One-Pot Synthesis of Pyrrolylamides and Pyrrolylimides by Tin- and Indium-Mediated Reductive Acylation of 2- and 3-Nitropyrroles

Liangfeng Fu, Gordon W. Gribble*

Department of Chemistry, Dartmouth College, Hanover, NH 03755, USA
Fax +1(603)6463946; E-mail: ggribble@dartmouth.edu

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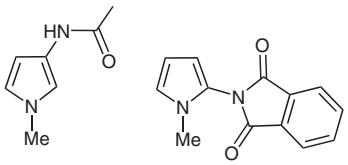
Abstract: A one-pot synthesis of pyrrolylamides and pyrrolylimides from nitropyrroles via reductive acylation under mild conditions in moderate to excellent yields is described.

Key words: tin, indium, reduction, nitropyrrole, pyrrolylamide, pyrrolylimide

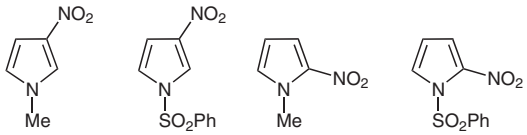
Aminopyrroles are well known to be relatively unstable,[1,2] but they are important in the synthesis of pyrrole-containing heterocycles and medicinal compounds.[3] Pyrrolylamides are also intermediates for the synthesis of pyrrole heterocycles.[4,5] For example, 3-acetylamino-1-methylpyrrole (**2a**) (Figure 1) is a key intermediate for the generation of pyrrolothiazines and pyrrolopyridines,[4,5] and was prepared by the catalytic hydrogenation acylation of 1-methyl-3-nitropyrrole (**1a**)[6] (Figure 2) the presence of acetic anhydride.[5] Pyrrolylimides have been used for the in situ generation of the corresponding aminopyrroles.[7,8] *N*-(1-Methyl-1*H*-pyrrol-2-yl)phthalimide (**9c**) (Figure 1) was the key intermediate for a synthesis of 2-amino-*N*-methylpyrrole,[7,8] and tetraphenylborate salts of this aminopyrrole can be isolated.[1,2] Phthalimide **9c** was prepared by the reaction of 1-methylpyrrole and *N*-chlorosuccinimide.[9] Furthermore, pyrrolylamide and pyrrolylimide building blocks are common features in a number of pyrrole-based anticancer drugs.[10–14] Thus, new routes to these compounds are an important synthetic goal and the objective of the present work.

Our recent work involving the indium-mediated reductive acylation of nitroindoles[15] prompted us to explore the related reductive acylation of 2- and 3-nitropyrroles as a simple route to pyrrolylamides and pyrrolylimides. Most of the previous examples of reductive acylation of 2-[5,16] and 3-nitropyrroles[4,17] involve catalytic hydrogenation of nitropyrroles substituted with electron-withdrawing groups, a feature that greatly stabilizes the aminopyrrole. Four nitropyrroles,1-methyl-3-nitropyrrole (**1a**), 1-methyl-2-nitropyrrole (**1c**), 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**),[18] and 2-nitro-1-(phenylsulfonyl)pyrrole (**1d**)[19,20] were selected as substrates (Figure 2).



2a **9c**

Figure 1 Pyrrolylamide **2a** and pyrrolylimide **9c**



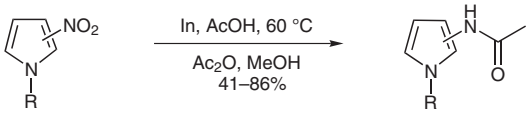
1a **1b** **1c** **1d**

Figure 2 Nitropyrroles **1a–d**

Thus, the reaction of **1a** with indium in acetic acid and methanol in the presence of acetic anhydride affords the desired acetamide **2a** in 73% yield (Table 1). Similarly, 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**) gives **2b** in 86% yield. Although reductive acylation of 1-methyl-2-nitropyrrole (**1c**) does furnish 2-acetylamino-1-methylpyrrole (**2c**), this compound decomposes during workup.[5] In contrast, the stable 2-acetylamino-1-(phenylsulfonyl)pyrrole (**2d**) is produced in 48% yield from **1d** (Table 1).

Whereas treatment of **1a** under the same conditions with indium in the presence of succinic anhydride does not afford succinimide **3a**, refluxing this mixture in acetic acid

Table 1 Reductive Acylation of **1a–d** with Indium and Acetic Anhydride



1a–d **2a–d**

Product	R	NO_2	Yield (%)[a]
2a	Me	3-NO_2	73
2b	SO_2Ph	3-NO_2	86
2c	Me	2-NO_2	–[b]
2d	SO_2Ph	2-NO_2	48

[a] Yield after column chromatography.
[b] Product decomposed during workup.

