Tetrahedron 67 (2011) 898–903

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Unique chemoselective Clauson–Kass reaction of substituted aniline catalyzed by MgI_2 etherate

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ARTICLE INFO

Article history:
Received 29 October 2010
Received in revised form 1 December 2010
Accepted 7 December 2010
Available online 10 December 2010

Keywords:
Chemoselective
Dimethoxytetrahydrofuran
Pyrrole
Clauson–Kaas reaction
MgI_2 etherate

ABSTRACT

Clauson–Kass reaction of various substituted aniline, primary aryl amide, and sufonyl amide with 2,5-dimethoxytetrahydrofuran was realized in the presence of 10 mol % of MgI_2 etherate in a mild, efficient, and highly chemoselective manner. Iodide counterion and solvents (i.e., MeCN) played the critical roles for the unique reactivity of this catalytic system.

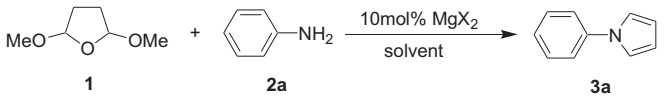
1. Introduction

Pyrrole derivatives are important species with remarkable biological activities[1] and useful intermediates in the synthesis of natural products and heterocycles.[2] Many methods for the synthesis of pyrrole derivatives have been developed, which involve conjugate addition,[3] transition metal-mediated cyclization,[4] aza-Michael addition,[5] multi-components reactions,[6] and other operations.[7] Among them, Paal–Knorr pyrrole synthesis and Clauson–Kaas pyrrole synthesis are the typical and commonly used protocols for the construction of pyrroles framework. A number of catalysts have been utilized into the condensation of Clauson–Kass pyrrole synthesis, such as glacial acetic acid,[8] TfOH,[9] P_2O_5,[10] montmorillonite K-10,[11] *p*-chloropyridine hydrochloride,[12] $FeCl_3\cdot 7H_2O$,[13] $Bi(NO_3)_3\cdot 5H_2O$,[14] and lanthanide triflate.[15] Magnesium, a practically ideal main group metal, which abundantly exists in nature, has been actively investigated as a catalyst in the field of C–C bond formation and functional group transformation.[16] In our previous papers,[17] we have demonstrated that MgI_2 etherate could efficiently catalyze the Mukaiyama aldol reaction of aldehydes with trimethylsilyl enolates, allylation of aldehydes with allylstannane and cycloaddition of isocyanates with oxiranes. In continuation of our research field, we will wish to report a mild, efficient, and highly chemoselective Clauson–Kass condensation of various primary amines with 2,5-dimethoxytetrahydrofuran catalyzed by 10% MgI_2 etherate.

2. Results and discussion

Initially, we have chosen aniline and 2,5-dimethoxytetrahydrofuran **1** as the model substrates for surveying the reaction parameters in the model reaction. The results are summarized in Table 1.

Table 1
Optimization of reaction conditions for MgI_2 etherate-catalyzed synthesis of pyrrole from aniline[a]



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

Entry	MgX_2	Solvent	Time (h)	Temp (°C)	Yield[b] (%)
1	MgI_2	DMF	6.0	100	Trace
2	MgI_2	CH_2Cl_2	6.0	40	Trace
3	MgI_2	EtOH	6.0	75	Trace
4	MgI_2	PhMe	6.0	100	35
5	MgI_2	THF	7.0	65	25
6	MgI_2	2-MeTHF	6.5	80	55
7	MgI_2	DMSO	5.5	100	55
8	MgI_2	Dioxane	6.0	100	65
9	MgI_2	CH_3CN	6.0	80	85
10	$MgBr_2$	CH_3CN	6.0	80	65
11	$MgCl_2$	CH_3CN	6.5	80	60
12	$MgClO_4$	CH_3CN	7.0	80	75

[a] The reaction was carried out by the condensation of aniline(5.0 mmol) and 2,5-dimethoxytetrahydrofuran (6.0 mmol) in the presence of 10 mol % $MgI_2\cdot(OEt_2)_n$ in above solvent at indicated temperature.
[b] Isolated yield by silica gel flash chromatography.

