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I_2-Catalyzed Synthesis of Substituted Pyrroles from α-Amino Carbonyl Compounds and Aldehydes

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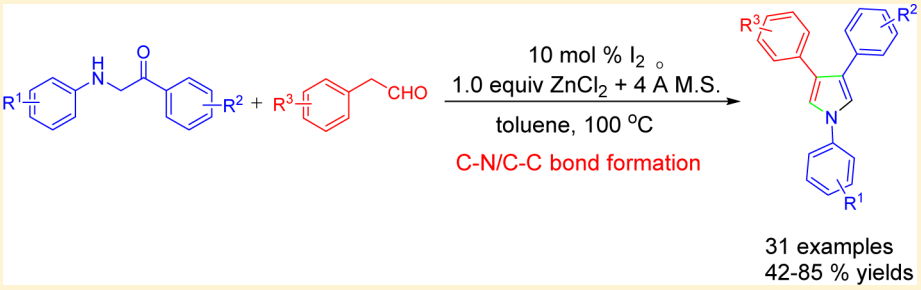
Supporting Information



ABSTRACT: A direct method for the synthesis of 1,3,4-triarylpyrroles was achieved easily from cyclization of α-amino carbonyl compounds and aldehydes catalyzed by I_2. Various substituted groups can be employed, and this reaction can proceed smoothly in moderate to good yields.

Substituted pyrroles represent one of the most important classes of heterocyclic molecules found in numerous natural and biologically active compounds.[1] Furthermore, substituted pyrroles are widely used as synthetic building blocks, pharmacophores, and various kinds of functional materials.[2] Since the pyrroles were found from coal tar and bone oil, chemists have been fascinated with their synthesis. Traditional methods for the synthesis of substituted pyrroles include the classical Knorr reaction, the Hantzsch reaction, and the Paal−Knorr condensation reaction.[3] Recently, new procedures based on multicomponent coupling,[4] tandem reactions, transition-metal-catalyzed cyclization,[5] and catalytic C−H bond functionalization strategies have been developed and drawn extensive and enduring attention.[6] However, it is still a great challenge to design a highly efficient chemical reaction that can be used to construct the skeleton of pyrroles with readily accessible substrates and few steps.

The use of commercially available amines and aldehydes to synthesize heterocyclic compounds in few steps has drawn more attention. Inspired by Jia's synthesis of substituted pyrroles using AgOAc-mediated cyclization of aldehydes and anilines,[7] we conceived a synthetic route for heterocyclic compounds via cyclization of α-amino carbonyl compounds and aldehydes (Scheme 1). As expected, substituted pyrroles were successfully obtained through this reaction. On the basis of our previous studies,[8] herein we report a facile and straightforward method to synthesize substituted pyrroles from α-amino carbonyl compounds and aldehydes via I_2 catalysis.

We began our study by investigating the reaction of 1-phenyl-2-(phenylamino)ethan-1-one (**1a**) and 2-phenylacetaldehyde (**2a**) with I_2 catalysis in toluene at 100 °C. Gratifyingly, the desired 1,3,4-triphenyl-1*H*-pyrrole (**3aa**) was isolated in 18% yield after 4 h (Table 1, entry 1). Obviously, I_2 promotes the reaction by coordinating with the oxygens of the organic carbonyl compounds,[9] and the high chemoselectivity of the pyrrole formation suggests that **2a** reacts with the NH group of **1a** to generate intermediate **6**, which directly produces intermediate **7** via intramolecular nucleophilic cyclization (Scheme 2). Then H_2O is eliminated from **7** to afford pyrrole **3aa**. There are very few examples of the synthesis of substituted pyrroles with phenylacetaldehyde directly. This interesting result encouraged us to optimize the reaction conditions to provide a general protocol for the synthesis of substituted pyrroles.