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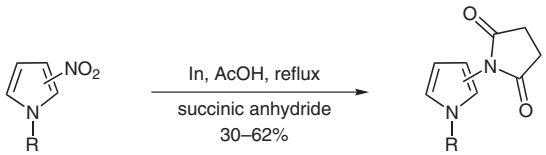
Table 2 Reductive Acylation of **1a–d** with Indium and Succinic Anhydride



1a–d **3a–d**

Product	R	NO_2	Yield [a] (%)
3a	Me	3-NO_2	53
3b	SO_2Ph	3-NO_2	62
3c	Me	2-NO_2	30
3d	SO_2Ph	2-NO_2	trace

[a] Yield after column chromatography.

Table 3 Reductive Acylation of **1a–d** with Tin in the Presence of Acetic Anhydride and Succinic Anhydride

Product	R	NO_2	Solvent	Temp (°C)	Yield (%)[a]
2a	Me	3-NO_2	$ClCH_2CH_2Cl$	60	77
2b	SO_2Ph	3-NO_2	$ClCH_2CH_2Cl$	60	75
2d	SO_2Ph	2-NO_2	MeOH	60	58
3a	Me	3-NO_2	toluene	reflux	52
3c	Me	2-NO_2	toluene	reflux	89
3d	SO_2Ph	2-NO_2	toluene	reflux	trace

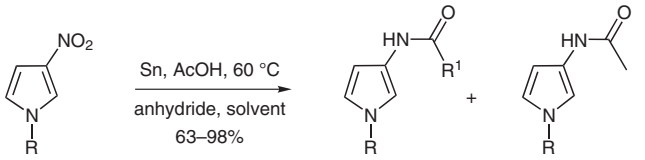
[a] Yield after column chromatography.

alone (no methanol) provides **3a** in 53% yield (Table 2). Likewise, succinimides **3b** and **3c** are obtained in 62% and 30% yield, respectively, but only trace amounts of **3d** are isolated from **1d** (Table 2).

Although indium is essentially nontoxic and highly suitable for 'green' chemistry,[15] it is expensive. Therefore, we turned our attention to the much cheaper tin. Thus, reductive acylations using tin under similar reaction conditions are comparable to those with indium (Table 3). In the case of **1c** succinimide **3c** is obtained in 89% yield (30% using indium).

To extend this reductive acylation of nitropyrroles, we examined other anhydrides as the acylation reagent. As summarized in Table 4, we observe competitive acylations involving mixed anhydrides with acetic acid as solvent. Thus, the reaction of **1a** with tin and benzoic anhydride in acetic acid and methanol gives a 50% yield of benzamide **4a** and a 13% yield of acetamide **2a**. This same reaction in dichloroethane also leads to a mixture of **4a** (33%) and **2a** (39%). Similarly, **1b** affords mixtures of benzamide **4b** and acetamide **2b**. The reductive acylation of **1b** with hexanoic anhydride provides an 84% yield of hexanamide **5b** and only 14% yield of acetamide **2b** (Table 4). Al-

Table 4 Reductive Acylation of **1a** and **1b** with Tin and Anhydrides

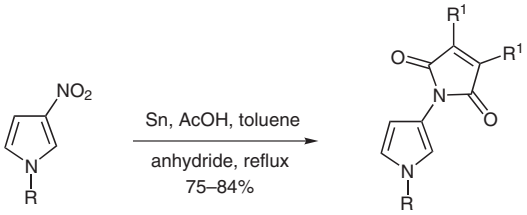


1a,b **4a,b, 5b, 6a,b** **2a,b**

Product	R	Anhydride	Solvent	R^1	Yield (%)[a]
4a	Me	benzoic anhydride	MeOH	Ph	50
2a					13
4a	Me	benzoic anhydride	$ClCH_2CH_2Cl$	Ph	33
2a					39
4b	SO_2Ph	benzoic anhydride	MeOH	Ph	36
2b					61
4b	SO_2Ph	benzoic anhydride	$ClCH_2CH_2Cl$	Ph	62
2b					26
5b	SO_2Ph	hexanoic anhydride	MeOH	Ph	84
2b					14
6a	Me	Boc anhydride	MeOH	O*t*-Bu	55
6b	SO_2Ph	Boc anhydride	MeOH	O*t*-Bu	48

[a] Yield after column chromatography.

Table 5 Reductive Acylation of **1a** and **1b** with Tin and Anhydrides



1a,b **7a,b, 8a,b**

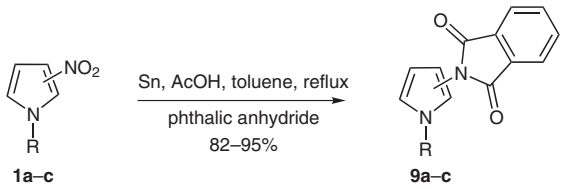
Product	R	Anhydride	R^1	Yield (%)[a]
7a	Me	2,3-dimethylmaleic anhydride	Me	77
7b	SO_2Ph	2,3-dimethylmaleic anhydride	Me	84
8a	Me	2,3-dichloromaleic anhydride	Cl	75
8b	SO_2Ph	2,3-dichloromaleic anhydride	Cl	80

[a] Yield after column chromatography.

though annoying, these mixtures of amides are separable by column chromatography. Only in the cases of **1a** and **1b**, the desired amides **6a** and **6b** are produced with Boc anhydride in 55% and 48% yield, respectively.

