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SYNTHESIS OF *N*-SUBSTITUTED PYRROLE DERIVATIVES VIA INDIUM-ASSISTED ONE-POT REDUCTION/*N*-ANNULATION SEQUENCE REACTION

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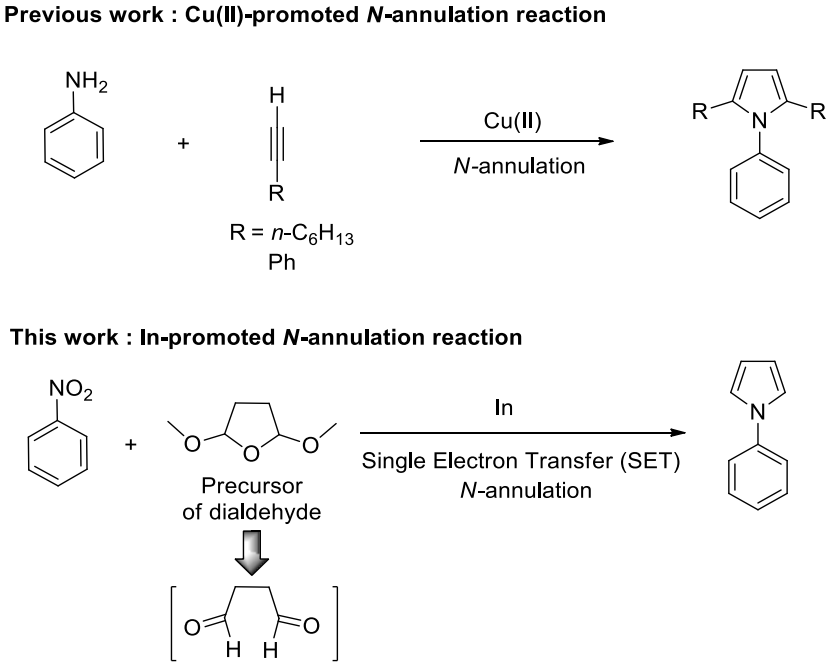
Abstract – A synthesis strategy toward diverse pyrrole derivatives *via* an indium-mediated one-pot reductive *N*-annulation reaction has been developed. This protocol provides easy access to versatile *N*-substituted pyrroles in the presence of an indium/AcOH co-activation promotor, with excellent yields.

Indium-mediated single-electron transfer (SET) reactions have attracted much attention in the field of organic synthesis because indium is an environment-friendly and moderate reducing reagent among electron-donating metals.[1] Our group developed the synthesis of various heterocyclic compounds by indium-mediated reductive annulation.[2] The pyrrole moiety is of much interest to researchers owing to the broad-spectrum biological activities of the related derivatives.[3] In particular, pyrrole derivatives are important pharmaceutical agents that show a wide range of biological activities such as antitubercular[4] and antimycobacterial[5] activities. Reactions involving nitro substrates could be a suitable alternative to the traditional methods for synthesizing pyrroles from amino derivatives as the nitro functional group in the starting materials could be easily converted into an amine group by using an indium/Brønsted-Lowry acid co-activation promotor.[2] Recently, Kumar's group reported the synthesis of pyrroles starting from nitroarenes with 2,5-dimethoxytetrahydrofuran in aqueous HCl solution at room temperature using indium, which was selected after screening several metals.[6] We believe it could be a good strategy if the reaction conditions are improved and tuned more precisely by avoiding the use of strong acidic solution. Based on data related to the SET ability of indium in our previous study, we hypothesized that various useful pyrrole derivatives can be prepared by the protocol using indium and the appropriate co-activation promotor. One advantage of this process is that it does not require amine-functionalized substrates as the starting material or any additional synthetic steps because the reduction/*N*-annulation can be

accomplished in one pot. Additionally, this method helps overcome the difficulty involved in the preparation of pyrroles with substituents on the ring, as opposed to conventional synthetic methods such as the Hantzsch reaction[7] and Paal-Knorr reaction.[8]

In a recent study, we reported a novel Cu(II)-catalyzed method for the synthesis of pyrrole derivatives from 1-alkynes with primary amines *via* the Glaser coupling/*N*-annulation reaction (Scheme 1).[9] This is an excellent method that provides 2,5-disubstituted symmetric pyrroles from terminal alkynes. However, it is not applicable for the synthesis of *N*-substituted pyrroles with no substitution on the pyrrole ring that are frequently shown in pharmaceutical agents. In the present study, we developed an efficient and mild one-pot indium-promoted method for preparing *N*-substituted pyrroles without ring substitution, which are found in biologically active compounds. Nitrobenzene (**NB**) and 2,5-dimethoxytetrahydrofuran (**MHF**) were used as the starting materials (dialdehyde and aniline precursors, respectively), and *N*-substituted pyrroles were produced in excellent yields *via* the reduction/*N*-annulation sequence reaction in the presence of the indium/AcOH system.