In order to improve the yield, 4 Å molecular sieves (M.S.) were added to the reaction mixture, and the yield increased to 61% (Table 1, entry 2). Moreover, various metal salts were screened, and we were pleased to find that $ZnCl_2$ as a typical activator for organic carbonyl compounds showed the highest activity, affording pyrrole **3aa** in 82% yield (entry 7).[10] Other metal salts such as $Pd(OAc)_2$, AgOAc, $FeCl_2$, and $FeCl_3$ showed no overall improvement (entries 3−6). Acids such as PivOH and HOAc were also examined, and no better results were obtained (entries 8 and 9). After screening on different parameters, including solvent and temperature (entries 10−13),

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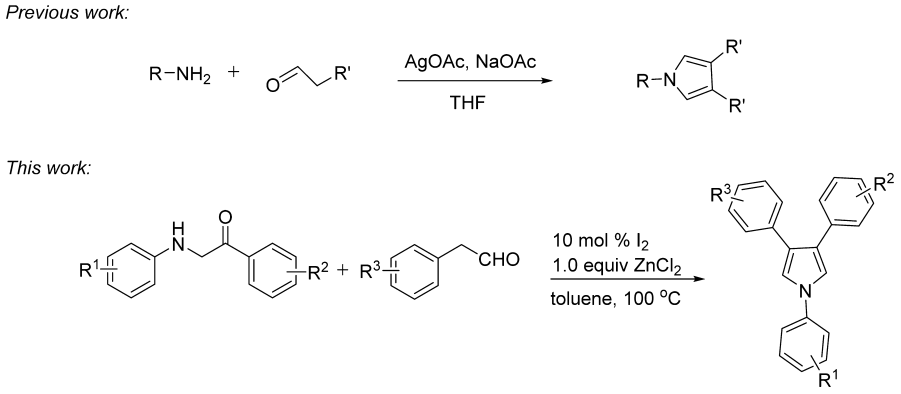
Scheme 1. Synthesis of Substituted Pyrroles Using Amines and Aldehydes



Scheme 2. Construction of Substituted Pyrrole 3aa from 1a and 2a

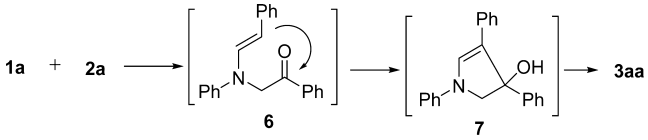
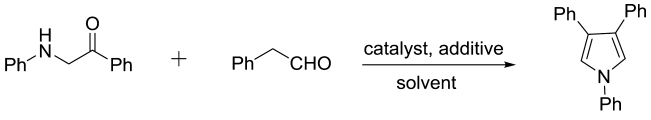


Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3aa

entry	catalyst	additive (equiv)	solvent	T (°C)	yield (%)[b]
1	I_2	none	toluene	100	18
2	I_2	4 Å M.S.	toluene	100	61
3	I_2	$Pd(OAc)_2$ (0.1) + 4 Å M.S.	toluene	100	27
4	I_2	AgOAc (0.1) + 4 Å M.S.	toluene	100	16
5	I_2	$FeCl_2$ (1.0) + 4 Å M.S.	toluene	100	72
6	I_2	$FeCl_3$ (1.0) + 4 Å M.S.	toluene	100	63
7	**I_2**	**$ZnCl_2$ (1.0) + 4 Å M.S.**	**toluene**	**100**	**82**
8	I_2	PivOH (1.0) + 4 Å M.S.	toluene	100	29
9	I_2	HOAc (1.0) + 4 Å M.S.	toluene	100	48
10	I_2	$ZnCl_2$ (1.0) + 4 Å M.S.	DCE	100	46
11	I_2	$ZnCl_2$ (1.0) + 4 Å M.S.	PhCl	100	57
12	I_2	$ZnCl_2$ (1.0) + 4 Å M.S.	DMF	100	34
13	I_2	$ZnCl_2$ (1.0) + 4 Å M.S.	toluene	80	71
14	none	$ZnCl_2$ (1.0) + 4 Å M.S.	toluene	100	–

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.36 mmol), catalyst (0.03 mmol), and additive (4 Å M.S., 100 mg) in 2 mL of solvent for 4 h. [b]Isolated yields.

the highest yield of **3aa** was achieved when the reaction was carried out with I_2 (0.1 equiv), $ZnCl_2$ (1.0 equiv), and 4 Å M.S. in toluene at 100 °C.