Maleic anhydride, 2,3-dimethylmaleic anhydride and 2,3-dichloromaleic anhydride were also tested in this reductive acylation (Table 5). Whereas maleic anhydride does not give the expected maleimides with 3-nitropyrroles **1a** and **1b**, 2,3-dimethyl- and 2,3-dichloromaleic anhydrides

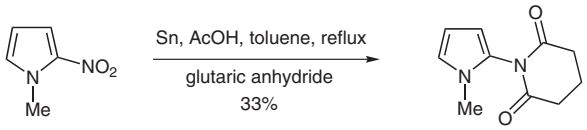
Table 6 Reductive Acylation of **1a–c** with Tin and Phthalic Anhydride



1a–c **9a–c**

Product	R	NO_2	Yield (%)[a]
9a	Me	3-NO_2	95
9b	SO_2Ph	3-NO_2	82
9c	Me	2-NO_2	86

[a] Yield after column chromatography.



1c **10c**

Scheme 1

provide substituted maleimides **7a**,**8a** and **7b**,**8b** from **1a** and **1b**, respectively, in 75–84% yields.

Similarly, phthalic anhydride gives the expected pyrrole phthalimides **9a–c** in excellent yields (Table 6).

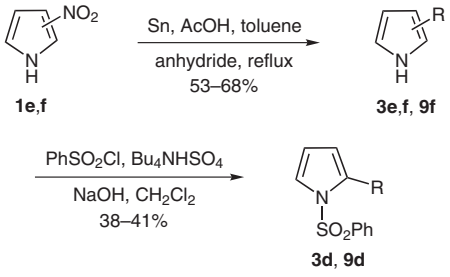
Glutaric anhydride only provides a 33% yield of the expected glutarimide **10c** from 2-nitropyrrole **1c** (Scheme 1). Unfortunately, other nitropyrroles gave much lower yields under the same reaction conditions.

During these reductive acylation studies, we were unable to produce imide **3d** from 2-nitropyrrole **1d** (Tables 2 and 3). To circumvent this problem, we have found that the reductive acylation of unprotected 2- (**1e**) and 3-nitropyrrole (**1f**) under the usual reaction conditions gives good yields of the desired succinimides **3e** and **3f** and phthalimide **9f** (Table 7). Protection of **3f** and **9f** under standard conditions affords **3d** and **9d**, respectively. The successful reductive acylation of **1e** and **1f** suggests that a steric effect operates in the lack of reaction of 2-nitro-1-(phenylsulfonyl)pyrrole (**1d**).

In summary, we have developed a mild reductive acylation of 2- and 3-nitropyrroles to furnish the corresponding pyrrolylamides and pyrrolylimides in moderate to excellent yields. Applications of this chemistry are ongoing in our laboratory and will be reported in due course.

Melting points were determined with a Mel-Temp Laboratory Device apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian 500 Fourier transform NMR spectrometer. Elemental analyses were performed by Atlantic Microlabs in Norcross, GA. Both low- and high-resolution mass spectra were carried out at the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois at Urbana Champaign. All solvents were used as received.

Table 7 Reductive Acylation and Protection of Unprotected Nitropyrroles **1e** and **1f** with Tin and Anhydrides



1e,**f** **3e**,**f**, **9f**

3d, **9d**

Product	NO_2	Anhydride	R	Yield[a] (%)
3e	3-NO_2	succinic anhydride	succinimido	68
3f	2-NO_2	succinic anhydride	succinimido	53
3d				41
9f	2-NO_2	phthalic anhydride	phthalimido	62
9d				38

[a] Yield after column chromatography.

Indium- and Tin-mediated Reductive Acylation of Pyrrolylamides; 3-Acetylamino-1-methylpyrrole (2a); Typical Procedure

To 1-methyl-3-nitropyrrole (**1a**; 0.10 g, 0.80 mmol) and tin powder (0.47 g, 4.0 mmol) in CH_2Cl_2 (6 mL) was added AcOH (4 mL) and Ac_2O (0.40 g, 4.0 mmol). The resulting mixture was heated to 60 °C under N_2. The progress of the reaction was checked by TLC. After the completion of the reaction, the mixture was cooled to r.t. and transferred to a beaker. Aq sat. $NaHCO_3$ was added carefully until the solution was no longer acidic. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with aq sat. $NaHCO_3$ (20 mL), brine (20 mL), and dried (Na_2SO_4). Removal of the solvent and column chromatography of the residue with hexanes–EtOAc (1:1) gave **2a** (0.085 g, 77%) as a yellow solid; mp 121–122 °C (Lit.[4] mp 120.5–121 °C).

^1H NMR (acetone-d_6): δ = 9.01 (br s, 1 H), 7.10 (dd, $J_{2,4}$ = 1.7 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 6.47 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 5.93 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 3.61 (s, 3 H), 2.02 (s, 3 H).

^{13}C NMR (acetone-d_6): δ = 166.1, 124.2, 119.3, 112.1, 100.0, 35.6, 22.6.

