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MONTMORILLONITE K-10 CATALYZED MICROWAVE-ASSISTED SYNTHESIS OF PYRROLES IN SOLVENT FREE CONDITIONS

Chaowei Ma[1]* and Guosheng Huang[2]

[1]College of Chemistry and Environmental Engineering, Xinjiang Institute of Engineering, Urumqi, 830091, China. e-mail: mcw11@163.com. [2]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, 730000, China.

Abstract – An effective microwave-induced, montmorillonite K-10 catalyzed, environmentally benign synthesis of substituted pyrroles from α-amino carbonyl compounds and aldehydes under solvent-free conditions is described. The reaction involving various substituted substrates proceeds smoothly, and substituted pyrroles are synthesized in moderate to excellent yields within minutes. The developed method offers advantages such as operational simplicity, solvent-free, rapid reaction rate and use of a commercially recyclable catalyst.

INTRODUCTION

As nitrogen-containing aromatic heterocycles, pyrroles are an important class of heterocyclic compounds and are structural units found in a vast array of natural products, synthetic pharmaceuticals, and organic conducting materials. The best-known natural pyrroles are the heme derivatives and chlorophyll, which contain four pyrrole groups joined by methine bridges. Furthermore, substituted pyrroles are widely used as synthetic building blocks. In particular, 1,3,4-trisubstituted pyrroles possess interesting biological activities.[1] Accordingly, substantial attention has been paid to develop new methods for the efficient synthesis of substituted pyrroles. Except for the traditional methods such as the Knorr reaction, Hantzsch reaction and Paal−Knorr condensation reaction,[2] a number of efficient synthetic methodologies have been developed and have drawn extensive and enduring attention in recent years.[3] Although many of these contemporary synthetic routes are efficient and effective, with the strengthening of environmental awareness, the development of green synthetic methods for the preparation of these chemicals is still at the forefront of synthesis research.

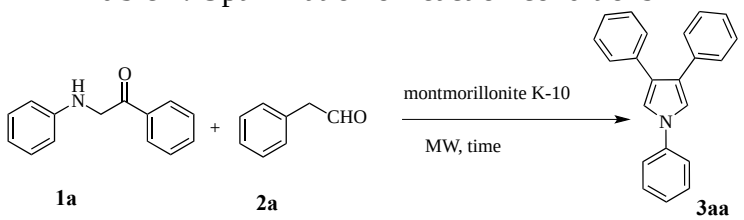
In recent years, solid acids as heterogeneous catalysts have received significant interest in organic

synthesis due to enviroeconomic factors. They have successfully minimized undesirable waste causing environmental pollution.[4] Solid acid catalysts, include clays, zeolites, metal oxides, and acidic ion-exchange resins,[5] and our catalyst of choice in this work is a synthetic clay, montmorillonite K-10. It is produced from natural montmorillonites by treatment with diluted mineral acid. It offers several advantages over conventional homogeneous acid catalysts, such as ease of handling and workup, non-corrosive properties, strong acidity, mild reaction conditions, low cost, high selectivity and yields, and recyclability. In many cases, it can be reused with only minor changes in activity and selectivity.[6,7] Montmorillonite K-10 has a substantial surface area (220-270 m^2/g) that makes it a useful and active catalyst and ensures excellent reaction rates. The Hammett acidity (Ho) value for K-10 is *ca*. -8 indicating strong acidity, which corresponds approximately to the acidity of concentrated nitric acid.[8] Montmorillonite K-10 is also an excellent catalyst for microwave-assisted organic synthesis (MAOs). This area has also attracted considerable attention in recent years.[9] As an effective and non-polluting method of activation, MAOs plays an important role in laboratory preparation. Commonly, these reactions occur under solvent-free (dry media) conditions using solid catalysts.[10] In fact, the absence of organic solvent is also advantageous for the process itself. On the other hand, montmorillonite K-10 is an excellent microwave absorber. This property is extremely useful in transforming the microwave irradiation to heat and providing rapid and evenly distributed energy to the MAOs.[11]

RESULTS AND DISCUSSION

Continuing our efforts in the synthesis of pyrroles,[12] in this study, we describe a more effective and progressive montmorillonite K-10 catalyzed, microwave-induced, solvent-free, environmentally-benign synthesis of substituted pyrroles. This results in excellent yields, shortens the reaction time and represents a highly eco-friendly approach. Moreover, the solid catalyst of the reaction is reusable with retention of its high activity.