With the optimized reaction conditions established (Table 1, entry 7), we then extended the scope of this reaction, and the results are illustrated in Table 2. Fortunately, a variety of α-amino carbonyl compounds and aldehydes successfully produced the desired products **3** in moderate to high yields. Different functionalities on the aryl rings of the α-amino carbonyl compounds and aldehydes demonstrated that both electron-withdrawing and electron-donating groups are compatible with this reaction. For example, alkyl, methoxy, bromo, chloro, and fluoro groups on the substrates all survived and gave the target molecule. As shown in Table 2, electron-donating groups for R^1 played a positive role in the reaction and resulted in higher yields than electron-withdrawing groups. Further studies showed that electron-rich and electron-deficient groups for R^2 and R^3 displayed similar efficiencies and did not significantly affect the yield of the products. Notably, *ortho*-substitution on the aryl rings had an obvious impact on the results, suggesting that the transformation is sensitive to steric hindrance of the α-amino carbonyl compounds and aldehydes. For example, the desired pyrrole (**3ba**) was generated only in 72% yield when **1b** was employed as a substrate. 1-(Naphthalen-1-yl)-3,4-diphenyl-1*H*-pyrrole (**3la**) was obtained in 52% yield when 2-(naphthalen-1-ylamino)-1-phenylethan-1-one (**1l**) was used as a substrate. However, the substituted pyrrole **3rd** was not obtained when **1r** and **2d** were used as substrates. Unfortunately, when butyraldehyde and **1a** were subjected to the standard conditions, no desired product was detected (Scheme 3).

It is worth mentioning that when 1-phenyl-2-(phenylamino)-ethan-1-one (**1a**) and 3-phenylpropanal (**4a**) were employed as substrates under the optimized conditions, the desired product 3-benzyl-1,4-diphenyl-1*H*-pyrrole (**4aa**) was isolated in 52% yield (Scheme 4).

In summary, we have developed a direct I_2-catalyzed method for synthesis of 1,3,4-triarylpyrroles from α-amino carbonyl compounds and aldehydes in a one-pot manner under air. A variety of substituents such as alkyl, methoxyl, bromo, chloro, and fluoro groups were tolerated by the cyclization reaction, which proceeded smoothly in moderate to good yields.

EXPERIMENTAL SECTION

General Remarks. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, in $CDCl_3$. All chemical shifts (δ) are given in parts per million with reference to tetramethylsilane (TMS) as an internal standard. HRMS was performed on an FT-ICR mass spectrometer using electrospray ionization (ESI). Copies of the ^1H and ^{13}C NMR spectra of the products are provided in the Supporting Information. Products were purified by flash chromatography on 200–300 mesh silica gels. All melting points were determined without correction. Commercially available reagents and solvents were used without further purification except as noted.

General Procedure for the Synthesis of the Desired Pyrroles 3. An oven-dried tube was charged with the α-amino carbonyl compound [e.g., 1-phenyl-2-(phenylamino)ethanone (**1a**)] (0.3 mmol) and toluene (2 mL). The mixture was stirred at room temperature until the solid was completely dissolved. Then the aldehyde [e.g., 2-phenylacetaldehyde (**2a**)] (0.36 mmol), anhydrous $ZnCl_2$ (0.3 mmol), I_2 (0.03 mmol), and 4 Å M.S. (100 mg) were

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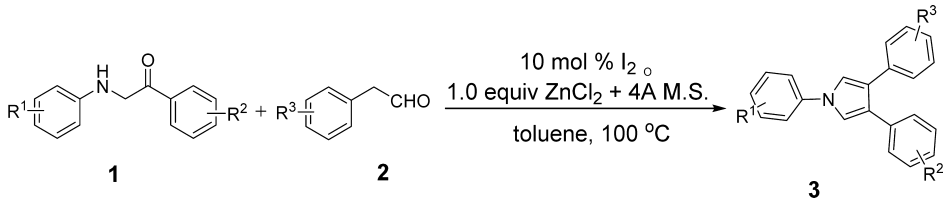
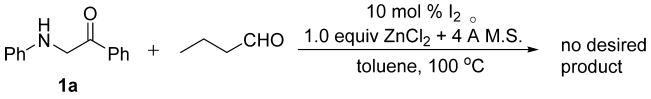
Table 2. Synthesis of Substituted Pyrroles from α-Amino Carbonyl Compounds and Aldehydes[a]