3-Acetylamino-1-(phenylsulfonyl)pyrrole (2b)

Prepared from 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**; 0.10 g, 0.40 mmol), indium powder (0.22 g, 2.0 mmol), MeOH (8 mL), AcOH (2 mL), and Ac_2O (0.20 g, 2.0 mmol). Column chromatography with hexanes–EtOAc (1:1) gave **2b** (0.091 g, 86%) as a white solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 169–170.5 °C.

^1H NMR (acetone-d_6): δ = 9.27 (br s 1 H), 7.94–7.97 (m, 2 H), 7.71–7.74 (m, 1 H), 7.69 (dd, $J_{2,4}$ = 1.7 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 7.62–7.66 (m, 2 H), 7.18 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.27 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 2.01 (s, 3 H).

^{13}C NMR (acetone-d_6): δ = 167.8, 139.8, 134.9, 130.4, 129.1, 127.6, 120.5, 109.6, 108.5, 23.1.

Anal. Calcd for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60; S, 12.13. Found: C, 54.36; H, 4.49; N, 10.49; S, 12.05.

2-Acetylamino-1-phenylsulfonylpyrrole (2d)
Prepared from 2-nitro-1-(phenylsulfonyl)pyrrole (**1d**; 0.10 g, 0.40 mmol), tin powder (0.24 g, 2.0 mmol), MeOH (8 mL), AcOH (2 mL), and Ac_2O (0.20 g, 2.0 mmol). Column chromatography with hexanes–EtOAc (1:1) gave **2d** (0.061 g, 58%) as a white solid. An analytical sample was obtained by several recrystallizations from hexanes–EtOAc (1:1); mp 128–129 °C.

^{1}H NMR ($CDCl_3$): δ = 8.57 (br s 1 H), 7.74–7.76 (m, 2 H), 7.62 (m, 2 H), 7.52 (m, 2 H), 6.90 (dd, $J_{3,5}$ = 1.8 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.55 (dd, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.8 Hz, 1 H), 6.24 (dd, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 2.18 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 166.8, 138.5, 134.6, 130.0, 128.6, 126.8, 116.7, 113.1, 104.0, 24.3.

Anal. Calcd for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60; S, 12.13. Found: C, 54.27; H, 4.58; N, 10.48; S, 12.28.

3-Benzoylamino-1-methylpyrrole (4a)
Prepared from 1-methyl-3-nitropyrrole (**1a**; 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), MeOH (8 mL), AcOH (2 mL), and benzoic anhydride (0.90 g, 4.0 mmol). Column chromatography with hexanes–EtOAc (4:1 and 1:1) gave **4a** (0.080 g, 50%) as a white solid together with **2a** (0.014 g, 13%). An analytical sample of **4a** was obtained by several recrystallizations from EtOAc; mp 169–170.5 °C.

^{1}H NMR ($CDCl_3$): δ = 7.84–7.86 (m, 2 H), 7.81 (br s 1 H), 7.45–7.53 (m, 3 H), 7.32 (dd, $J_{2,4}$ = 1.9 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 6.49 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.05 (dd, $J_{2,4}$ = 1.9 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 3.65 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 164.6, 135.1, 131.6, 128.9, 127.1, 122.8, 120.0, 113.5, 100.7, 36.8.

Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.92; H, 6.06; N, 14.02.

3-Benzoylamino-1-(phenylsulfonyl)pyrrole (4b)
Prepared from 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**; 0.10 g, 0.40 mmol), tin powder (0.24 g, 2.0 mmol), dichloroethane (6 mL), AcOH (4 mL), and benzoic anhydride (0.45 g, 2.0 mmol). Column chromatography with hexanes–EtOAc (4:1 and 1:1) gave **4b** (0.081 g, 62%) as a white solid together with **2b** (0.028 g, 26%). An analytical sample was obtained by several recrystallizations from EtOAc; mp 170.5–172 °C.

^{1}H NMR ($CDCl_3$): δ = 7.90–7.92 (m, 2 H), 7.85 (dd, $J_{2,4}$ = 1.5 Hz, $J_{2,5}$ = 2.6 Hz, 1 H), 7.80–7.82 (m, 3 H), 7.45–7.60 (m, 6 H), 7.14 (dd, $J_{2,5}$ = 2.6 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.32 (dd, $J_{2,4}$ = 1.5 Hz, $J_{4,5}$ = 3.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 165.0, 138.9, 134.2, 134.1, 132.2, 129.7, 129.1, 127.2, 127.1, 127.0, 120.0, 110.3, 107.7.

Anal. Calcd for $C_{17}H_{14}N_2O_3S$: C, 62.56; H, 4.32; N, 8.58; S, 9.83. Found: C, 62.40; H, 4.28; N, 8.56; S, 9.90.

3-Hexanoylamino-1-(phenylsulfonyl)pyrrole (5b)
Prepared from 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**; 0.10 g, 0.40 mmol), tin powder (0.47 g, 4.0 mmol), MeOH (8 mL), AcOH (2 mL), and hexanoic anhydride (0.95 mL, 4.0 mmol). Column chromatography with hexanes–EtOAc (2:1 and 1:1) gave **5b** (0.11 g, 84%) as a brown oil together with **2b** (0.015 g, 14%).