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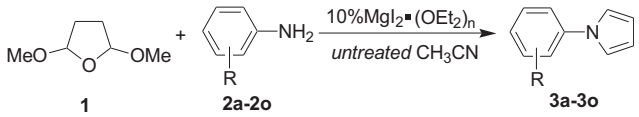
doi:10.1016/j.tet.2010.12.018

By screening various solvents we have found that *untreated* reagent-grade CH_3CN is the best solvent for this reaction (Table 1, entry 9). Poor yields were given in toluene, THF, 2-MeTHF, DMSO, and dioxane (Table 1, entries 4–8). No reaction was almost carried out in CH_2Cl_2, EtOH, and DMF (Table 1, entries 1–3). To examine the halide anion effect, halogen analogs of MgI_2 etherate, $MgCl_2$ etherate, $MgBr_2$ etherate, and $Mg(ClO_4)_2$ were compared under parallel reaction conditions (Table 1, entries 9–12), respectively. The best result has been observed with MgI_2 etherate as the catalyst. Good yield was also given by using 10 mol % of $MgClO_4$. However, $MgCl_2$ etherate and $MgBr_2$ etherate are less effective in terms of substrate conversion.

With these optimal conditions in hand, we further explored the scope and limitation of this simple process by reaction of electronically, sterically and functionally diverse amines under the same conditions. The results are listed in Table 2. As shown in Table 2, the reaction proceeded smoothly in MeCN at 80 °C and provided a single product without any side-products in good to excellent yields. Furthermore, we have observed the following delicate electronic effects: (1) anilines bearing an electron-donating group (i.e., OMe, Me) reacted *much faster* than aniline and provided the corresponding products in excellent yields (Table 2. entries 2 and 3). In addition, the reaction of less sterically hindered 2-methylaniline **2c** with 2,5-dimethoxytetrahydrofuran could give a good yield (Table 2. entry 4). However, the more sterically hindered 2,6-diisopropylaniline gave a moderate yield (Table 2, entry 5). (2) anilines bearing electron-withdrawing group (i.e., Cl, Br, F, NO_2, CF_3) *deactivated* aryl amine remarkably and afforded the corresponding pyrrole derivatives in moderate yields (Table 2. entries 6–12). Seemingly, this reactivity of aromatic amine is principally dependent on the electron density of the amino group, which is fur-

Table 2
Synthesis of *N*-aryl pyrrole derivatives catalyzed by MgI_2 etherate[a]



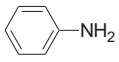
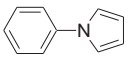
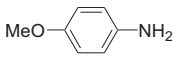
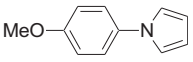
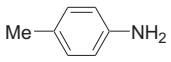
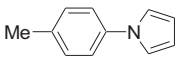
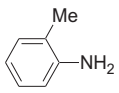
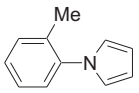
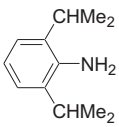
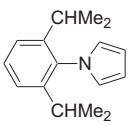
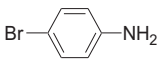
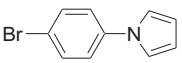
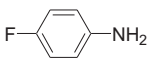
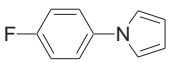
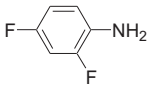
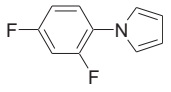
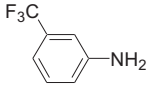
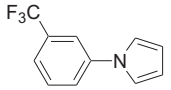
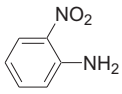
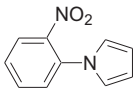
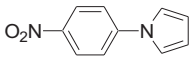
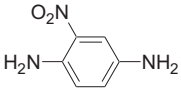
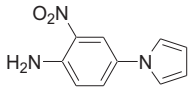
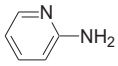
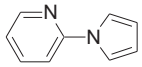
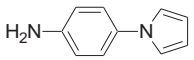
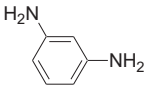
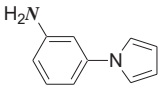
Entry	Amine	Time (h)	Product	Yield[b] (%)
1	 **2a**	6.0	 **3a**	85
2	 **2b**	2.0	 **3b**	98
3	 **2c**	2.0	 **3c**	94
4	 **2d**	6.0	 **3d**	84
5	 **2e**	10.0	 **3e**	70
6	 **2f**	6.0	 **3f**	66
7	 **2g**	6.0	 **3g**	73
8	 **2h**	6.0	 **3h**	65
9	 **2i**	8.0	 **3i**	77
10	 **2j**	12.0	 **3j**	65