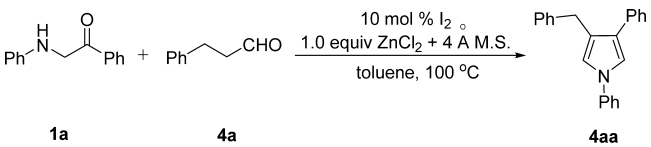
entry	1	R^1	R^2	2	R^3	product	yield (%)[b]
1	**1a**	H	H	**2a**	H	**3aa**	82
2	**1b**	2-Me	H	**2a**	H	**3ba**	72
3	**1c**	3-Me	H	**2a**	H	**3ca**	85
4	**1d**	4-Me	H	**2a**	H	**3da**	83
5	**1e**	2,3-Me_2	H	**2a**	H	**3ea**	76
6	**1f**	3,5-Me_2	H	**2a**	H	**3fa**	80
7	**1g**	4-^{i}Pr	H	**2a**	H	**3ga**	70
8	**1h**	4-^{t}Bu	H	**2a**	H	**3ha**	76
9	**1i**	4-Cl	H	**2a**	H	**3ia**	74
10	**1j**	3-Br	H	**2a**	H	**3ja**	62
11	**1k**	4-F	H	**2a**	H	**3ka**	66
12	**1l**	1-naphthyl	H	**2a**	H	**3la**	52
13	**1m**	H	4-Me	**2a**	H	**3ma**	60
14	**1n**	H	4-MeO	**2a**	H	**3na**	64
15	**1o**	H	4-Cl	**2a**	H	**3oa**	75
16	**1p**	H	4-Br	**2a**	H	**3pa**	72
17	**1a**	H	H	**2b**	2-Me	**3ab**	61
18	**1a**	H	H	**2c**	3-Me	**3ac**	72
19	**1a**	H	H	**2d**	4-Me	**3ad**	74
20	**1a**	H	H	**2e**	4-Et	**3ae**	61
21	**1a**	H	H	**2f**	3-MeO	**3af**	78
22	**1a**	H	H	**2g**	2-F	**3ag**	42
23	**1a**	H	H	**2h**	4-F	**3ah**	70
24	**1d**	4-Me	H	**2i**	3,4-Me_2	**3di**	55
25	**1d**	4-Me	H	**2d**	4-Me	**3dd**	50
26	**1d**	4-Me	H	**2g**	2-F	**3dg**	65
27	**1i**	4-Cl	H	**2d**	4-Me	**3id**	55
28	**1i**	4-Cl	H	**2f**	3-MeO	**3if**	76
29	**1q**	4-Me	4-MeO	**2a**	H	**3qa**	61
30	**1r**	4-Cl	4-Br	**2a**	H	**3ra**	42
31	**1r**	4-Cl	4-Br	**2d**	4-Me	**3rd**	trace
32	**1s**	2-COOMe	H	**2a**	H	**3sa**	trace
33	**1t**	4-NO_2	H	**2a**	H	**3ta**	trace

[a]Conditions: see Table 1, entry 7. [b]Isolated yields.

Scheme 3. Attempted Reaction of 1a and Butyraldehyde



Scheme 4. Reaction of 1a and 4a To Give 4aa



added, and the reaction mixture was stirred at 100 °C for 4 h. After cooling to room temperature, the mixture was filtered to remove suspended particles and washed with EtOAc. The solvent was diluted with 20 mL of ethyl acetate, washed with 10 mL of brine, and dried over anhydrous Na_2SO_4. After the solvent was evaporated in vacuo, the residue was purified by column chromatography, eluting with petroleum ether/EtOAc (20:1) to afford the desired pyrrole (e.g., **3aa**).

1,3,4-Triphenyl-1*H*-pyrrole (3aa). Yellow solid (72.8 mg, 82% yield), mp 98.3−102.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.42 (m, 4H), 7.34−7.20 (m, 13H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 135.3, 129.7, 128.5, 128.2, 126.0, 125.8, 125.6, 120.2, 118.5. HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{18}N$ $[M + H]^+$ 296.1434, found 296.1436.

3,4-Diphenyl-1-*o*-tolyl-1*H*-pyrrole (3ba). Yellow solid (66.7 mg, 72% yield), mp 117.3−118.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.24 (m, 12H), 7.22−7.18 (m, 2H), 6.90 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 135.6, 133.5, 131.2, 128.5, 128.2, 127.6, 126.7, 126.4, 125.7, 124.0, 121.5, 18.1. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ $[M + H]^+$ 310.1589, found 310.1587.