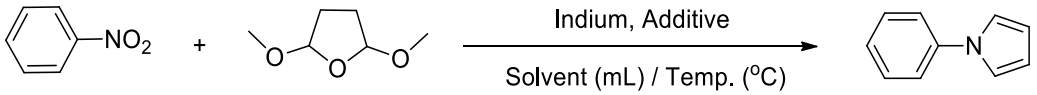


Scheme 1

A co-interactive indium/Brønsted-Lowry acid system was introduced as an activation promotor for the indium-mediated reduction/*N*-annulation sequence reaction. Then, reaction variables such as the amounts of indium, additive, and starting materials, as well as the solvent, temperature, and reaction time, were investigated. As shown in Table 1, the reaction of **NB** with **MHF** to afford 1-phenyl-(1*H*)-pyrrole (**1**) was applied as the delegate to optimize the aforementioned conditions. When the reaction of **NB** with **MHF**

was carried out in the presence of indium (4 equiv.) and AcOH (10 equiv.) with MeOH as the solvent at 60 °C for 24 h, the desired *N*-annulated product **1** was not obtained at all, even though **NB** disappeared completely; instead, aniline was obtained as the major product in 57% yield (Table 1, entry 1). When H_2O was used as the polar protic solvent instead of MeOH, the yield of **1** increased to 29%, with residual aniline (24%) (entry 2). However, both these reactions fell short of our expectation because of the poor product yield. Polar protic solvents worked well for the reduction but were ineffective for the following

Table 1. Optimization of reaction conditions for *N*-phenylpyrrole synthesis



NB **MHF** **1**

Entry	Molar equiv.			Additive (equiv.)	Solvent (mL) / Temp. (°C)	Time (h)	Yield[a] (%)
	NB	**MHF**	Indium				**1**
1	1	1	4	AcOH (10)	MeOH (10)/60	24	0[b]
2	1	1	4	AcOH (10)	H_2O (10)/60	24	29[b]
3	1	1	4	AcOH (10)	DMF (5)/reflux	24	0[b]
4	1	1	4	AcOH (10)	MeCN (10)/60	24	38[b]
5	1	1.2	4	AcOH (10)	MeCN (10)/reflux	24	54[b]
6	1	1.2	4	AcOH (10)	MeOH (8)· H_2O (2)/80	24	28[b]
7	1	1.2	4	AcOH (10)	MeOH (2)· H_2O (8)/80	12	32[b]
8	1	1.2	2	AcOH (3)	MeCN (10)/reflux	24	15[a,c,d]
9	1	1.2	2	AcOH (7)	MeCN (10)/reflux	24	55[b,d]
10	1	1.2	3	AcOH (3)	MeCN (10)/reflux	24	24[b]
11	1	1.2	3	AcOH (7)	MeCN (10)/reflux	24	65[b]
12	1	1.2	3	AcOH (7)	MeCN (9)· H_2O (1)/reflux	24	50[b]
13	1	1.2	3	AcOH (7)	MeCN (8)· H_2O (2)/reflux	24	74[b]
14	1	1.2	3	AcOH (10)	MeCN (8)· H_2O (2)/60	24	36[b]
15	1	1.2	3	AcOH (10)	MeCN (9)· H_2O (1)/reflux	24	76[b]
16	1	1.2	3	AcOH (10)	MeCN (8)· H_2O (2)/reflux	24	52[b]
17	1	1.2	3	AcOH (10)	MeCN (9)→add H_2O (1)/reflux	3→5	96
18	1	1.2	3	AcOH (10)	MeCN (8)→add H_2O (2)/reflux	2→2	98 (97[c])

[a]GC yield with an internal standard (*n*-octane). [b]Aniline was obtained or remained. [c]Isolated yield. [d]**NB** was remained.

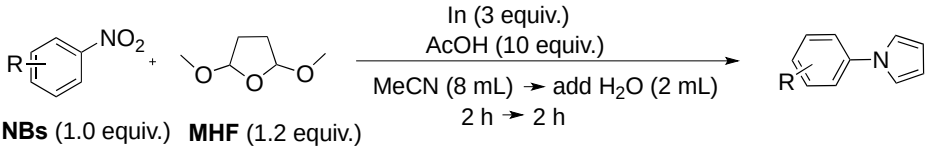
N-annulation reaction. The reaction failed to proceed in aprotic solvents such as DMF (entry 3), toluene, ethyl acetate, and dichloromethane. Fortunately, the use of the polar aprotic solvent MeCN led to the desired product **1** in 38% yield (entry 4). To improve the yield of **1**, more control experiments were performed. The reaction of **NB** with **MHF** (1.2 equiv.) in MeCN under reflux gave a better yield of **1** (54%, entry 5). On the basis of our investigation, we used MeCN/H_2O co-solvent system and obtained a higher yield of **1** (76%, entry 15). To our surprise, in one of the trials, *i.e.*, when co-solvent system was adopted in the middle of the reaction, the yield improved drastically. First, a mixture of **NB** (1 equiv.), **MHF** (1.2 equiv.), indium (3 equiv.), and acetic acid (10 equiv.) in MeCN was refluxed for 2–3 h, followed by the addition of H_2O (1–2 mL) and further refluxing for 2–5 h (entries 17–18). In those control experiments, the product was obtained in almost quantitative yield. It is believed this optimistic effect of adding H_2O later may come from different solvent effect for the reductive reaction versus for the following *N*-annulation reaction. Therefore, the best conditions for the synthesis of *N*-substituted pyrroles were as follows: reaction of **NB** (1 equiv.), **MHF** (1.2 equiv.), indium (3 equiv.), and AcOH (10 equiv.) under reflux in MeCN (8 mL/2 h), followed by the addition of H_2O and refluxing (2 mL/2 h).