Table 1. Optimization of reaction conditions[a]



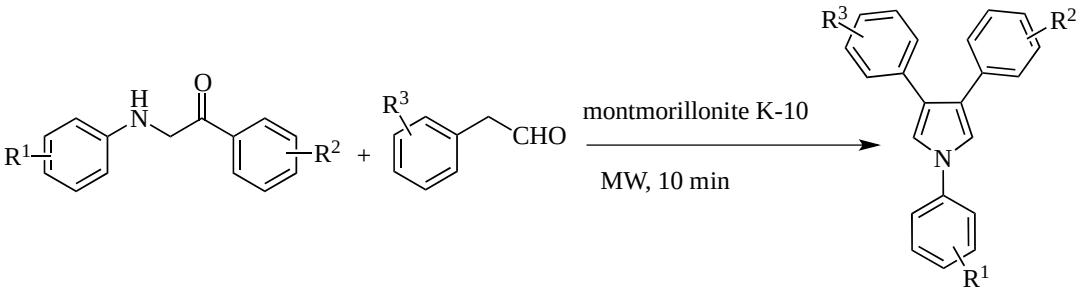
1a **2a** **3aa**

Entry	Mont K-10 (mg)	Time (min)	Power (W)	Yields (%)[b]
1	100	10	800	56
2	**200**	**10**	**800**	**98**
3	300	10	800	93
4	200	5	800	61
5	200	10	400	73

[a] Reactions were performed with **1a** (0.3 mmol), **2a** (0.3 mmol).

[b] Isolated yields.

Table 2. Synthesis of substituted pyrroles from α-amino carbonyl compounds and aldehydes[a]



1 **2** **3**

Entry	**1**	R^1	R^2	**2**	R^3	Product	Yields (%)[b]
1	**1a**	H	H	**2a**	H	**3aa**	98
2	**1b**	3-Me	H	**2a**	H	**3ba**	93
3	**1c**	4-Me	H	**2a**	H	**3ca**	90
4	**1d**	2,3-Me_2	H	**2a**	H	**3da**	81
5	**1e**	3,4-Me_2	H	**2a**	H	**3ea**	87
6	**1f**	4-MeO	H	**2a**	H	**3fa**	79
7	**1g**	4-Ph	H	**2a**	H	**3ga**	73
8	**1h**	4-F	H	**2a**	H	**3ha**	75
9	**1i**	4-Cl	H	**2a**	H	**3ia**	72
10	**1j**	4-Br	H	**2a**	H	**3ja**	76
11	**1k**	3,4-Cl_2	H	**2a**	H	**3ka**	71
12	**1l**	H	4-Me	**2a**	H	**3la**	68
13	**1m**	H	4-MeO	**2a**	H	**3ma**	65
14	**1n**	H	3-MeO	**2a**	H	**3na**	76
15	**1o**	H	4-F	**2a**	H	**3oa**	73
16	**1p**	H	4-Cl	**2a**	H	**3pa**	79
17	**1q**	H	4-Br	**2a**	H	**3qa**	84
18	**1r**	H	4-CF_3	**2a**	H	**3ra**	68
19	**1s**	H	1-naphthyl	**2a**	H	**3sa**	59
20	**1a**	H	H	**2b**	3-Me	**3ab**	89
21	**1a**	H	H	**2c**	4-MeO	**3ac**	87
22	**1a**	H	H	**2d**	4-Me	**3ad**	84
23	**1a**	H	H	**2e**	4-F	**3ae**	82
24	**1a**	H	H	**2f**	4-Cl	**3af**	95
25	**1a**	H	H	**2g**	4-Br	**3ag**	80
26	**1a**	H	H	**2h**	1-naphthyl	**3ah**	93
27	**1a**	H	H	**2i**	piperonyl	**3ai**	91
28	**1t**	4-Me	4-Cl	**2a**	H	**3ta**	80
29	**1u**	4-Cl	4-Cl	**2a**	H	**3ua**	71

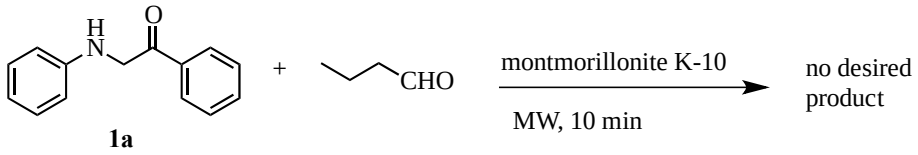
[a] Reaction conditions: **1** (0.3 mmol), **2** (0.3 mmol), montmorillonite K-10 (200 mg), 800 W, 10 min.

