123.6, 123.4, 116.5, 102.0, 28.7, 15.6; HRMS *m/z* ($M + Na^+$) calcd 313.0948, found 313.0948. *Anal*. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.62; H, 5.32; N, 9.31.

2-(3-Methoxyphenyl)-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (61). The general method with 2-(methylthio)indole **53** (0.066 g, 0.195 mmol) was used, giving **61** (57 mg, 100%) as light-yellow crystals: mp 202–203°C; ^{1}H NMR (300 MHz, DMSO-d_6, δ) 12.02 (bs, 1H, 6-H), 7.87 (dd, J = 8.3, 0.8 Hz, 1H, 5-H), 7.82 (dd, J = 2.9, 2.9 Hz, 1H, 5′-H), 7.63 (d, J = 8.1 Hz, 1H, 4-H), 7.43 (dd, J = 8.1, 8.1 Hz, 1H, 4′-H), 6.98–7.07 (m, 3H, 7-H, 2′-H, 6′-H), 6.85–6.88 (m, 1H, 8-H), 3.79 (s, 3H, OCH_3); ^{1}H NMR (300 MHz, acetone-d_6) 11.2 (bs, 1H, 6-H), 7.95 (dd, J = 8.1, 0.9 Hz, 1H, 5-H), 7.82 (dd, J = 2.9, 2.9 Hz, 1H, 7-H), 7.68 (d, J = 8.4 Hz, 1H, 4-H), 7.45 (dd, J = 8.3, 8.3 Hz, 1H, 5'-H), 7.14–7.16 (m, 1H, 4′-H or 6′-H), 7.12 (dd, J = 1.8, 0.9 Hz, 1H, 2′-H), 7.01 (ddd, J = 3.3, 2.3, 1.1 Hz, 1H, 8-H), 6.98–7.01 (m, 1H, 4′-H or 6′-H), 3.79 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6, δ) 168.8, 168.5, 160.0, 141.4, 134.0, 132.6, 130.0, 124.2, 123.1, 123.0, 120.1, 117.6, 115.9, 113.8, 100.5, 55.9; IR (KBr, cm^{-1}) 3362(m), 3304(m), 2922(w), 1762(m), 1703(s), 1606(m), 1496(m), 1461(m), 1387(m), 1370(m), 1343(w), 1319(w), 1262(m), 1217(w), 1154(w), 1097(w), 1072(w), 1039(w), 1009(w), 972(w), 906(w), 852(w), 740(w), 715(w); HRMS *m/z* ($M + Na^+$) calcd 315.0741, found 315.0733. *Anal*. Calcd for $C_{17}H_{12}N_2O_3$: C, 69.86; H, 4.14; N, 9.58. Found: C, 69.61; H, 4.32; N, 9.36.

2-Dimethylamino-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (62). The general method was used with 2-(methylthio) indole **54** (19 mg, 0.069 mmol), giving **62** (8.6 mg, 54%) as bright-yellow crystals: ^{1}H and ^{13}C NMR spectra matched the literature values [6].

6-Methyl-2-phenyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (63) [6]. The general method was used with 2-(methylthio) indole **55** (0.081 g, 0.251 mmol), giving **63** (66 mg, 95%) as yellow crystals: mp 221–222°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.77 (d, J = 8.4 Hz, 1H, 4-H), 7.64 (dd, J = 8.3, 0.8 Hz, 1H, 5-H), 7.48–7.54 (m, 4H, Ph), 7.35–7.41 (m, 2H, 7-H, Ph), 7.05 (dd, J = 3.3, 0.9 Hz, 1H, 8-H), 3.92 (s, 3H, NCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 169.6, 169.1, 141.9, 135.2, 133.0, 129.7, 128.2, 127.3, 125.0, 124.4 (likely two overlapping peaks), 116.8, 115.1, 101.6, 34.2; IR (KBr, cm^{-1}) 3100(m), 3080(m), 2920(m), 2905(m), 1757(s), 1705 (s), 1625(w), 1591(m), 1502(s), 1456(m), 1413(w), 1379(s), 1291(m), 1239(w), 1219(m), 1182(w), 1758(w), 1124(w), 1096 (m), 1066(w), 1024(w), 989(w), 953(w), 901(w), 843(w), 823 (w), 785(w), 780(m), 741(s), 690(m), 624(m); HRMS *m/z* ($M + Na^+$) calcd 299.0792, found 299.0785. *Anal*. Calcd for $C_{17}H_{12}N_2O_2$: C, 73.90; H, 4.38; N, 10.14. Found: C, 73.67; H, 4.18; N, 10.38.