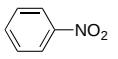
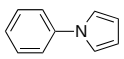
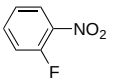
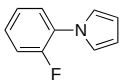
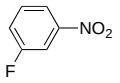
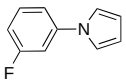
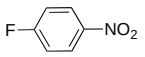
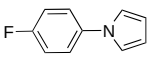
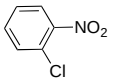
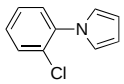
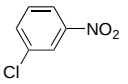
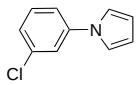
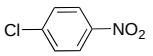
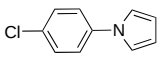
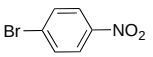
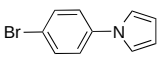
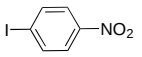
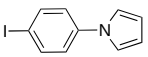
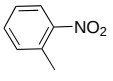
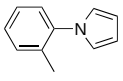
With the optimal conditions in hand, we examined the substrate scope for the preparation of diverse *N*-substituted pyrroles for synthetic applications (Table 2). In most cases, the indium-mediated reduction/*N*-annulation reactions proceed to give high products yield within four hours, irrespective of the substituent type or position. The reaction of **MHF** with substituted nitroarenes, which had electron-withdrawing (entries 2–9) as well as electron-donating (entries 10–18) groups on the aryl ring, was hardly affected by the substituent position (*ortho*-, *meta*-, *para*-), and the product was obtained in 72%–98% yield. Di-oxygen-containing aryl compounds such as 5-nitrobenzo[*d*][1,3]dioxole also produced the corresponding *N*-substituted pyrrole in high yield under the optimum condition (94%, entry 18). In particular, the reaction of a nitroarene with an iodo-moiety at *para*-position gave **9** in high yield (92%) along with the dehalogenated product in ~3% GC yield, which was strong evidence for the radical/radical anion intermediacy during the reaction (entry 9). Without doubt, indium-mediated SET processes to **NB** were involved prior to cyclization reaction with **MHF**. As an exception, the reaction of *o*-cyano-substituted nitroarene gave the corresponding product in trace amounts (entry 20) even though all the substrate was disappeared, presumably because *ortho*-cyano group inhibits further reaction of in situ formed 2-cyanoaniline intermediate towards the next *N*-annulation reaction by intramolecular H-bonding between *ortho*-oriented amino and cyano group.

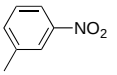
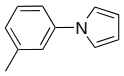
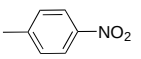
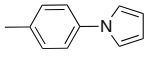
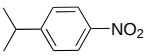
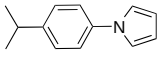
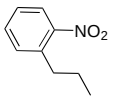
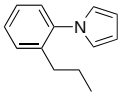
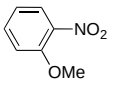
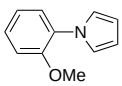
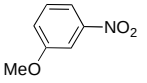
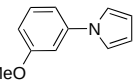
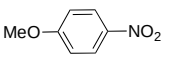
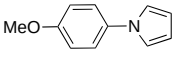
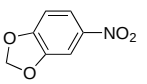
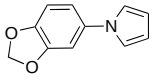
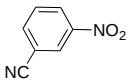
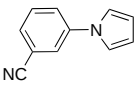
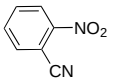
Then, we investigated the scope of heteroatom-containing nitroarene derivatives, π-extended conjugated aromatic compounds, and aliphatic hydrocarbons with **MHF** (Table 3). However, the reactions of heteroatom compounds such as 2-nitrofuran and 2-nitrothiophene were unsuccessful (entries 1 and 2),

and the corresponding products were not obtained with the mostly recovered starting substrate even when the reaction time was increased up to 12 h. To our delight, heteroatom-substituted 5-(1*H*-pyrrol-1-yl)quinoline **20** was obtained successfully by appropriate control of the reaction time after adding H_2O (86%, entry 3).

Table 2. Indium-mediated reduction/*N*-annulation reaction of nitroarene derivatives (**NBs**) with **MHF** at reflux



Entry	Substrate	Product		Yield (%)[a]
1			**1**	97
2			**2**	86
3			**3**	84
4			**4**	98
5			**5**	85
6			**6**	96
7			**7**	82
8			**8**	88
9			**9**	92[b]
10			**10**	91

Entry	Substrate	Product		Yield (%)[a]
11			**11**	85
12			**12**	86
13			**13**	92
14			**14**	92
15			**15**	95
16			**16**	81
17			**17**	95
18			**18**	94
19			**19**	72
20			-	trace[c]

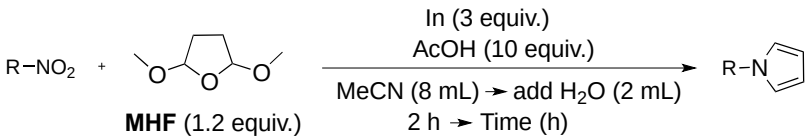
[a]Isolated yield. [b]Dehalogenated product was observed (~3% GC yield). [c]Substrate was disappeared.