3,4-Diphenyl-1-*m*-tolyl-1*H*-pyrrole (3ca). Yellow solid (78.8 mg, 85% yield), mp 101.7−103.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.19 (m, 15H), 7.09−7.07 (d, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 139.7, 135.4, 129.5, 128.5, 128.2, 126.6, 126.0, 125.5, 120.9, 118.6, 117.3, 21.5. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ $[M + H]^+$ 310.1589, found 310.1586.

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3,4-Diphenyl-1-*p*-tolyl-1*H*-pyrrole (3da). Yellow solid (76.9 mg, 83% yield), mp 107.3−110.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.21 (m, 14H), 7.17 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 135.7, 135.4, 130.2, 128.5, 128.2, 125.9, 125.3, 120.1, 118.6, 20.9. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ [M + H]$^+$ 310.1589, found 310.1587.

1-(2,3-Dimethylphenyl)-3,4-diphenyl-1*H*-pyrrole (3ea). Yellow solid (73.6 mg, 76% yield), mp 138.8−142.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.17 (m, 13H), 6.87 (s, 2H), 2.36 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 138.4, 135.7, 132.7, 129.2, 128.5, 128.2, 125.9, 125.7, 124.4, 123.8, 121.8, 20.5, 14.5. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{22}N$ [M + H]$^+$ 324.1746, found 324.1743.

1-(3,5-Dimethylphenyl)-3,4-diphenyl-1*H*-pyrrole (3fa). Yellow solid (77.5 mg, 80% yield), mp 125.7−128.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.18 (m, 12H), 7.09 (s, 2H), 6.91 (s, 1H), 2.37 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 139.4, 135.4, 128.5, 128.2, 127.6, 125.9, 125.3, 118.7, 118.1, 21.4. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{22}N$ [M + H]$^+$ 324.1746, found 324.1742.

1-(4-Isopropylphenyl)-3,4-diphenyl-1*H*-pyrrole (3ga). Yellow oil (77.8 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.37 (d, 2H), 7.33−7.17 (m, 14H), 2.99−2.92 (m, *J* = 7.2 Hz, 1H), 1.29−1.28 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 138.2, 135.4, 128.5, 128.2, 127.6, 125.9, 125.3, 120.3, 118.7, 33.6, 24.0. HRMS (ESI) *m*/*z*: calcd for $C_{25}H_{24}N$ [M + H]$^+$ 338.1902, found 338.1900.

1-(4-*tert*-Butylphenyl)-3,4-diphenyl-1*H*-pyrrole (3ha). Yellow oil (80.0 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.45 (d, 2H), 7.40−7.38 (d, 2H), 7.33−7.17 (m, 12H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 137.8, 135.4, 128.5, 128.2, 126.5, 125.9, 125.3, 119.9, 118.6, 34.5, 31.4. HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{26}N$ [M + H]$^+$ 352.2059, found 352.2055.

1-(4-Chlorophenyl)-3,4-diphenyl-1*H*-pyrrole (3ia). Yellow oil (73.3 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.37 (m, 4H), 7.33−7.20 (m, 10H), 7.14 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 135.0, 131.3, 129.8, 128.5, 128.3, 126.2, 126.1, 121.2, 118.4. HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}ClN$ [M + H]$^+$ 330.1043, found 330.1039.

1-(3-Bromophenyl)-3,4-diphenyl-1*H*-pyrrole (3ja). Yellow solid (69.4 mg, 62% yield), mp 97.3−98.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.63 (t, 1H), 7.41−7.38 (m, 2H), 7.32−7.27 (m, 9H), 7.26−7.20 (m, 2H), 7.17 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3, 134.9, 131.0, 128.7, 128.5, 128.3, 126.3, 126.2, 123.3, 123.2, 118.5, 118.3. HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}BrN$ [M + H]$^+$ 374.0538, found 374.0535.