2-(4-Ethylphenyl)-6-methyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (64). The general method was used with 2-(methylthio) indole **56** (0.101 g, 0.288 mmol), giving **64** (77 mg, 88%) as yellow crystals: mp 192–193°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.76 (d, J = 8.4 Hz, 1H, 4-H), 7.63 (d, J = 8.4H, 1H, 5-H), 7.39 (d, J = 8.1 Hz, 2H, Ph), 7.33 (d, J = 8.4 Hz, 2H, Ph), 7.36 (d, J = 2.4 Hz, 1H, 7-H), 7.05 (d, J = 2.4 Hz, 1H, 8-H), 3.91 (s, 3H, NCH_3), 2.71 (q, J = 7.5 Hz, 2H, CH_2CH_3), 1.28 (t, J = 7.5 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 169.8, 169.2, 144.4, 141.9, 135.1, 130.4, 129.2, 127.2, 125.1, 124.5, 124.4, 116.7, 115.0, 101.6, 34.2, 29.3, 16.2; IR (KBr, cm^{-1}) 3140(w), 3106(m), 3040(w), 2969(m), 2934(m), 2880(w), 2860(w), 1757(s), 1703(s), 1626(w), 1590(w), 1511(s), 1458(m), 1418(w), 1379(s), 1366(s), 1297(m), 1263(w), 1241(w), 1233(m), 1178(m), 1120(m), 1086(s), 1046(w), 989(w), 969(w), 951(w), 880(w), 852(w), 828(w), 815(w), 803(m), 770(m), 750(m), 661(w), 638(w); HRMS *m/z* ($M + Na^+$) calcd 327.1105, found 327.1110. *Anal*. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20, for $C_{19}H_{16}N_2O_2 \cdot 0.13H_2O$: C, 74.41; H, 5.34; N, 9.13. Found: C, 74.40; H, 5.32; N, 8.93.

2-(3-Methoxyphenyl)-6-methyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (65). The general method was used with 2-(methylthio)indole **57** (0.101 g, 0.287 mmol), giving **65** (76 mg, 87%) as yellow crystals: mp 180–181°C; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.76 (d, J = 8.3, 1H, 4-H), 7.63 (dd, J = 8.1, 1.1 Hz, 1H, 5-H), 7.40 (dd, J = 8.3, 8.3 Hz, 1H, 5′-H), 7.37 (d, J = 3.0 Hz, 1H, 7-H), 7.04–7.11 (m, 3H, 8-H, 2′-H, 6′-H), 6.91–6.96 (m, 1H, 4′-H), 3.92 (s, 3H, NCH_3), 3.85 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ) 169.6, 169.0, 160.6, 141.9, 135.2, 134.0, 130.3, 125.0, 124.42, 124.39, 119.6, 116.8, 115.1, 114.5, 112.9, 101.6, 56.1, 34.2; IR (KBr, cm^{-1}) 3150(w), 3105(m), 3010(m), 2962(m), 2934(m), 2820(w), 1811(m), 1760(m), 1704(s), 1603(m), 1588(m), 1513(w), 1492(m), 1457(m), 1440(w), 1379(s), 1366(s), 1286(m), 1255(s), 1229(m), 1212(m), 1116(w), 1093(m), 1044(m), 989(w), 967(w), 876(w), 827(w), 814(w), 779(w), 743(s), 705(w), 624(w); HRMS *m/z* ($M + Na^+$) calcd 329.0897, found 329.0899. *Anal*. Calcd for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.65; H, 4.79; N, 8.97.

2-Dimethylamino-6-methyl-2H,6H-pyrrolo[3,4-e]indole-1,3-dione (66). The general method was used with 2-(methylthio) indole **58** (0.057 g, 0.20 mmol), giving **66** (44 mg, 92%) as orange crystals: ^{1}H and ^{13}C NMR spectra matched the literature data [6].

Acknowledgment. N.P.L., R.R.D., M.E.M., and H.N.N. thank the Wayland E. Noland Research Fund for the generous financial support of this project.

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