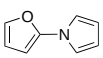
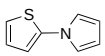
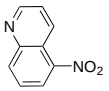
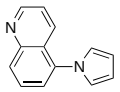
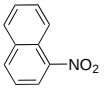
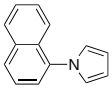
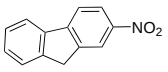
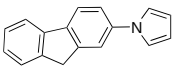
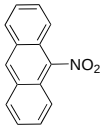
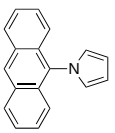
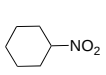
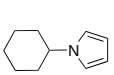
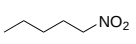
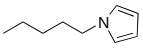
Further, pyrrole derivatives containing extended conjugate compounds were successfully formed when the reaction time in MeCN/H_2O was controlled (78%–96%, entries 4–6). In the case of aliphatic nitro substrates such as nitrocyclohexane and nitropentane, unexpected good result was obtained with the extended reaction time in MeCN and/or in MeCN/H_2O (entries 7, 8). The reaction was performed for 4 h in MeCN and then for 2 h (nitrocyclohexane) or 16 h (nitropentane) after adding H_2O, additionally. Thus,

the corresponding product was obtained in moderate yield (52% and 45% respectively). Even though it produces relatively lower yield compared to that of nitroarenes reactions probably because of the higher reduction potential of the aliphatic substrates as compared to aromatic compounds, it is a valuable result since aliphatic substrates were poorly worked for our previous indium-mediated reductive reactions.

A plausible mechanism for the formation of **1** from the indium-mediated reduction/*N*-annulation reaction between **NB** and **MHF** is outlined in Scheme 2. On the basis of the abovementioned experimental results and previous reports, the formation of **1** occurs as follows. The nitro group of **NB** might initially be converted into an amine group *via* SET reaction by the indium/AcOH co-activation promotor. The starting material **MHF** that acts as the masked form of the dialdehyde is transformed to intermediate 2,5-dihydroxytetrahydro-1*H*-furan cation **A** under acid/water conditions.[10] Ring-opening of **A** gives intermediate **B**, which is transformed into intermediate **C** by a sequential dehydration step. Nucleophilic attack of aniline (**D**) onto the carbonyl group of **C** generates intermediate **E**, which is then converted into intermediate **F** by proton transfer. Subsequent dehydration/proton transfer/nucleophilic attack produces intermediate **G**. Finally, *N*-substituted pyrrole **1** is furnished *via* aromatization of intermediate **F**.

Table 3. Indium-mediated reduction/*N*-annulation reaction of various nitro compounds with **MHF** at reflux

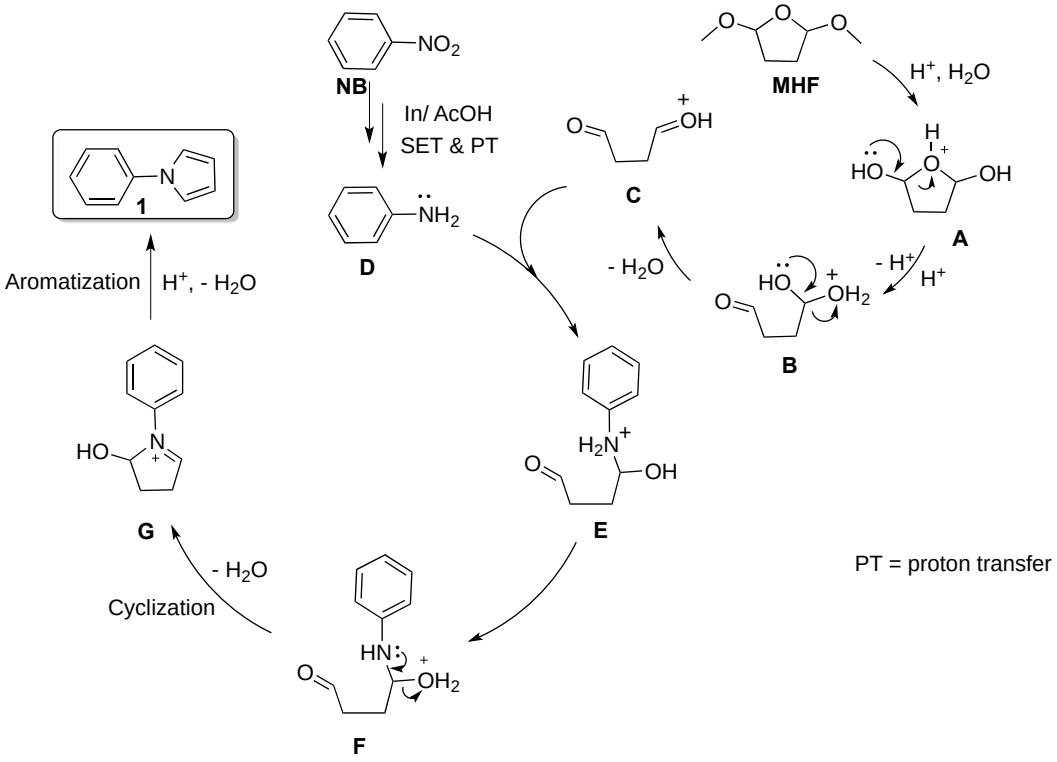


Entry	Substrate (**2**)	Product (**3**)		TIme (h)	Yield (%)[a]
1				12	0
2				12	0
3			**20**	4	86
4			**21**	3	92
5			**22**	2	78
6			**23**	2	96
7			**24**	2[b]	52
8			**25**	16[c]	45

[a]Isolated yield. [b]Reaction time : 4 h (in MeCN) → 2 h (in MeCN/H_2O). [c]Reaction time : 4 h (in MeCN) → 16 h (in MeCN/H_2O)

In conclusion, we have developed a one-pot indium-mediated reduction/*N*-annulation reaction of 2,5-dimethoxytetrahydrofuran with nitroarenes in the presence of MeCN/H_2O co-solvent system. Interestingly,

co-solvent system adoption in the middle of the reaction was critical for obtaining the best yield, which proved that the indium/AcOH-mediated reduction and following *N*-annulation differ in efficiency in each reaction step. It is also worthy to note that aliphatic nitro compounds work well for our one-pot reductive *N*-annulation reaction as far as their reduction reactivity concerned. Our protocol would be valuable for the preparation of diverse pyrrole analogs without ring substitution. We have demonstrated that the synthetic method for *N*-substituted pyrroles is eco-friendly and efficient because the reaction proceeds under mild one-pot conditions in the presence of an indium/AcOH activation promotor.