^{1}H NMR ($CDCl_3$): δ = 7.89 (br s 1 H), 7.81–7.82 (m, 2 H), 7.66 (dd, $J_{2,4}$ = 1.7 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 7.42–7.56 (m, 3 H), 7.03 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.18 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 2.26 (t, J = 8.0 Hz, 2 H), 1.59–1.65 (m, 2 H), 1.22–1.28 (m, 4 H), 0.84 (t, J = 7.0 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 171.3, 138.8, 134.1, 129.6, 127.3, 127.1, 119.8, 109.8, 107.8, 36.9, 31.6, 25.5, 22.6, 14.1.

MS (EI): m/z = 320 ([M^+]), 277, 264, 238, 222 (100%), 179, 157, 141, 126, 99, 81.

HRMS (EI): m/z calcd for $C_{16}H_{20}N_2O_3S$: 320.1195; found: 320.1190.

3-*tert*-Butoxycarbonylamino-1-methylpyrrole (6a)
Prepared from 1-methyl-3-nitropyrrole (**1a**; 0.050 g, 0.40 mmol), tin powder (0.24 g, 2.0 mmol), MeOH (5 mL), AcOH (1 mL), and *tert*-butoxycarbonyl anhydride (0.44 g, 2.0 mmol). Column chromatography with hexanes–EtOAc (4:1) gave **6a** (0.043 g, 55%) as a white solid; mp 88–89 °C.

^{1}H NMR ($CDCl_3$): δ = 6.84 (m, 1 H), 6.41 (m, 1 H), 6.27 (br s, 1 H), 5.88 (m, 1 H), 3.59 (s, 3 H), 1.50 (s, 9 H).

^{13}C NMR ($CDCl_3$): δ = 153.6, 123.0, 120.0, 111.8, 100.7, 79.9, 36.7, 28.7.

MS (EI): m/z = 196 ([M^+]), 153, 140 (100%), 123, 96, 81, 68, 57.

HRMS (EI): m/z calcd for $C_{10}H_{16}N_2O_2$: 196.1212; found: 196.1213.

3-*tert*-Butoxycarbonylamino-1-(phenylsulfonyl)pyrrole (6b)
Prepared from 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**; 0.050 g, 0.20 mmol), tin powder (0.24 g, 2.0 mmol), MeOH (5 mL), AcOH (1 mL), and *tert*-butoxycarbonyl anhydride (0.22 g, 1.0 mmol). Column chromatography with hexanes–EtOAc (4:1) gave **6b** (0.031 g, 48%) as a white solid; mp 172–173 °C.

^{1}H NMR ($CDCl_3$): δ = 7.86 (m, 2 H), 7.58 (m, 1 H), 7.48 (m, 2 H), 7.35 (br s, 1 H), 7.05 (m, 1 H), 6.34 (m, 1 H), 6.14 (m, 1 H), 1.48 (s, 9 H).

^{13}C NMR ($CDCl_3$): δ = 152.7, 139.1, 134.0, 129.5, 128.1, 127.8, 127.1, 120.1, 107.9, 80.8, 28.5.

MS (EI): m/z = 322 ([M^+]), 266 (100%), 248, 222, 191, 158, 141, 125, 108, 77.

HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O_4S$: 322.0987; found: 322.0988.

Indium/Tin-Mediated Reductive Formation of Pyrrolylimides; *N*-(1-Methyl-1*H*-pyrrol-3-yl)succinimide (3a); Typical Procedure
To a mixture of 1-methyl-3-nitropyrrole (**1a**; 0.050 g, 0.40 mmol), indium powder (0.22 g, 2.0 mmol), and succinic anhydride (0.40 g, 4.0 mmol) was added AcOH (6 mL). The resulting mixture was heated to reflux under N_2. The progress of the reaction was checked by TLC. After the completion of the reaction, it was cooled to r.t., and transferred to a beaker. Aq sat. $NaHCO_3$ was carefully added until the mixture was no longer acidic. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), brine (20 mL), and dried (Na_2SO_4). Removal of solvent and column chromatography with hexanes–EtOAc (1:1) gave **3a** (0.037 g, 53%) as a yellowish solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 99.5–101 °C.

^{1}H NMR (acetone-d_6): δ = 7.11 (m, 1 H), 6.61 (m, 1 H), 6.48 (m, 1 H), 3.68 (s, 3 H), 2.77 (s, 4 H).

^{13}C NMR (acetone-d_6): δ = 176.0, 119.9, 117.9, 115.6, 103.3, 35.8, 28.1.

Anal. Calcd for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.62; H, 5.66; N, 15.71.