[b] Isolated yields.

In our initial study, 1-phenyl-2-(phenylamino)ethan-1-one (**1a** 0.3 mmol) was treated with phenylacetaldehyde (**2a** 0.3 mmol) using commercial montmorillonite K-10 as the catalyst under solvent-free conditions. The general procedure for the reaction involves the adsorption of substrates on the K-10 surface with a small amount of dichloromethane (DCM). Evaporation of DCM gives the dry mixture of K-10 and substrates adsorbed on its surface. The dry mixture is then irradiated in the microwave reactor at the desired power for the specified time at atmospheric pressure in an open system. The effects of microwave power, catalyst dosage and reaction time were studied, with results summarized in Table 1. As the data indicate, while the microwave power was set to 800 W (the temperature of the IR

detector is 155 ˚C at the end of the reaction), the best yield of **3aa** was achieved when the reaction was carried out with 200 mg of montmorillonite K-10 after a 10-minute reaction time.

After determining the optimum conditions, the scope and generality of this method were investigated and the results are given in Table 2. Fortunately, most α-amino carbonyl compounds (**1**) and acetaldehydes (**2**), including those with electron-donating, -neutral, -withdrawing or heterocyclic aryl groups, produced the corresponding pyrroles in moderate to excellent yields. In general, electron-neutral (H) and electron-donating groups for R^1 played a positive role in the reaction and resulted in higher yields than electron-withdrawing groups (Table 2, entries 1-11). In contrast, α-amino carbonyl compounds with electron-rich groups for R^2 gave relatively lower yields than those with electron-deficient groups (Table 2, entries 12-18). Further studies showed that electron-donating and electron-withdrawing groups of acetaldehydes (R^3) showed similar reactivity and did not obviously affect the yield of the products (Table 2, entries 20-27). To further explore the synthetic potential of this methodology, we also tested some chlorine-substituted α-amino carbonyl compounds, as shown, these reactions also gave the expected products in excellent yields (Table 2, entries 28-29).



1a

Scheme 1. Attempted reaction of **1a** and butyraldehyde

Unfortunately, when substrate **1a** and butyraldehyde were subjected to the standard conditions, no desired final compound was detected (Scheme 1).

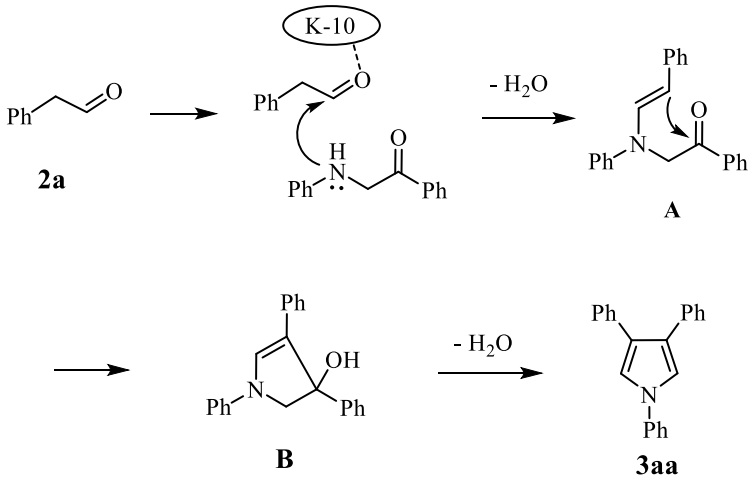
To further explore the advantages of this approach, we studied the recyclability of the catalyst after the reaction. We found that montmorillonite K-10 could be easily separated from the reaction system and the recovered catalyst was reusable with retention of its high catalytic performance, even in the six recycling experiments (Table 3).