Scheme 2

EXPERIMENTAL

1. General considerations

Most of the chemical reagents were purchased from Sigma-Aldrich Co. (St. Louis, Missouri, USA) and used without further purification. Solvents were purchased and dried using standard methods. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively (JEOL, Tokyo, Japan). Chemical shifts are reported in parts per million relative to the residual solvent as an internal standard or tetramethylsilane (TMS). GC–MS spectra were recorded on an Agilent 6890N GC system connected to an Agilent 5975 mass-selective detector (Hewlett-Packard Co., Palo Alto, CA, USA). HRMS spectra were recorded on a JEOL JMS-DX 303 mass spectrometer (JEOL, Tokyo, Japan). Infrared (IR) spectra were recorded using an MB104 FTIR (ABB Bomem, Inc., Zurich, Switzerland) apparatus. Melting points were

determined on an M3000 (Krüss Optronic, Hamburg, Germany) system and reported uncorrected. All major products were isolated by flash column chromatography on silica gel (230–400 mesh ATSM, purchased from Merck & Co., Inc., Whitehouse Station, NJ, USA) using a mixed solvent (EtOAc/hexane) as the eluent. Analytical thin-layer chromatography (TLC) was performed using 0.25 mm silica gel 60 F_{254} precoated-glass plates.

2. General procedure for indium-mediated reaction of NBs with 2,5-dimethoxytetrahydrofuran to obtain pyrroles.

The **NB** derivative (1.0 mmol) and indium powder (344 mg, 3.0 mmol) were added to MeCN (4 mL), and then, AcOH (600 mg, 573 μL, 10.0 mmol) and 2,5-dimethoxytetrahydrofuran (134 mg, 164 μL, 1.2 mmol) in MeCN (4 mL) were added. The reaction mixture was stirred under reflux in a nitrogen atmosphere. After 2 h, H_2O (2 mL) was added. After the reaction was complete, the mixture was diluted with CH_2Cl_2 (30 mL), filtered through Celite, and poured into 10% aqueous $NaHCO_3$ solution (30 mL). The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was eluted through a neutral silica gel column with EtOAc/hexane (3:97, v/v) to give the corresponding pyrroles. The structures of the known pyrroles were characterized by ^{1}H NMR, ^{13}C NMR, FTIR, and GC–MS analyses. For unknown compounds, HRMS data were reported additionally.

1-Phenyl-1*H*-pyrrole[11] **(1) :** White liquid; TLC (30% EtOAc/hexane) R_f 0.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.56 (m, 4H), 7.43–7.39 (m, 1H), 7.28 (t, 2H, J = 2.1 Hz), 7.55 (t, 2H, J = 2.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.41, 140.87, 133.73, 124.76, 123.64, 114.12, 26.16; GC–MS *m/z* (rel. intensity) 143 (M^+, 100), 115 (82), 77 (20), 51 (7).

1-(2-Fluorophenyl)-1*H*-pyrrole[13] **(2) :** Brown liquid; TLC (30% EtOAc/hexane) R_f 0.72; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (td, 1H, J = 7.8, 1.8 Hz), 7.25–7.18 (m, 3H), 7.04 (dd, 2H, J = 4.1, 1.8 Hz), 6.35 (t, 2H, J = 2.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.19, 153.70, 129.00, 128.89, 127.17, 127.09, 124.92, 124.90, 124.78, 124.74, 121.37, 121.32, 117.12, 116.91, 109.93; IR (neat) 3101, 1612, 1512, 1474, 1396, 1072, 756, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 161 (M^+, 100), 133 (75), 95 (13), 75 (19).

1-(3-Fluorophenyl)-1*H*-pyrrole[15] **(3) :** Brown liquid; TLC (30% EtOAc/hexane) R_f 0.78; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (td, 1H, J = 8.1, 6.5 Hz), 7.05–7.02 (m, 1H), 6.98–6.93 (m, 3H), 6.79 (td, 1H, J = 8.5, 1.9 Hz), 6.23 (t, 1H, J = 2.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.45, 162.00, 142.09, 141.99, 130.78, 130.69, 119.08, 115.61, 115.58, 112.27, 112.05, 110.92, 107.74, 107.49; IR (neat) 3101, 3032,

2924, 2854, 1612, 1458, 1203, 1072, 849, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 161 (M^+, 100), 133 (71), 95 (13), 75 (12).