Table 2 (*continued*)

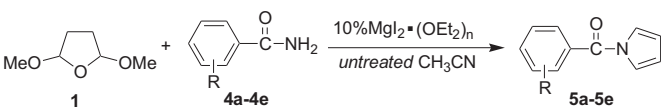
Entry	Amine	Time (h)	Product	Yield[b] (%)
11	 **2k**	12.0	 **3k**	62
12	 **2l**	12.0	 **3l**	70
13	 **2m**	12.0	 **3m**	68
14	 **2n**	10.0	 **3n**	65
15	 **2o**	10.0	 **3o**	63

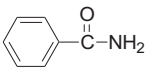
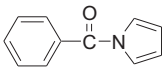
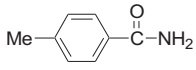
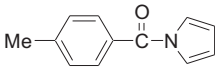
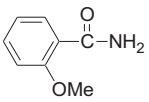
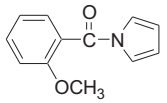
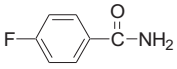
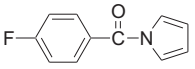
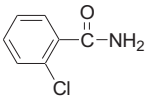
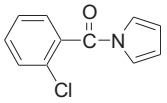
[a] The reaction was carried out by the condensation of aniline (5.0 mmol) and 2,5-dimethoxytetrahydrofuran (6.0 mmol) in the presence of 10 mol % $MgI_2 \cdot (OEt_2)_n$ in MeCN at 80 °C.
[b] Isolated yield by silica gel flash chromatography.

thered suggested by the exclusively regioselective condensation of 2-nitro-benzene-1,4-diamine **2l** (Table 2, entry 12). Moreover, we examined the reactivity of heteroaromatic amines, such as 2-aminopyridine **2m**, with 2,5-dimethoxytetrahydrofuran **1** in the presence of 10 mol % MgI_2 etherate. Moderate yield was also obtained by prolonging the reaction time (Table 2, entry 13). Additionally, the Clauson–Kass reaction of aromatic diamine with 2,5-dimethoxytetrahydrofuran **1** was selectively conducted (Table 2, entries 14 and 15). Moreover, we also studied the condensation of aliphatic amines with 2,5-dimethoxytetrahydrofuran **1**. Unfortunately, aliphatic amines are inert in the presence of MgI_2 etherate.