***N*-(1-Phenylsulfonyl-1*H*-pyrrol-3-yl)succinimide (3b)**
Prepared from 3-nitro-1-phenylsulfonylpyrrole (**1b**; 0.050 g, 0.20 mmol), indium powder (0.12 g, 1.0 mmol), succinic anhydride (0.20 g, 2.0 mmol) in AcOH (6 mL). Column chromatography with hexanes–EtOAc (1:1) gave **3b** (0.038 g, 62%) as a white solid. An

analytical sample was obtained by several recrystallizations from EtOAc; mp 161–162 °C.

^{1}H NMR (acetone-d_6): δ = 8.02 (m, 2 H), 7.77–7.80 (m, 2 H), 7.67 (m, 2 H), 7.34 (dd, $J_{2,5}$ = 2.6 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.99 (dd, $J_{2,4}$ = 1.5 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 2.82 (s, 4 H).

^{13}C NMR (acetone-d_6): δ = 175.8, 138.9, 134.8, 130.1, 127.2, 123.1, 119.6, 112.8, 109.0, 28.2.

Anal. Calcd for $C_{14}H_{12}N_2O_4S$: C, 55.26; H, 3.97; N, 9.16; S, 10.59. Found: C, 55.00; H, 4.16; N, 9.16; S, 10.59.

***N*-(1-Methyl-1*H*-pyrrol-2-yl)succinimide (3c)**
Prepared from 1-methyl-2-nitropyrrole (**1c**; 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), succinic anhydride (0.40 g, 4.0 mmol), and AcOH (2 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (1:1) gave **3c** (0.13 g, 89%) as a white solid; mp 166–167 °C (Lit.[9] mp 163–164 °C).

^{1}H NMR (acetone-d_6): δ = 6.72 (dd, $J_{3,5}$ = 1.9 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.05 (dd, $J_{3,4}$ = 3.8 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 5.93 (dd, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.9 Hz, 1 H), 3.41 (s, 3 H), 2.89 (s, 4 H).

^{13}C NMR (acetone-d_6): δ = 176.8, 121.5, 120.6, 106.7, 106.4, 32.4, 28.5.

***N*-(1*H*-Pyrrol-3-yl)succinimide (3e)**
Prepared from 3-nitropyrrole (**1e**; 0.090 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), succinic anhydride (0.40 g, 4.0 mmol), and AcOH (3 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (1:1) gave **3e** (0.090 g, 68%) as a white solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 150.5–151.5 °C.

^{1}H NMR ($CDCl_3$): δ = 8.38 (br s, 1 H), 7.22 (m, 1 H), 6.78 (m, 1 H), 6.60 (m, 1 H), 2.84 (s, 4 H).

^{13}C NMR ($CDCl_3$): δ = 176.3, 117.2, 117.1, 112.7, 104.2, 28.4.

Anal. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.06. Found: C, 58.55; H, 4.99; N, 16.99.

***N*-(1*H*-Pyrrol-2-yl)succinimide (3f)**
Prepared from 2-nitropyrrole (**1f**; 0.090 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), succinic anhydride (0.40 g, 4.0 mmol) and AcOH (3 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (2:1) gave **3f** (0.070 g, 53%) as a white solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 195–196 °C.

^{1}H NMR ($CDCl_3$): δ = 10.02 (br s, 1 H), 6.70 (m, 1 H), 6.68 (m, 1 H), 6.22 (m, 1 H), 2.87 (s, 4 H).

^{13}C NMR ($CDCl_3$): δ = 175.0, 123.5, 114.1, 107.8, 99.8, 28.4.

Anal. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.06. Found: C, 58.61; H, 4.97; N, 17.13.

***N*-(1-Methyl-1*H*-pyrrol-3-yl)dimethylmaleimide (7a)**
Prepared from 1-methyl-3-nitropyrrole (**1a**; 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), 2,3-dimethylmaleic anhydride (0.50 g, 4.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) gave **7a** (0.13 g, 77%) as an orange solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 120.5–122 °C.

^{1}H NMR ($CDCl_3$): δ = 6.88 (m, 1 H), 6.55 (m, 1 H), 6.35 (m, 1 H), 3.65 (s, 3 H), 2.01 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 171.3, 137.4, 120.8, 116.4, 115.7, 104.1, 36.9, 9.1.

Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.80; H, 6.05; N, 13.65.

***N*-(1-Phenylsulfonyl-1*H*-pyrrol-3-yl)dimethylmaleimide (7b)**
Prepared from 3-nitro-1-phenylsulfonylpyrrole (**1b**; 0.10 g, 0.40 mmol), tin powder (0.25 g, 2.0 mmol), 2,3-dimethylmaleic anhydride (0.25 g, 2.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) gave **7b** (0.11 g, 84%) as a yellow solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 166.5–168 °C.

^{1}H NMR ($CDCl_3$): δ = 7.88–7.90 (m, 2 H), 7.66 (dd, $J_{2,4}$ = 1.7 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 7.59–7.62 (m, 1 H), 7.49–7.53 (m, 2 H), 7.15 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.7 Hz, 1 H), 6.87 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.7 Hz, 1 H), 2.01 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 170.1, 138.9, 138.0, 134.2, 130.0, 127.2, 122.3, 120.0, 111.6, 108.4, 9.1.