1-(4-Fluorophenyl)-1*H*-pyrrole[11] (4) : White solid; Mp 50.4−51.2 °C; TLC (30% EtOAc/hexane) R_f 0.83; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 7.13–7.07 (m, 2H), 7.00 (t, 2H, *J* = 2.2 Hz), 6.34 (t, 1H, *J* = 2.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.84, 159.40, 137.10, 122.27, 122.19, 119.60, 116.39, 116.16, 110.43; IR (neat) 3132, 2924, 1504, 1497, 1327, 1072, 918 cm^{-1}; GC–MS *m/z* (rel. intensity) 161 (M^+, 100), 133 (76), 95 (26), 83 (20), 57 (46).

1-(2-Chlorophenyl)-1*H*-pyrrole[11] (5) : Brown liquid; TLC (30% EtOAc/hexane) R_f 0.80; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, 1H, *J* = 6.8 ,1.6 Hz), 7.36–7.26 (m, 3H), 6.91 (t, 2H, *J* = 2.1 Hz), 6.34 (t, 2H, *J* = 2.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.65, 130.66, 129.50, 128.21, 127.78, 127.56, 122.13, 109.24; IR (neat) 3101, 3070, 1589, 1497, 1443, 1072, 725, 625 cm^{-1}; GC–MS *m/z* (rel. intensity) 177 (M^+, 100), 142 (35), 115 (84), 75 (18), 50 (7).

1-(3-Chlorophenyl)-1*H*-pyrrole[11] (6) : White solid; Mp 50.0–50.9 °C; TLC (30% EtOAc/hexane) R_f 0.74; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.19 (m, 4H), 7.06 (t, 2H, *J* = 2.1 Hz), 6.35 (t, 2H, *J* = 2.15 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.71, 135.16, 130.56, 125.56, 120.59, 119.17, 118.39, 110.97; IR (neat) 3132, 3078, 2924, 2854, 1597, 1489, 802, 725 cm^{-1}; GC–MS m/z (rel. intensity) 177 (M^+, 100), 142 (15), 115 (64), 75 (12).

1-(4-Chlorophenyl)-1*H*-pyrrole[11] (7) : White solid; Mp 87.9–88.3 °C; TLC (30% EtOAc/hexane) R_f 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, 2H, *J* = 8.5 Hz), 7.17 (d, 2H, *J* = 8.5 Hz), 6.92–6.91 (m, 2H), 6.25–6.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.20, 130.91, 129.57, 121.47, 119.17, 110.79; IR (neat) 3132, 3101, 2962, 2924, 2854, 1597, 1504, 1327, 818, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 177 (M^+, 100), 115 (85), 75 (25), 50 (18).

1-(4-Bromophenyl)-1*H*-pyrrole[11] (8) : White solid; Mp 88.7–89.5 °C; TLC (30% EtOAc/hexane) R_f 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 2H, *J* = 8.5 Hz), 7.12 (d, 2H, *J* = 8.7 Hz), 6.92 (m, 2H), 6.25 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.65, 132.53, 121.79, 119.11, 118.60, 110.86; IR (neat) 3132, 2924, 2854, 1597, 1497, 1327, 1257, 818. 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 222 ($(M+2)^+$, 79), 220 (M^+, 79), 154 (5), 156 (5), 142 (29), 166 (100), 75 (17).

1-(4-Iodophenyl)-1*H*-pyrrole[14] (9) : White solid; Mp 127.8–128.3 °C; TLC (30% EtOAc/hexane) R_f

0.74; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2H, *J* = 7.1 Hz), 7.05 (d, 2H, *J* = 6.8 Hz), 6.96–6.96 (m, 4H), 6.27–6.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.37, 138.49, 122.16, 119.05, 110.91, 89.36; IR (neat) 3140, 2924, 2854, 1582, 1497, 1257, 1072, 1026, 810, 563 cm^{-1}; GC–MS *m/z* (rel. intensity) 269 (M^+, 100), 142 (3), 115 (32), 76 (7), 50 (7).

1-(2-Methylphenyl)-1*H*-pyrrole[13] (10) : Brown oil; TLC (30% EtOAc/hexane) R_f 0.83; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.23 (m, 4H), 6.78 (t, 2H, *J* = 2.0 Hz), 6.31 (t, 2H, *J* = 2.0 Hz), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.55, 133.79, 131.02, 127.45, 126.59, 126.51, 122.02, 108.65, 17.84; IR (neat) 3024, 2970, 1543, 1504, 1497, 1373, 1327, 1072, 764, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 157 (M^+, 100), 131 (19), 77 (7), 65 (9), 51 (4).

1-(3-Methylphenyl)-1*H*-pyrrole[11] (11) : Brown oil; TLC (30% EtOAc/hexane) R_f 0.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (td, 2H, *J* = 8.0, 1.2 Hz), 7.19 (t, 2H, *J* = 9.1 Hz), 7.07–7.03 (m, 3H), 6.32 (ddd, 2H, *J* = 4.12, 2.0, 2.0 Hz), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.70, 139.48, 129.29, 126.36, 121.25, 119.31, 117.63, 110.18, 21.46; IR (neat) 2970, 1612, 1504, 1335, 1072, 910, 779, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 157 (M^+, 100), 131 (22), 115 (7), 91 (6), 77 (4), 65 (9).