To expand the scope of this reaction we investigated the one-step preparation of *N*-acyl pyrroles from primary aryl amides using MgI_2 etherate. *N*-Acyl pyrroles can be regarded as activated carboxylic acid equivalents and are usually prepared by the addition of pyrrolyl anion with the appropriate acylating agents.[18,19] However, the harsh reaction conditions and strict avoidance from moisture limited this method. Recently, Azizi et al. reported a simple, practical and economical procedure for synthesis of *N*-acyl pyrrole catalyzed by $FeCl_3 \cdot 7H_2O$ in water.[13] Herein, we attempted to examined the scope and generality of our protocol using different substituted amides with 2,5-dimethoxytetrahydrofuran **1**. The results are summarized in Table 3. As shown in Table 3, the results showed that aryl amides are also good substrates in this catalytic system, and the desired acyl pyrroles are formed in moderate to good yield. We have also observed the same delicate electronic effects: (1) the reactivity of primary aryl amides with an electron-donating substitution (i.e., OMe, Me) is *much better* than primary benzamide (Table 3, entries 2 and 3). (2) An electron-withdrawing substitution (i.e., F, Cl, NO_2,) *deactivated* aryl amides remarkably (Table 3, entries 4 and 5). For example, primary aromatic amides with electronic-rich functionality, such as 4-methylbenzamide **4b**, underwent efficiently condensation with 2,5-dimethoxytetrahydrofuran **1** to afford the corresponding *N*-acyl pyrroles **5b** in 82% yields. The condensation of primary aromatic amides with electronic-poor functionality, such as 4-fluorobenzamide **4d** and 2-chlorobenzamide **4e**, with 2,5-dimethoxytetrahydrofuran **1** afforded the corresponding *N*-acyl pyrroles in moderate yields. Especially, 4-nitrobenzamide could not reacted with 2,5-dimethoxytetrahydrofuran **1** under the same condition. Apparently, the reactivity of these substituted aromatic amides is dependent on the inherent nucleophilicity of the amino group.

Table 3
Synthesis of *N*-acyl pyrrole derivatives catalyzed by MgI_2 etherate[a]

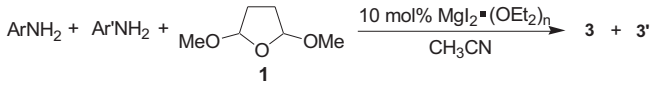


Entry	Substrate	Time (h)	Product	Yield[b] (%)
1	 **4a**	6.0	 **5a**	71
2	 **4b**	6.0.	 **5b**	82
3	 **4c**	6.0	 **5c**	78
4	 **4d**	10.0	 **5d**	65
5	 **4e**	10.0	 **5e**	62

[a] The reaction was carried out by the condensation of aryl amide (5.0 mmol) and 2,5-dimethoxytetrahydrofuran (6.0 mmol) in the presence of 10 mol % $MgI_2 \cdot (OEt_2)_n$ in MeCN at 80 °C.
[b] Isolated yield by silica gel flash chromatography.

This interesting chemoselectivity was further evaluated by crossover experiments of various aniline with 2,5-dimethoxytetrahydrofuran **1**, respectively. The MgI_2 etherate catalysis shows high levels of aromatic amines discrimination in the competitive reactions with 2,5-dimethoxytetrahydrofuran **1** (Table 4). Firstly, the catalyst can differentiate the steric difference in aromatic amines to much higher extents (Table 4, entries 1 and 2). Secondly, the MgI_2 etherate catalyst can uniquely recognize the delicate difference in electronic effect involved in aniline. Interestingly enough, 4-nitroaniline is much less reactive than aniline, 4-methylaniline, and 4-methoxyaniline in the MgI_2 etherate-catalyzed process. Only the Clauson–Kass condensation product of aniline, 4-methylaniline, and 4-methoxyaniline was obtained, respectively. In crossover-reaction of 4-nitroaniline with 4-bromoaniline or 4-fluoroaniline, the former is also less reactive than the latter (Table 4, entries 6 and 7) and the reaction exclusively gave the 1-(4-bromophenyl)-1*H*-pyrrole or 1-(4-fluorophenyl)-1*H*-pyrrole. More significantly, the MgI_2 etherate catalyst shows the remarkable preference for 4-methoxyaniline or 4-methylaniline over aniline, 4-bromoaniline, and 4-fluoroaniline (Table 4, entries 8–12). These results suggest that the relative reactivity of aromatic amines in the MgI_2 etherate-catalyzed process is determined almost solely by nucleophilicity of aromatic amines themselves.