Table 3. Re-use of the montmorillonite K-10 [a]

Recycle number	Fresh	2nd	3rd	4th	5th	6th
Isolated yield (%)	98	93	97	90	96	95

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), montmorillonite K-10 (200 mg), 800 W, 10 min.

On the basis of the present results and the literatures reported before,[13] a proposed mechanism for this transformation is illustrated in Scheme 2. It is proposed that the reaction proceeds via activation of the carbonyl group of the phenylacetaldehyde (**2a**) on the acidic surface of montmorillonite K-10 and simultaneous nucleophilic attack of the NH group of **1a** to generate intermediate **A**. Subsequently, intermediate **B** is formed via intramolecular nucleophilic cyclization of **A**. Finally, H_2O is eliminated from **B** to give the product **3aa**.



Scheme 2. Proposed mechanism

In summary, we have developed a direct montmorillonite K-10 catalyzed method for synthesis of pyrroles from α-amino carbonyl compounds and aldehydes in a green and economical manner under microwave irradiation. Compared with methods reported before, advantages of the present method are the rapid reaction rate, excellent yields, absence of solvents and recyclability of the catalyst, which give it great potential for large-scale applications.

EXPERIMENTAL

^{1}H NMR and ^{13}C NMR spectra were recorded on 400MHz and 100MHz in $CDCl_3$. All chemical shifts are given as δ value (ppm) with reference to tetramethylsilane (TMS) as an internal standard. All compounds were further characterized by HRMS; Products were purified by flash chromatography on 200–300 mesh silica gels. All melting points were determined without correction. Unless otherwise noted, commercially available reagents and solvents were used without further purification.

Pyrroles 3; General Experimental Procedure:

Substrates **1** (0.3 mmol) and **2** (0.3 mmol) were dissolved in 3 mL CH_2Cl_2 in a round bottomed flask, 200 mg of montmorillonite K-10 was mixed with the above mixture. After 5 min of stirring, the solvent was evaporated under reduced pressure. The dry mixture was then transferred to a reaction vial and irradiated

in the microwave reactor for the specified time. After the reaction was completed, CH_2Cl_2 (2 mL) was added to the reaction mixture and filtered, and then washed with CH_2Cl_2 (3×2 mL). The filtrate was concentrated, and the residue was subjected to column chromatography [silica gel (300–400 mesh); PET/EA (20:1)]. Meanwhile, the recovered catalyst was washed with EtOH (3×2 mL), dried in air and calcinated at 150 ˚C for 1 h.

1,3,4-Triphenyl-1*H*-pyrrole (**3aa**)**:** Yield: 98% (86 mg). White solid. mp 100-102 ˚C (lit.[12] 98.3−102.4 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.49 – 7.41 (m, 4H), 7.37 – 7.16 (m, 13H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.2, 135.2, 129.6, 128.4, 128.2, 126.0, 125.8, 125.5, 120.1, 118.5. HRMS calcd for $C_{22}H_{17}N$ $[M+H]^+$ 296.1434; found: 296.1431.

3,4-Diphenyl-1-(*m*-tolyl)-1*H*-pyrrole (**3ba**)**:** Yield: 93% (86 mg). White solid. mp 102-104 ˚C (lit.[12] 101.7−103.5 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 15H), 7.1 (d, *J* = 7.3 Hz, 1H), 2.4 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.1, 139.6, 135.3, 129.4, 128.4, 128.2, 126.6, 125.9, 125.3, 120.9, 118.6, 117.2, 21.5. HRMS calcd for $C_{23}H_{19}N$ $[M+H]^+$ 310.1590 ; found: 310.1593.

3,4-Diphenyl-1-(*p*-tolyl)-1*H*-pyrrole (**3ca**)**:** Yield: 90% (83 mg). White solid. mp 105-108 ˚C (lit.[12] 107.3−110.4 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 14H), 7.1 (s, 2H), 2.4 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 137.8, 135.6, 135.3, 130.1, 128.4, 128.2, 125.9, 125.2, 120.1, 118.6, 20.9. HRMS calcd for $C_{23}H_{19}N$ $[M+H]^+$ 310.1590 ; found: 310.1595.