1-(4-Methylphenyl)-1*H*-pyrrole[11] (12) : White solid; Mp 81.1–81.9 ºC; TLC (30% EtOAc/hexane) R_f 0.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 2H, *J* = 8.6 Hz), 7.23–7.19 (m, 2H), 7.05 (t, 2H, *J* = 2.3 Hz), 6.33 (t, 2H, *J* = 2.3 Hz), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.44, 135.34, 130.01, 120.50, 119.36, 110.02, 20.82; IR (neat) 2962, 2924, 1520, 1373, 1072, 810, 710 cm^{-1}; GC–MS *m/z* (rel. intensity) 157 (M^+, 100), 131 (13), 115 (21), 91 (7), 77 (6), 85 (9).

1-(4-Isopropylphenyl)-1*H*-pyrrole[16] (13) : White solid; Mp 65.2–66.1 ºC; TLC (30% EtOAc/hexane) R_f 0.71; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.10 (m, 4H), 6.92 (m, 2H), 6.21 (m, 2H), 2.78 (quin, 1H), 1.13 (d, 6H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.27, 138.64, 127.38, 120.51, 119.30, 110.02, 33.43, 23.88; IR (neat) 3140, 3101, 2955, 2924, 1504, 1466, 1327, 1072, 818 cm^{-1}; GC–MS *m/z* (rel. intensity) 185 (M^+, 41), 170 (100), 128 (12), 115 (12), 77 (7).

(2-Propylphenyl)-1*H*-pyrrole[17] (14) : Brown liquid; TLC (30% EtOAc/hexane) R_f 0.77; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.21 (m, 2H), 7.15–7.14 (m, 2H), 6.68 (t, 2H, *J* = 2.1 Hz), 6.21 (t, 2H, *J* = 2.1 Hz), 2.37 (t, 2H, *J* = 7.8 Hz), 1.39 (sixlet, 2H, *J* = 7.5 Hz), 0.75 (t, 2H, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.27, 138.69, 129.93, 127.67, 127.12, 126.35, 122.32, 108.56, 32.99, 23.93, 13.92; IR (neat) 2962, 2870, 1504, 1458, 1373, 1327, 1234, 1072, 764, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 185 (M^+,

100), 170 (55), 156 (64), 128 (18), 77 (15), 65 (9).

1-(2-Methoxyphenyl)-1*H*-pyrrole[12] (15) : Brown liquid; TLC (30% EtOAc/hexane) R_f 0.75; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.19–7.13 (m, 2H), 6.91–6.89 (m, 4H), 6.22 (t, 2H, *J* = 1.9 Hz), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.59, 130.07, 127.42, 125.66, 122.00, 120.79, 112.08, 108.70, 55.58; IR (neat) 3124, 3101, 2955, 2924, 2847, 1597, 1504, 1474, 1072, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 173 (M^+, 100), 158 (15), 144 (15), 130 (15), 115 (16) , 77 (22), 63 (7).

1-(3-Methoxyphenyl)-1*H*-pyrrole[11] (16) : Brown liquid; TLC (30% EtOAc/hexane) R_f 0.79; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, 1H, *J* = 8.2 Hz), 6.95–6.94 (m, 2H), 6.84–6.79 (m, 2H), 6.63 (dd, 1H, *J* = 8.2, 2.7 Hz), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.37, 141.75, 130.19, 119.19, 112.64, 110.65, 110.28, 106.53, 55.18; IR (neat) 3063, 2932, 1605, 1497, 1257, 1219, 1041, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 173 (M^+, 100), 130 (38), 103 (15), 77 (15), 63 (7).

1-(4-Methoxyphenyl)-1*H*-pyrrole[11] (17) : White solid; Mp 109.8–110.2 ºC; TLC (30% EtOAc/ hexane) R_f 0.69; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, 2H, *J* = 6.6, 2.1 Hz), 6.99 (t, 2H, *J* = 2.3 Hz), 6.94 (dd, 2H, *J* = 6.8, 2.3 Hz), 6.32 (t, 2H, *J* = 2.3 Hz), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.59, 134.45, 122.15, 119.65, 114.57, 109.79, 55.51; IR (neat) 3148, 3109, 3055, 3016, 2962, 1512, 1486, 1250, 1026, 717 cm^{-1}; GC–MS *m/z* (rel. intensity) 173 (M^+, 87), 158 (100), 130 (35), 103 (15), 77 (17), 63 (6).

1-(1,3-Benzo[*b*][1,4]dioxol-5-yl)-1*H*-pyrrole[13] (18) : Brown solid; TLC (30% EtOAc/hexane) R_f 0.64; Mp 79.5−80.0 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (m, 2H), 6.87 (s, *J* = 1.8, 1H), 6.82 (m, 2H), 6.30–6.29 (m, 2H), 5.99 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.28, 145.59, 135.65, 119.78, 113.95, 109.92, 108.38, 102.96, 101.54; IR (neat) 3101, 2916, 1643, 1504, 1450, 1227, 1034, 802 cm^{-1}; GC–MS *m/z* (rel. intensity) 187 (M^+, 100), 129 (33), 102 (20), 63 (8), 51 (8).

3-(1*H*-Pyrrol-1-yl)benzonitrile[18] (19) : White solid; Mp 66.3–66.9 ºC; TLC (30% EtOAc/hexane) R_f 0.66; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.47 (m, 2H), 7.43–7.37 (m, 2H), 6.69 (t, 2H, *J* = 2.0 Hz), 6.28 (t, 2H, *J* = 1.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.96, 130.48, 128.67, 124.12, 123.05, 118.83, 118.05, 113.46, 111.58; IR (neat) 3078, 2962, 2924, 2230, 1582, 1497, 1335, 1257, 879 cm^{-1}; GC–MS *m/z* (rel. intensity) 168 (M^+, 100), 141 (30), 114 (19), 75 (12), 51 (12).