Table 4
Crossover condensation of **1** with aromatic amines[a]



Entry	Ar	Ar′	Ratio (**3**/**3′**)[b]	Yield[c] (%)
1	C_6H_5	2,6-$(CH_3)_2CHC_6H_3$	80:20	90
2	2-MeC_6H_4	2,6-$(CH_3)_2CHC_6H_3$	70:30	88
3	C_6H_5	4-$NO_2C_6H_4$	>99/<1	84
4	4-MeC_6H_4	4-$NO_2C_6H_4$	>99/<1	93
5	4-$MeOC_6H_4$	4-$NO_2C_6H_4$	>99/<1	98
6	4-BrC_6H_4	4-$NO_2C_6H_4$	>99/<1	65
7	4-FC_6H_4	4-$NO_2C_6H_4$	>99/<1	71
8	4-$MeOC_6H_4$	C_6H_5	92/8	98
9	4-$MeOC_6H_4$	4-BrC_6H_4	97/3	97
10	4-$MeOC_6H_4$	4-FC6H4	95/5	97
11	4-MeC_6H_4	4-BrC_6H_4	85/15[d]	92
12	4-MeC_6H_4	C_6H_5	75/25[d]	95
13	C_6H_5	4-BrC_6H_4	74/26[d]	86

[a] Reactions were run with a mixture of 5.0 mmol of each aromatic amine, 5.0 mmol of 2,5-dimethoxytetrahydrofuran **1** and 10 mol % of MgI_2 etherate in MeCN at 80 °C.
[b] The ratio was determined by flash column chromatography.
[c] Isolated overall yield.
[d] The ratio was determined by GC analysis.

To the best of our knowledge, commonly used strong Lewis acids, i.e., $FeCl_3\cdot 7H_2O$,[13] $Bi(NO_3)_3\cdot 5H_2O$,[14] and $Sc(OTf)_3$,[15] are usually non- or poor-chemoselective. Thus, MgI_2 etherate represents a novel type of main group Lewis acid catalyst, which selectively activates the electron-rich functionality aromatic amines. The uniqueness of MgI_2 etherate is attributed to the dissociative character of iodide counterion, which is cooperating with the coordination of Lewis basic oxygen atom of acetal function with Mg(II) leading to a more Lewis acidic cationic Mg-coordinate as a result of Lewis base activation of Lewis acid.[20] The reactive intermediate **6** on reaction with amines **2** can lead to pyrroles **3** following a nucleophilic addition and subsequent expulsion of MeOH, dehydration, and aromatization steps as shown in the proposed catalytic cycle (Scheme 1). This reaction suggests the capability of MgI_2 etherate to serve as Lewis acid activator.

In conclusion, we have developed a mild, convenient, and environmentally friendly procedure for efficient synthesis of *N*-aryl pyrroles and *N*-acyl pyrroles by the condensation of amines with 2,5-dimethoxytetrahydrofuran in the presence of 10 mol % of MgI_2 etherate. Furthermore, we have demonstrated that the MgI_2 etherate catalysis system has unique chemoselectivity to the substrates. Exploitation of this protocol for generation of novel multicyclic structures is actively pursued in our lab.

3. Experimental section

3.1. General procedure for the synthesis of *N*-aryl pyrroles 3a–o

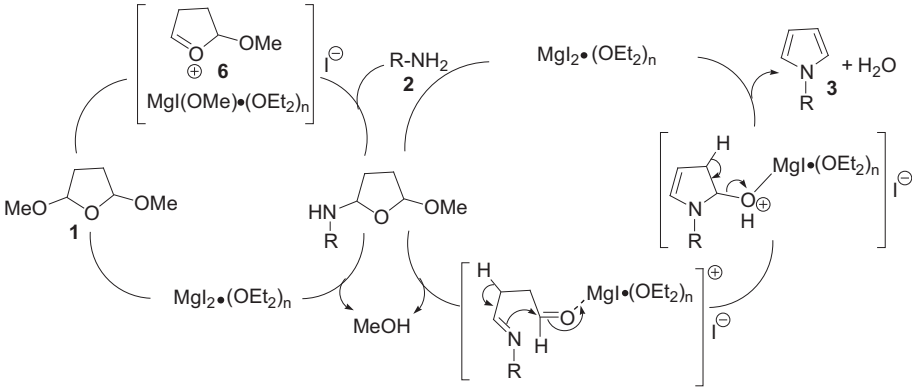
A Schlenk reaction tube was charged with primary aromatic amine (5.0 mmol), 2,5-dimethoxytetrahydrofuran (6.0 mmol), MgI_2 etherate (10% mmol), and acetonitrile (10 mL). The reaction mixture was stirred at 80 °C for several hours and then concentrated in vacuo. The residue was purified by flash column chromatography on a silica gel to give the desired product.