1-(2,3-Dimethylphenyl)-3,4-diphenyl-1*H*-pyrrole (**3da**)**:** Yield: 81% (78 mg). White solid. mp 138-141 ˚C (lit.[12] 138.8−142.3 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 13H), 6.9 (s, 2H), 2.4 (s, 3H), 2.2 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.2, 138.4, 135.7, 132.6, 129.2, 128.5, 128.2, 125.9, 125.7, 124.3, 123.7, 121.8, 20.5, 14.6. HRMS calcd for $C_{24}H_{21}N$ $[M+H]^+$ 324.1747 ; found: 324.1745.

1-(3,4-Dimethylphenyl)-3,4-diphenyl-1*H*-pyrrole (**3ea**)**:** Yield: 87% (84 mg). Yellow solid. mp 133-135 ˚C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 13H), 7.2 (s, 2H), 2.3 (s, 3H), 2.3 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 138.2, 138.0, 135.4, 134.3, 130.6, 128.5, 128.2, 125.9, 125.1, 121.6, 118.7, 117.6, 20.0, 19.2. HRMS calcd for $C_{24}H_{21}N$ $[M+H]^+$ 324.1747 ; found: 324.1744.

1-(4-Methoxyphenyl)-3,4-diphenyl-1*H*-pyrrole (3fa): Yield: 79% (77 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 12H), 7.1 (s, 2H), 7.0 – 6.9 (m, 2H), 3.8 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 157.7, 135.3, 133.8, 128.4, 128.2, 125.9, 124.9, 121.8, 118.9, 114.7, 55.5. HRMS calcd for $C_{23}H_{19}NO$ $[M+H]^+$ 326.1539 ; found: 326.1536.

1-([1,1'-Biphenyl]-4-yl)-3,4-diphenyl-1*H*-pyrrole (**3ga**)**:** Yield: 73% (81 mg). Yellow solid. mp 129-132 ˚C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.7 – 7.6 (m, 2H), 7.6 – 7.5 (m, 2H), 7.5 – 7.1 (m, 17H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.8, 140.1, 138.6, 135.2, 134.2, 129.7, 128.7, 128.7,

128.5, 128.3, 127.0, 126.9, 126.9, 126.1, 125.9, 125.5, 125.0, 120.1, 118.7, 118.5. HRMS calcd for $C_{28}H_{21}N$ $[M+H]^+$ 372.1747 ; found: 372.1743.

1-(4-Fluorophenyl)-3,4-diphenyl-1*H*-pyrrole (**3ha**)**:** Yield: 75% (70 mg). White solid. mp 91-94 ˚C (lit.[12] 93.4–96.8 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 12H), 7.1 – 7.0 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 160.7 (d, J_{C-F} = 244Hz), 136.5 (d, J_{C-F} = 3Hz), 135.1, 128.4, 128.2, 126.0, 125.6, 121.8 (d, J_{C-F} = 8Hz), 118.7, 116.4 (d, J_{C-F} = 23Hz). HRMS calcd for $C_{22}H_{16}FN$ $[M+H]^+$ 314.1340 ; found: 314.1344.

1-(4-Chlorophenyl)-3,4-diphenyl-1*H*-pyrrole (**3ia**)**:** Yield: 72% (71 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.4 (m, 4H), 7.3 – 7.2 (m, 10H), 7.1 (s, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 138.7, 135.0, 131.2, 129.7, 128.4, 128.3, 126.2, 126.0, 121.2, 118.4. HRMS calcd for $C_{22}H_{16}ClN$ $[M+H]^+$ 330.1044 ; found: 330.1046.

1-(4-Bromophenyl)-3,4-diphenyl-1*H*-pyrrole (**3ja**)**:** Yield: 76% (85 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.6 – 7.5 (m, 2H), 7.4 – 7.2 (m, 12H), 7.1 (s, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 139.2, 134.9, 132.7, 128.4, 128.3, 126.2, 126.1, 121.5, 118.9, 118.3. HRMS calcd for $C_{22}H_{16}BrN$ $[M+H]^+$ 374.0539 ; found: 374.0535.