1-(4-Fluorophenyl)-3,4-diphenyl-1*H*-pyrrole (3ka). Yellow solid (62.0 mg, 66% yield), mp 93.4−96.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.40 (m, 2H), 7.32−7.20 (m, 10H), 7.16−7.12 (t, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0−159.6 (d, *J* = 243 Hz), 136.7−136.6 (d, *J* = 3 Hz), 135.2, 128.5, 128.3, 126.1, 125.7, 122.0−121.9 (d, *J* = 8 Hz), 118.8, 116.6−116.4 (d, *J* = 23 Hz). HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}FN$ [M + H]$^+$ 314.1339, found 314.1335.

1-(Naphthalen-2-yl)-3,4-diphenyl-1*H*-pyrrole (3la). Yellow oil (53.8 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02−7.99 (t, 1H), 7.95−7.88 (m, 2H), 7.57−7.51 (m, 4H), 7.39−7.37 (d, 4H), 7.31−7.27 (t, 4H), 7.24−7.20 (m, 2H), 7.12 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 135.5, 134.3, 129.4, 128.5, 128.2, 128.2, 128.0, 127.1, 126.7, 125.8, 125.3, 124.3, 123.2, 123.1, 122.6. HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{20}N$ [M + H]$^+$ 346.1589, found 346.1587.

1,3-Diphenyl-4-*p*-tolyl-1*H*-pyrrole (3ma). Yellow oil (55.6 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.45 (t, 3H), 7.34−7.18 (m, 11H), 7.10−7.08 (d, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 135.6, 135.4, 132.3, 129.6, 129.0, 128.4, 128.3, 128.2, 125.9, 125.7, 125.5, 120.1, 118.4, 118.3, 21.1. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ [M + H]$^+$ 310.1589, found 310.1587.

3-(4-Methoxyphenyl)-1,4-diphenyl-1*H*-pyrrole (3na). Yellow oil (62.4 mg, 64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.41 (m, 4H), 7.33−7.19 (m, 9H), 7.15−7.14 (d, 1H), 6.84−6.82 (d, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 140.3, 135.4, 129.6, 129.6, 128.4, 128.2, 127.8, 125.9, 125.7, 125.5, 125.3, 120.1, 118.3, 118.0, 113.7, 55.2. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}NO$ [M + H]$^+$ 326.1539, found 326.1534.

3-(4-Chlorophenyl)-1,4-diphenyl-1*H*-pyrrole (3oa). Yellow solid (74.0 mg, 75% yield), mp 108.3−111.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.45 (d, 4H), 7.30−7.28 (t, 5H), 7.23 (s, 5H), 7.18 (t, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 135.0, 133.8, 131.8, 129.7, 129.6, 128.5, 128.4, 128.3, 126.2, 126.0, 125.5, 124.4, 120.2, 118.7, 118.5. HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}ClN$ [M + H]$^+$ 330.1043, found 330.1041.

3-(4-Bromophenyl)-1,4-diphenyl-1*H*-pyrrole (3pa). Yellow solid (80.6 mg, 72% yield), mp 108.8−112.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.45 (d, 4H), 7.40−7.38 (d, 2H), 7.30−7.22 (m, 6H), 7.18−7.16 (d, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 135.0, 134.3, 131.4, 130.0, 129.7, 128.5, 128.4, 126.2, 126.0, 125.5, 124.4, 120.2, 119.9, 118.8, 118.5. HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}BrN$ [M + H]$^+$ 374.0538, found 374.0532.

1,3-Diphenyl-4-*o*-tolyl-1*H*-pyrrole (3ab). Yellow solid (56.5 mg, 61% yield), mp 101.3−104.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.43 (m, 4H), 7.32−7.22 (m, 10H), 7.21−7.12 (m, 1H), 7.06−7.05 (d, 1H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 137.2, 135.8, 135.4, 131.0, 130.0, 129.6, 128.3, 127.0, 126.8, 126.4, 125.7, 125.6, 125.5, 125.1, 120.0, 119.0, 116.9, 20.4. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ [M + H]$^+$ 310.1589, found 310.1585.

1,3-Diphenyl-4-*m*-tolyl-1*H*-pyrrole (3ac). Yellow oil (66.7 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.43 (m, 4H), 7.34−7.14 (m, 10H), 7.10−7.03 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 137.8, 135.3, 135.2, 129.7, 129.1, 128.4, 128.2, 128.1, 126.8, 126.0, 125.8, 125.7, 125.6, 120.1, 118.5, 118.4, 21.4. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ [M + H]$^+$ 310.1589, found 310.1586.