5-(1*H*-Pyrrol-1-yl)quinoline (20) : White solid; Mp 70.8–71.2 ºC; TLC (30% EtOAc/hexane) R_f 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, 1H, *J* = 4.1, 1.8 Hz), 8.16–8.10 (m, 2H), 7.77–7.73 (m, 1H) 7.53

(dd, 1H, *J* = 7.3, 1.0 Hz), 7.41 (dd, 1H, *J* = 8.7, 4.1 Hz), 6.97 (t, 2H, *J* = 2.3 Hz), 6.42 (t, 2H, *J* = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.91, 148.57, 137.89, 131.87, 129.19, 128.74, 124.98, 123.45, 123.09, 121.80, 109.56; IR (neat) 3094, 2924, 1612, 1489, 1396, 1088, 802 cm^{-1}; GC–MS *m/z* (rel. intensity) 194 (M^+, 100), 166 (30), 139 (12), 101 (9), 75 (7), 51 (7); HRMS *m/z* calc. for $C_{13}H_{10}N_2$ 194.0844, found 194.0841.

1-(Naphthalen-1-yl)-1*H*-pyrrole[12] (21) : Brown oil; TLC (30% EtOAc/hexane) R_f 0.83; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, 1H, *J* = 8.2 Hz), 7.89 (d, 2H, *J* = 7.3 Hz), 7.80 (dd, 1H, *J* = 8.2, 0.9 Hz), 7.57–7.47 (m, 4H), 7.04–7.03 (m, 2H) 6.46–6.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.16, 134.19, 129.83, 128.07, 127.83, 126.91, 126.52, 125.26, 123.25, 123.23, 123.17, 108.99; IR (neat) 3055, 2955, 2924, 1597, 1489, 1088, 802, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 193 (M^+, 100), 166 (29), 96 (12), 65 (4).

1-(9*H*-Fluoren-2-yl)-1*H*-pyrrole[13] (22) : Beige solid; Mp 199.0–199.2 ºC; TLC (30% EtOAc/hexane) R_f 0.70; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, 2H, *J* = 7.8 Hz), 7.41 (m, 2H), 7.26–7.24 (m, 2H), 7.18 (td, 1H, *J* = 6.6, 1.4 Hz), 7.01 (m, 2H), 7.26 (m, 2H), 3.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.66, 143.07, 140.89, 139.55, 139.31, 126.85, 126.59, 124.96, 120.51, 119.71, 119.47, 119.40, 117.34, 110.24, 36.91; IR (neat) 1962, 1620, 1551, 1504, 1458, 1366, 1227, 1072, 764, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 231 (M^+, 100), 202 (20), 165 (16), 115 (9), 101 (12).

1-(Anthracen-9-yl)-1*H*-pyrrole[12] (23) : Light yellow solid; Mp 153.7–153.9 ºC; TLC (30% EtOAc/hexane) R_f 0.85; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.41 (d, 2H, *J* = 8.7 Hz), 7.52–7.40 (m, 6H), 6.97 (t, 2H, *J* = 8.7 Hz), 7.41 (ddd, 2H, *J* = 4.0, 1.98, 1.95 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.40, 131.31, 129.19, 128.10, 127.24, 126.81, 125.65, 124.47, 123.39, 108.81; IR (neat) 3186, 3140, 2962, 2924, 1620, 1504, 1420, 1072, 818, 725 cm^{-1}; GC–MS *m/z* (rel. intensity) 243 (M^+, 100), 216 (15), 177 (12), 121 (16), 88 (6).

1-Cyclohexyl-1*H*-pyrrole[13] (24) : Brown liquid; TLC (30% EtOAc/hexane) R_f 0.86; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (t, 2H, *J* = 2.0 Hz), 6.20 (t, 2H, *J* = 1.8 Hz), 3.90–3.83 (m, 1H), 2.16 (dd, 2H, *J* = 12.8, 1.9 Hz), 1.95 (dd, 2H, *J* = 16.4, 2.7 Hz), 1.79 (d, 1H, *J* = 12.9 Hz), 1.74–1.64 (m, 2H), 1.51–1.40 (m, 2H), 1.34–1.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.38, 107.28, 58.62, 34.63, 29.68, 25.68, 25.44; IR (neat) 3101, 2932, 2854, 1643, 1450, 1257, 1088, 810, 717 cm^{-1}; GC–MS *m/z* (rel. intensity) 149 (M^+, 9), 148 (59), 119 (22), 105 (22), 94 (22), 67 (100), 55 (21).

1-Pentyl-1*H*-pyrrole[19] **(25) :** Beige liquid; TLC (10% EtOAc/hexane) R_f 0.69; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (t, 2H, *J* = 2.1 Hz), 6.13 (t, 2H, *J* = 2.1 Hz), 3.84 (t, 2H, *J* = 7.3 Hz), 1.17 (dt, 2H, *J* = 14.6, 7.3 Hz), 3.65-1.24 (m, 4H), 0.87 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.56, 107.83, 49.72, 31.38, 29.01, 22.39, 14.06; IR (neat) 2956, 2933, 1688, 1258, 1093, 805, 732 cm^{-1}; GC–MS *m/z* (rel. intensity) 137 (M^+, 64), 81 (100), 80 (62), 67 (14).

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