1-(3,4-Dichlorophenyl)-3,4-diphenyl-1*H*-pyrrole (**3ka**)**:** Yield: 71% (77 mg). Yellow solid. mp 143-146 ˚C ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 (d, *J* = 5.1 Hz, 5H), 7.3 – 7.2 (m, 7H), 7.2 (q, *J* = 2.5 Hz, 2H), 7.1 (dd, *J* = 8.3, 2.0 Hz, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 139.9, 135.5, 134.6, 132.1, 130.1, 129.7, 128.5, 128.4, 127.8, 126.4, 126.2, 125.5, 123.2, 120.3, 118.9, 118.8. HRMS calcd for $C_{22}H_{15}Cl_2N$ $[M+H]^+$ 364.0654 ; found: 364.0650.

1,3-Diphenyl-4-(*p*-tolyl)-1*H*-pyrrole (**3la**)**:** Yield: 68% (63 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.4 – 7.2 (m, 10H), 7.1 (d, *J* = 7.9 Hz, 2H), 2.3 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) 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 calcd for $C_{23}H_{19}N$ $[M+H]^+$ 310.1590 ; found: 310.1592.

3-(4-Methoxyphenyl)-1,4-diphenyl-1*H*-pyrrole (**3ma**)**:** Yield: 65% (63 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.3 – 7.1 (m, 10H), 6.8 (d, *J* = 8.7 Hz, 2H), 3.8 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 158.1, 140.2, 135.3, 129.6, 129.6, 128.4, 128.2, 127.7, 125.9, 125.7, 125.5, 125.2, 120.1, 118.3, 118.0, 113.7, 55.2. HRMS calcd for $C_{23}H_{19}NO$ $[M+H]^+$ 326.1539 ; found: 326.1535 .

3-(3-Methoxyphenyl)-1,4-diphenyl-1*H*-pyrrole (**3na**)**:** Yield:76 % (74 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.4 – 7.2 (m, 9H), 6.9 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.9 (dd, *J* = 2.6, 1.5 Hz, 1H), 6.8 (ddd, *J* = 8.2, 2.7, 1.0 Hz, 1H), 3.7 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 159.4, 140.2, 136.6, 135.2, 129.6, 129.2, 128.6, 128.2, 126.1, 125.9, 125.6, 125.4, 120.9, 120.1, 118.5, 113.6, 112.0, 55.0. HRMS calcd for $C_{23}H_{19}NO$ $[M+H]^+$ 326.1539 ; found: 326.1537.

3-(4-Fuorophenyl)-1,4-diphenyl-1*H*-pyrrole (**3oa**)**:** Yield: 73% (68 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.3 – 7.1 (m, 10H), 7.0 (t, *J* = 8.6 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 161.5 (J_{C-F} = 243 Hz), 140.1, 135.1, 131.3 (J_{C-F} = 4 Hz), 130.0 (J_{C-F} = 8 Hz), 129.7, 128.4, 128.3, 126.1, 125.9, 125.5, 124.6, 120.1, 118.5, 118.3, 115.1 (J_{C-F} = 21Hz). HRMS calcd for $C_{22}H_{16}FN$ $[M+H]^+$ 314.1340 ; found: 314.1343.

3-(4-Chlorophenyl)-1,4-diphenyl-1*H*-pyrrole (**3pa**)**:** Yield: 79% (78 mg). Yellow solid. mp 108-110 ˚C (lit.[12] 108.3−111.5 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 (d, *J* = 4.2 Hz, 4H), 7.4 – 7.4 (m, 2H), 7.3 (d, *J* = 4.3 Hz, 4H), 7.3 – 7.1 (m, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.0, 134.9, 134.2, 131.3, 130.0, 129.7, 128.5, 128.3, 126.2, 126.0, 125.5, 124.3, 120.2, 119.9, 118.8, 118.5. HRMS calcd for $C_{22}H_{16}ClN$ $[M+H]^+$ 330.1044 ; found: 330.1040.

3-(4-Bromophenyl)-1,4-diphenyl-1*H*-pyrrole (**3qa**)**:** Yield: 84% (94 mg). Yellow solid. mp 108-112 ˚C (lit.[12] 108.8−112.5 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 (d, *J* = 4.2 Hz, 4H), 7.3 – 7.2 (m, 12H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.1, 134.9, 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 calcd for $C_{22}H_{16}BrN$ $[M+H]^+$ 374.0539; found: 374.0536.