1,3-Diphenyl-4-*p*-tolyl-1*H*-pyrrole (3ad). Yellow oil (68.6 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.44 (t, 3H), 7.34−7.17 (m, 11H), 7.10−7.08 (t, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 135.6, 135.4, 132.3, 129.6, 129.0, 128.5, 128.4, 128.2, 126.0, 125.8, 125.6, 120.1, 118.4, 118.3, 21.1. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ [M + H]$^+$ 310.1589, found 310.1587.

3-(4-Ethylphenyl)-1,4-diphenyl-1*H*-pyrrole (3ae). Yellow oil (59.1 mg, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.08 (m, 16H), 2.68−2.62 (q, *J* = 7.6 Hz, 2H), 1.27−1.23 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 140.3, 135.4, 132.5, 129.6, 128.5, 128.4, 128.2, 127.7, 125.9, 125.7, 125.6, 120.1, 118.4, 118.3, 28.5, 15.4. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{22}N$ [M + H]$^+$ 324.1746, found 324.1743.

3-(3-Methoxyphenyl)-1,4-diphenyl-1*H*-pyrrole (3af). Yellow solid (76.0 mg, 78% yield), mp 97.3−99.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.43 (m, 4H), 7.35−7.17 (m, 9H), 6.93−6.91 (d, 1H), 6.86−6.85 (d, 1H), 6.78−6.76 (m, 1H), 3.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 140.2, 136.6, 135.3, 129.7, 129.2, 128.6, 128.2, 126.1, 125.9, 125.7, 125.5, 120.9, 120.2, 118.5, 113.7, 112.0, 55.0. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}NO$ [M + H]$^+$ 326.1539, found 326.1531.

3-(2-Fluorophenyl)-1,4-diphenyl-1*H*-pyrrole (3ag). White oil (39.4 mg, 42% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.43 (m, 4H), 7.30−7.19 (m, 9H), 7.10−7.01 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2−158.8 (d, *J* = 244 Hz, 1C), 140.2, 135.4, 131.8−131.7 (d, *J* = 3 Hz, 1C), 129.7, 128.3, 127.9−127.8 (d, *J* = 5 Hz, 1C), 127.7, 126.4, 126.0−126.0 (d, *J* = 8 Hz, 1C), 123.7−123.7 (d, *J* = 3 Hz, 1C), 123.1, 122.9, 120.3, 120.2−120.2 (d, *J* = 4 Hz, 1C), 118.2, 118.1, 115.8−115.6 (d, *J* = 22 Hz, 1C). HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}FN$ [M + H]$^+$ 314.1339, found 314.1335.

3-(4-Fluorophenyl)-1,4-diphenyl-1*H*-pyrrole (3ah). Yellow oil (65.7 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.45 (t, 4H), 7.29−7.16 (m, 10H), 6.99−6.95 (t, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8−160.4 (d, *J* = 243 Hz, 1C), 140.2, 135.1, 131.3−131.3 (d, *J* = 3 Hz, 1C), 130.0−129.9 (d, *J* = 8 Hz, 1C), 129.7, 128.4, 128.3, 126.1, 125.9, 125.6, 124.6, 120.2, 118.5, 118.4, 115.2−115.0 (d, *J* = 21 Hz, 1C). HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}FN$ [M + H]$^+$ 314.1339, found 314.1334.

3-(3,4-Dimethylphenyl)-4-phenyl-1-(*p*-tolyl)-1*H*-pyrrole (3di). Yellow oil (55.6 mg, 55% yield). ^{1}H NMR (400 MHz, $CDCl_3$):

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δ 7.36−7.27 (m, 4H), 7.25−7.13 (m, 8H), 7.02 (s, 2H), 2.38 (s, 3H), 2.25 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 136.3, 135.5, 135.5, 134.2, 132.8, 130.1, 129.6, 129.5, 128.4, 128.1, 126.0, 125.8, 125.3, 125.2, 120.1, 118.4, 20.9, 19.8, 19.4. HRMS (ESI) *m*/*z*: calcd for $C_{25}H_{24}N$ $[M + H]^+$ 338.1902, found 338.1896.