The physical and spectra data of the compounds **3a–o** are shown as follows.

*3.1.1. 1-Phenyl-1H-pyrrole (**3a**).* White solid;[13] mp 60.0–62.0 °C (lit. 62 °C); R_f 0.64 (100% petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.35 (t, J=2.0 Hz, 2H), 7.09 (t, J=2.0 Hz, 2H), 7.22–7.25 (m, 1H), 7.37–7.43 (m, 4H) ppm.

*3.1.2. 1-(4-Methoxyphenyl)-1H-pyrrole (**3b**).* White solid;[13] mp 112.1–112.9 °C; R_f 0.18 (100% petroleum ether); ^{1}H NMR(500 MHz, $CDCl_3$): δ=3.83 (s, 3H), 6.32 (t, J=2.0 Hz, 2H), 6.94 (d, J=9.0 Hz, 2H), 7.0 (t, J=2.0 Hz, 2H), 7.31 (d, J=9.0 Hz, 2H) ppm.

*3.1.3. 1-(4-Tolyl)-1H-pyrrole (**3c**).* Pale yellowish solid;[13] mp 82.9–83.1 °C (lit. 81.5–83.0 °C); R_f 0.59 (100% petroleum ether);



Scheme 1. The proposed mechanism of MgI_2 etherate-catalyzed pyrrole synthesis.

^{1}H NMR: (500 MHz, $CDCl_3$): δ=2.40 (s, 3H), 6.36 (t, J=2.0 Hz, 2H), 7.09 (t, J=2.0 Hz, 2H), 7.25 (s, 2H), 7.31 (d, J=8.5 Hz, 2H) ppm.

*3.1.4. 1-(2-Tolyl)-1H-pyrrole (**3d**).* Yellowish oil;[13] R_f 0.79 (100% petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=2.25 (s, 3H), 6.36 (t, J=2.0 Hz, 2H), 6.83 (t, J=2.0 Hz, 2H), 7.28–7.33 (m, 4H) ppm.

*3.1.5. 1-(2,6-Diisopropylphenyl)-1H-pyrrole (**3e**).* White crystalline solid;[21] mp 62.2–63.0 °C; R_f 0.84 (100% petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.123 (s, 6H), 1.137 (s, 6H), 2.401–2.456 (m, 2H), 6.31 (t, J=2.0 Hz, 2H), 6.63 (t, J=2.0 Hz, 2H), 7.21 (d, J=8.0 Hz, 2H), 7.38 (t, J=8.0 Hz, 1H) ppm.

*3.1.6. 1-(4-Bromophenyl)-1H-pyrrole (**3f**).* White solid;[13] mp 96.0–97.0 °C; R_f 0.68 (100% petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.38 (t, J=2.0 Hz, 2H), 7.01 (t, J=2.0 Hz, 2H), 7.28 (d, J=9.0 Hz, 2H), 7.55 (t, J=7.0 Hz, 2H) ppm.

*3.1.7. 1-(4-Fluorophenyl)-1H-pyrrole (**3g**).* Pale yellowish solid;[22] mp 50.6–51.7 °C; R_f 0.68 (100% petroleum ether); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=6.38 (t, J=2.0 Hz, 2H), 7.05 (t, J=2.0 Hz, 2H), 7.15 (t, J=8.5 Hz, 2H), 7.36–7.39 (m, 2H) ppm.

*3.1.8. 1-(2,4-Difluorophenyl)-1H-pyrrole (**3h**).* Pale yellowish oil;[23] R_f 0.33 (100% petroleum ether); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=6.34 (t, J=2.0 Hz, 2H), 6.91–6.99 (m, 4H), 7.31–7.36 (m, 1H) ppm.