1,3-Diphenyl-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole (**3ra**)**:** Yield: 68% (74 mg). White solid. mp 113-116 ˚C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 (d, *J* = 8.2 Hz, 2H), 7.5 (d, *J* = 4.3 Hz, 4H), 7.4 (d, *J* = 8.1 Hz, 2H), 7.3 – 7.2 (m, 7H), 7.2 (d, *J* = 2.5 Hz, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.0, 139.0, 139.0, 134.8, 129.7, 128.6,128.4, 128.3, 127.8(q, $^{2}J_{C-F}$ = 32 Hz), 125.2 (q, $^{3}J_{C-F}$ = 4.0Hz), 126.2, , 125.7, 124.5(q, $^{1}J_{C-F}$= 270 Hz), 124.2, 120.3, 119.1, 119.0. HRMS calcd for $C_{23}H_{16}F_3N$ $[M+H]^+$ 364.1308 ; found: 364.1305.

3-(Naphthalen-1-yl)-1,4-diphenyl-1*H*-pyrrole (**3sa**)**:** Yield: 59% (61 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.9 – 7.7 (m, 4H), 7.5 – 7.2 (m, 15H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.2, 135.2, 133.7, 132.9, 132.0, 129.7, 128.5, 128.3, 128.3, 127.8, 127.6, 127.6, 126.3, 126.1, 125.9, 125.7, 125.5, 125.3, 120.2, 118.8, 118.6. HRMS calcd for $C_{26}H_{19}N$ $[M+H]^+$ 346.1590 ; found: 346.1594.

1,3-Diphenyl-4-(m-tolyl)-1*H*-pyrrole (**3ab**)**:** Yield: 89% (82 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.6 – 7.4 (m, 4H), 7.4 – 7.0 (m, 12H), 2.3 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.2, 137.8, 135.3, 135.1, 129.6, 129.1, 128.4, 128.2, 128.1, 126.8, 126.0, 125.8, 125.7, 125.6, 125.5, 120.1, 118.5, 118.4, 21.5. HRMS calcd for $C_{23}H_{19}N$ $[M+H]^+$ 310.1590; found: 310.1593.

3-(4-Methoxyphenyl)-1,4-diphenyl-1*H*-pyrrole (**3ac**)**:** Yield: 87% (85 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.3 – 7.2 (m, 9H), 7.2 (d, *J* = 2.5 Hz, 1H), 6.8 (d, *J* = 8.7 Hz, 2H), 3.8 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 158.0, 140.2, 135.3, 129.6, 129.5, 128.4, 128.2, 127.7, 125.9, 125.7, 125.4, 125.2, 120.0, 118.3, 118.0, 113.7, 55.2. HRMS calcd for $C_{23}H_{19}NO$ $[M+H]^+$

326.1539; found: 326.1535.

1,3-Diphenyl-4-(*p*-tolyl)-1*H*-pyrrole (**3ad**)**:** Yield: 84% (78 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.3 – 7.2 (m, 10H), 7.1 (d, *J* = 7.9 Hz, 2H), 2.3 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.2, 135.6, 135.3, 132.2, 129.6, 129.0, 128.4, 128.3, 128.2, 125.9, 125.7, 125.5, 120.1, 118.4, 118.3, 21.2. HRMS calcd for $C_{23}H_{19}N$ $[M+H]^+$ 310.1590; found: 310.1592.

3-(4-Fluorophenyl)-1,4-diphenyl-1*H*-pyrrole (**3ae**)**:** Yield: 82% (77 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.4 (m, 4H), 7.3 – 7.1 (m, 10H), 6.9 (td, *J* = 8.7, 1.8 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) 161.5 (d, J_{C-F} = 243Hz), 140.0, 135.0, 131.3 (d, J_{C-F} = 4Hz), 129.9 (d, J_{C-F} = 8Hz), 129.6, 128.4, 128.3, 126.6 (d, J_{C-F} = 22Hz), 125.5, 124.6, 120.1, 118.4, 118.3, 115.2, 115.0. HRMS calcd for $C_{22}H_{16}FN$ $[M+H]^+$ 314.1340 ; found: 314.1343.