Anal. Calcd for $C_{16}H_{14}N_2O_4S$: C, 58.17; H, 4.27; N, 8.48; S, 9.71. Found: C, 57.89; H, 4.36; N, 8.49; S, 9.81.

***N*-(1-Methyl-1*H*-pyrrol-3-yl)dichloromaleimide (8a)**
Prepared from 1-methyl-3-nitropyrrole (**1a**, 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), 2,3-dichloromaleic anhydride (0.66 g, 4.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) gave **8a** (0.15 g, 75%) as a red solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 138.5–139.5 °C.

^{1}H NMR ($CDCl_3$): δ = 6.89 (dd, $J_{2,4}$ = 1.7 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 6.58 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.34 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 3.67 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 162.1, 121.2, 116.4, 115.0, 104.3, 37.0.

Anal. Calcd for $C_9H_6Cl_2N_2O_2$: C, 44.11; H, 2.47; Cl, 28.93; N, 11.43. Found: C, 44.18; H, 2.51; Cl, 29.08; N, 11.29.

***N*-(1-Phenylsulfonyl-1*H*-pyrrol-3-yl)dichloromaleimide (8b)**
Prepared from 3-nitro-1-phenylsulfonylpyrrole (**1b**; 0.10 g, 0.40 mmol), tin powder (0.25 g, 2.0 mmol), 2,3-dichloromaleic anhydride (0.33 g, 2.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) gave **8b** (0.12 g, 80%) as a yellow solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 188–189 °C.

^{1}H NMR ($CDCl_3$): δ = 7.90 (m, 2 H), 7.62–7.65 (m, 2 H), 7.52–7.55 (m, 2 H), 7.18 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.79 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 161.1, 138.6, 134.5, 134.0, 129.8, 127.3, 120.9, 120.3, 112.7, 108.3.

Anal. Calcd for $C_{14}H_8Cl_2N_2O_4S$: C, 45.30; H, 2.17; Cl, 19.10; N, 7.55; S, 8.64. Found: C, 45.35; H, 2.18; Cl, 19.12; N, 7.43; S, 8.53.

***N*-(1-Methyl-1*H*-pyrrol-3-yl)phthalimide (9a)**
Prepared from 1-methyl-3-nitropyrrole (**1a**; 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), phthalic anhydride (0.60 g, 4.0 mmol), and AcOH (4 mL) in toluene (4 mL). Column chromatography with hexanes–EtOAc (2:1) and recrystallization from EtOAc gave **9a** (0.17 g, 95%) as a yellow solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 172.5–174 °C.

^{1}H NMR ($CDCl_3$): δ = 7.73–7.91 (m, 4 H), 7.07 (dd, $J_{2,4}$ = 1.9 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 6.63 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.53 (dd, $J_{2,4}$ = 1.9 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 3.71 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 167.5, 134.3, 132.3, 123.6, 121.0, 116.4, 116.3, 104.5, 37.0.

Anal. Calcd for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.46; N, 12.38. Found: C, 68.80; H, 4.40; N, 12.33.

***N*-(1-Phenylsulfonyl-1*H*-pyrrol-3-yl)phthalimide (9b)**
Prepared from 3-nitro-1-(phenylsulfonyl)pyrrole (**1b**; 0.10 g, 0.40 mmol), tin powder (0.25 g, 2.0 mmol), phthalic anhydride (0.30 g,

2.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) gave **9b** (0.12 g, 82%) as a yellow solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 166–168 °C.

^{1}H NMR ($CDCl_3$): δ = 7.89–7.94 (m, 4 H), 7.85 (dd, $J_{2,4}$ = 1.7 Hz, $J_{2,5}$ = 2.4 Hz, 1 H), 7.75–7.85 (m, 2 H), 7.52–7.64 (m, 3 H), 7.22 (dd, $J_{2,5}$ = 2.4 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 7.03 (dd, $J_{2,4}$ = 1.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 166.5, 138.9, 134.7, 134.4, 131.9, 130.0, 127.3, 123.9, 122.1, 120.0, 112.9, 108.9.

Anal. Calcd for $C_{18}H_{12}N_2O_4S$: C, 61.35; H, 3.43; N, 7.95; S, 9.10. Found: C, 61.56; H, 3.44; N, 8.03; S, 9.10.

***N*-(1-Methyl-1*H*-pyrrol-2-yl)phthalimide (9c)**

Prepared from 1-methyl-2-nitropyrrole (**1c**; 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), phthalic anhydride (0.60 g, 4.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) and recrystallization from EtOAc gave **9c** (0.15 g, 86%) as a yellow solid; mp 202.5–204 °C (Lit. [9] mp 205–206 °C).

^{1}H NMR ($CDCl_3$): δ = 7.82–8.00 (m, 4 H), 6.73 (dd, $J_{3,5}$ = 1.8 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.25 (dd, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.20 (dd, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.8 Hz, 1 H), 3.49 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 167.9, 134.9, 132.0, 124.3, 122.4, 118.8, 107.8, 107.7, 33.5.