3-Phenyl-1,4-di-*p*-tolyl-1*H*-pyrrole (3dd). Yellow oil (48.4 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.20 (m, 11H), 7.16−7.14 (m, 2H), 7.10−7.08 (d, 2H), 2.38 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 135.6, 135.5, 132.4, 130.1, 129.1, 129.0, 128.7, 128.4, 128.4, 128.2, 125.9, 125.2, 120.1, 118.5, 118.4, 21.1, 20.9. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{22}N$ $[M + H]^+$ 324.1746, found 324.1742.

3-(2-Fluorophenyl)-4-phenyl-1-*p*-tolyl-1*H*-pyrrole (3dg). White solid (63.8 mg, 65% yield), mp 131.1−135.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.35 (d, 2H), 7.28−7.18 (m, 11H), 7.09−6.99 (m, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2−158.8 (d, *J* = 245 Hz, 1C), 137.9, 135.8−135.6 (d, *J* = 20 Hz, 1C), 131.8−131.8 (d, *J* = 4 Hz, 1C), 130.2, 128.3, 127.9, 127.7−127.6 (d, *J* = 8 Hz, 1C), 126.1, 126.0, 123.7, 123.7, 123.2, 123.0, 120.3, 118.2, 117.9, 115.8−115.6 (d, *J* = 22 Hz, 1C), 20.9. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{19}FN$ $[M + H]^+$ 328.1495, found 328.1490.

1-(4-Chlorophenyl)-3-phenyl-4-(*p*-tolyl)-1*H*-pyrrole (3id). Yellow oil (56.6 mg, 55% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.39 (d, 3H), 7.32−7.18 (m, 7H), 7.14−7.07 (m, 5H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 135.8, 135.1, 132.0, 131.2, 129.7, 129.0, 128.4, 128.3, 128.2, 126.1, 126.0, 121.2, 118.3, 118.2, 21.1. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{19}ClN$ $[M + H]^+$ 344.1200, found 344.1196.

1-(4-Chlorophenyl)-3-(3-methoxyphenyl)-4-phenyl-1*H*-pyrrole (3if). Yellow oil (81.8 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.31 (m, 4H), 7.30−7.26 (m, 4H), 7.24−7.14 (m, 4H), 6.91−6.89 (d, 1H), 6.84−6.83 (t, 1H), 6.79−6.76 (m, 1H), 3.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 138.8, 136.4, 135.0, 131.3, 129.8, 129.2, 128.6, 128.2, 126.2, 126.1, 125.9, 121.2, 120.9, 118.4, 113.7, 112.1, 55.0. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{19}ClNO$ $[M + H]^+$ 360.1149, found 360.1147.

3-(4-Methoxyphenyl)-4-phenyl-1-*p*-tolyl-1*H*-pyrrole (3qa). Yellow oil (62.0 mg, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.22 (m, 11H), 7.16−7.15 (d, 1H), 7.12−7.11 (d, 1H), 6.84−6.82 (d, 2H), 3.80 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 138.0, 135.5, 135.5, 130.1, 129.6, 128.4, 128.2, 127.9, 125.8, 125.2, 124.9, 120.1, 118.4, 118.2, 113.7, 55.2, 20.8. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{22}NO$ $[M + H]^+$ 340.1695, found 340.1692.

3-(4-Bromophenyl)-1-(4-chlorophenyl)-4-phenyl-1*H*-pyrrole (3ra). Yellow oil (51.3 mg, 42% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.38 (m, 6H), 7.30−7.26 (m, 5H), 7.17−7.14 (t, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 134.7, 134.0, 131.5, 131.4, 130.0, 129.8, 128.5, 128.4, 126.4, 126.0, 124.8, 121.3, 120.1, 118.7, 118.4. HRMS *m*/*z*: calcd for $C_{22}H_{15}BrClN$ $[M + H]^+$ 408.0148, found 408.0145.

3-Benzyl-1,4-diphenyl-1*H*-pyrrole (4aa). Yellow oil (48.2 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.34 (m, 8H), 7.28−7.19 (m, 8H), 6.74−6.73 (d, 1H), 4.01 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 140.4, 135.7, 129.5, 128.8, 128.4, 128.3, 128.0, 126.8, 126.0, 125.8, 125.4, 123.5, 120.0, 118.9, 117.2, 32.3. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N$ $[M + H]^+$ 310.1589, found 310.1586.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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