3-(4-Chlorophenyl)-1,4-diphenyl-1*H*-pyrrole (**3af**)**:** Yield: 95% (94 mg). Yellow solid. mp 108-110 ˚C (lit.[12] 108.3−111.5 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.3 (t, *J* = 4.6 Hz, 5H), 7.2 (s, 5H), 7.2 – 7.2 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.1, 134.9, 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 calcd for $C_{22}H_{16}ClN$ $[M+H]^+$ 330.1044 ; found: 330.1040.

3-(4-Bromophenyl)-1,4-diphenyl-1*H*-pyrrole (**3ag**)**:** Yield: 80% (89 mg). Yellow solid. mp 109-112 ˚C (lit.[12] 108.8−112.5 ˚C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 (d, *J* = 4.3 Hz, 4H), 7.4 – 7.4 (m, 2H), 7.3 – 7.2 (m, 6H), 7.2 – 7.1 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.1, 134.9, 134.2, 131.3, 130.0, 129.7, 128.5, 128.3, 126.2, 126.0, 125.5, 124.4, 120.2, 119.9, 118.8, 118.5. HRMS calcd for $C_{22}H_{16}BrN$ $[M+H]^+$ 374.0539 ; found: 374.0536.

3-(Naphthalen-1-yl)-1,4-diphenyl-1*H*-pyrrole (**3ah**)**:** Yield: 93% (96 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.0 (d, *J* = 8.5 Hz, 1H), 7.9 – 7.7 (m, 2H), 7.5 – 7.4 (m, 8H), 7.3 – 7.1 (m, 5H), 7.1 – 7.0 (m, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 140.2, 135.1, 133.7, 133.5, 132.7, 129.7, 128.2, 128.1, 128.0, 127.2, 127.1, 126.9, 126.7, 125.7, 125.6, 125.6, 125.5, 125.4, 123.4, 120.2, 120.0, 117.3. HRMS calcd for $C_{26}H_{19}N$ $[M+H]^+$ 346.1590 ; found: 346.1594.

3-(Benzo[*d*][1,3]dioxol-5-yl)-1,4-diphenyl-1*H*-pyrrole (**3ai**)**:** Yield: 91% (92 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.5 – 7.4 (m, 4H), 7.3 – 7.1 (m, 7H), 7.1 (d, *J* = 2.5 Hz, 1H), 6.8 – 6.7 (m, 3H), 5.9 (s, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 147.4, 146.0, 140.2, 135.1, 129.6, 129.3, 128.4, 128.2, 126.0, 125.8, 125.5, 125.3, 121.8, 120.1, 118.3, 118.2, 109.2, 108.2, 100.8. HRMS calcd for $C_{23}H_{17}NO_2$ $[M+H]^+$ 340.1332 ; found: 340.1335.

3-(4-Chlorophenyl)-4-phenyl-1-(*p*-tolyl)-1*H*-pyrrole (**3ta**)**:** Yield: 80% (82 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.2 (m, 13H), 7.1 (q, *J* = 2.5 Hz, 2H), 2.4 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 137.8, 135.8, 135.1, 133.9, 131.7, 130.2, 129.6, 128.5, 128.4, 128.3, 126.1,

125.2, 124.0, 120.2, 118.8, 118.6, 20.9. HRMS calcd for $C_{23}H_{18}ClN$ $[M+H]^+$ 344.1201 ; found: 344.1205.

1,3-Bis(4-chlorophenyl)-4-phenyl-1*H*-pyrrole (**3ua**)**:** Yield: 71% (77 mg). Yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.4 – 7.3 (m, 4H), 7.3 – 7.2 (m, 9H), 7.1 – 7.1 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ = 138.6, 134.7, 133.5, 131.9, 131.4, 129.8, 129.6, 128.4, 128.4, 126.3, 125.9, 124.8, 121.2, 118.6, 118.4. HRMS calcd for $C_{22}H_{15}Cl_2N$ $[M+H]^+$ 364.0654 ; found: 364.0656.

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SUPPORTING INFORMATION

Supplementary (^{1}H and ^{13}C NMR spectra) data associated with this article can be found, in the online version, at URL: https://www.heterocycles.jp/newlibrary/downloads/PDFsi/27012/100/12.

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