***N*-(1*H*-Pyrrol-2-yl)phthalimide (9f)**

Prepared from 2-nitropyrrole (**1f**; 0.090 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), phthalic anhydride (0.60 g, 4.0 mmol), and AcOH (3 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (4:1) gave **9f** (0.11 g, 62%) as an orange solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 187–188 °C.

^{1}H NMR ($CDCl_3$): δ = 9.80 (br s, 1 H), 7.75–7.80 (m, 4 H), 6.72 (m, 1 H), 6.67 (m, 1 H), 6.27 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 166.4, 134.8, 131.8, 123.9, 123.8, 114.4, 108.1, 99.6.

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 67.59; H, 3.88; N, 13.02.

***N*-(1-Methyl-1*H*-pyrrol-2-yl)glutarimide (10c)**

Prepared 1-methyl-3-nitropyrrole (**1a**; 0.10 g, 0.80 mmol), tin powder (0.47 g, 4.0 mmol), glutaric anhydride (0.46 g, 4.0 mmol), and AcOH (4 mL) in toluene (6 mL). Column chromatography with hexanes–EtOAc (1:1) gave **10c** (0.050 g, 33%) as a white solid. An analytical sample was obtained by several recrystallizations from EtOAc; mp 162–163 °C.

^{1}H NMR ($CDCl_3$): δ = 6.67 (dd, $J_{3,5}$ = 1.9 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.20 (dd, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 3.0 Hz, 1 H), 6.00 (dd, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.9 Hz, 1 H), 3.34 (s, 3 H), 2.82–2.86 (m, 4 H), 2.11 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 173.0, 122.0, 121.6, 107.5, 106.4, 33.3, 32.9, 17.5.

Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.26; H, 6.27; N, 14.45.

***N*-(1-Phenylsulfonyl-1*H*-pyrrol-2-yl)succinimide (3d)**

To a solution of *N*-(1*H*-pyrrol-2-yl)succinimide (**3f**; 0.37 g, 2.3 mmol) in CH_2Cl_2 (30 mL) were added NaOH (0.35 g, 6.9 mmol) and Bu_4NHSO_4 (0.10 g, 0.29 mmol) under stirring. The resulting suspension was cooled to 0 °C and stirred for 10 min, and $PhSO_2Cl$ (0.13 g, 2.7 mmol) was added via a syringe. The mixture was warmed to r.t. and stirred for 6 h. The mixture was poured onto H_2O (50 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). Removal of solvent and column chromatography with hexanes–EtOAc (1:1) gave **3d** (0.28 g, 41%) as a yellow oil.

^{1}H NMR ($CDCl_3$): δ = 7.80–7.83 (m, 2 H), 7.62–7.65 (m, 1 H), 7.51–7.55 (m, 2 H), 7.26 (dd, $J_{3,5}$ = 1.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.37 (m, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 3.4 Hz, 1 H), 6.30 (dd, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.7 Hz, 1 H), 2.84–2.96 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 176.4, 138.9, 134.6, 129.6, 127.4, 123.4, 120.6, 114.7, 112.3, 28.8.

MS (EI): *m*/*z* = 304 ([M$^+$], 100%), 240, 222, 212, 163, 149, 135, 107, 93, 77.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}N_2O_4S$: 304.0518; found: 304.0521.

***N*-(1-Phenylsulfonyl-1*H*-pyrrol-2-yl)phthalimide (9d)**

To a solution of *N*-(1*H*-pyrrol-2-yl)phthalimide (**9f**; 0.21 g, 0.99 mmol) in CH_2Cl_2 (30 mL) were added NaOH (0.35 g, 3.0 mmol) and Bu_4NHSO_4 (0.25 g, 0.74 mmol) under stirring. The resulting suspension was cooled to 0 °C and stirred for 10 min; thereafter $PhSO_2Cl$ (0.22 g, 0.12 mmol) was added via a syringe. The mixture was warmed to r.t. and stirred overnight. The mixture was poured onto H_2O (50 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). Removal of solvent and column chromatography over hexanes–EtOAc (1:1) gave **9d** (0.13 g, 38%) as a yellowish solid in 38% yield. An analytical sample was obtained by several recrystallizations from EtOAc; mp 211.5–212.5 °C.

^{1}H NMR ($CDCl_3$): δ = 7.82–8.00 (m, 4 H), 7.74 (m, 2 H), 7.61–7.64 (m, 1 H), 7.46–7.50 (m, 2 H), 7.37 (dd, $J_{3,5}$ = 1.9 Hz, $J_{4,5}$ = 3.7 Hz, 1 H), 6.42 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 3.7 Hz, 1 H), 6.39 (dd, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 1.9 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 167.3, 138.8, 134.9, 134.5, 132.0, 129.6, 127.5, 124.4, 123.5, 120.1, 115.7, 112.0.

Anal. Calcd for $C_{18}H_{12}N_2O_4S$: C, 61.35; H, 3.43; N, 7.95; S, 9.10. Found: C, 61.38; H, 3.43; N, 7.85; S, 8.98.

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