*3.1.9. 1-(3-Trifluoromethylphenyl)-1H-pyrrole (**3i**).* White solid;[11] mp 49.7–50.0 °C; R_f 0.67 (100% petroleum ether); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=6.38 (t, J=2.0 Hz, 2H), 7.11 (t, J=2.0 Hz, 2H), 7.48–7.58 (m, 3H), 7.63 (s, 1H) ppm.

*3.1.10. 1-(2-Nitrophenyl)-1H-pyrrole (**3j**).* Yellowish oil;[15] R_f 0.38 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.37 (t, J=2.0 Hz, 2H), 6.80 (t, J=2.0 Hz, 2H), 7.48 (dd, J=5.0, 8.0 Hz, 2H), 7.65 (dd, J=1.5, 8.0 Hz, 1H), 7.86 (dd, J=2.0, 7.0 Hz, 1H) ppm.

*3.1.11. 1-(4-Nitrophenyl)-1H-pyrrole (**3k**).* Yellowish solid;[15] mp 183.1–184.4 °C; R_f 0.50 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.45 (t, J=2.0 Hz, 2H), 7.20 (t, J=2.0 Hz, 2H), 7.54 (dd, J=9.0, 7.0 Hz, 2H), 8.33 (dd, J=2.0, 7.0 Hz, 2H) ppm.

*3.1.12. 1-(3-Nitro-4-aminophenyl)-1H-pyrrol (**3l**).* Red-brown solid;[24] mp 178.8–179.7 °C; R_f 0.42 (17% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.11 (s, 2H), 6.36 (t, J=2.0 Hz, 2H), 6.91 (d, J=9.0 Hz, 1H), 7.02(t, J=2.0 Hz, 2H), 7.48 (dd, J=2.0, 6.5 Hz, 1H), 8.16 (d, J=3.0 Hz, 1H) ppm.

*3.1.13. 1-(2-Pyridinyl)-1H-pyrrol (**3m**).* Yellowish oil;[14] R_f 0.33 (2.5% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.36 (s, 2H), 7.10 (t, J=6.0 Hz, 1H), 7.32 (d, J=8.0 Hz, 2H), 7.52 (s, 2H), 7.74 (t, J=8.0 Hz, 1H), 8.43 (d, J=4.0 Hz, 1H) ppm.

*3.1.14. 1-(4-Aminophenyl)-1H-pyrrol (**3n**).* Pale yellowish solid;[25] mp 155.5–156.5 °C; R_f 0.32 (17% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.30 (t, J=2.0 Hz, 2H), 6.72 (dd, J=2.0, 6.5 Hz, 2H), 6.97 (t, J=2.0 Hz, 2H), 7.18 (dd, J=2.0, 6.5 Hz, 2H), 8.16 (d, J=3.0 Hz, 1H) ppm.

*3.1.15. 1-(3-Aminophenyl)-1H-pyrrol (**3o**).* Yellowish oil;[26] R_f 0.33 (17% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.32 (t, J=2.0 Hz, 2H), 6.55 (dd, J=2.0, 8.0 Hz, 1H), 6.70 (t, J=2.0 Hz, 1H), 6.78 (dd, J=1.5, 8.0 Hz, 1H), 7.05 (t, J=2.0 Hz, 2H), 7.18 (t, J=2.0 Hz, 1H) ppm.

3.2. General procedure for preparation of *N*-acyl pyrrole 5a–e

A Schlenk reaction tube was charged with primary aromatic amide (5.0 mmol), 2,5-dimethoxytetrahydrofuran (6.0 mmol), MgI_2 etherate (10% mmol), and acetonitrile (10 mL). The reaction mixture was stirred at 80 °C for several hours and then concentrated in vacuo. The residue was purified by flash column chromatography on a silica gel to give the desired product.

The physical and spectra data of the compounds **5a–e** are as follows.

*3.2.1. 1-Benzoyl-1H-pyrrole (**5a**).* Yellowish oil;[13] R_f 0.65 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.35 (t, J=2.5 Hz, 2H), 7.29 (t, J=2.5 Hz, 2H), 7.51 (t, J=7.5 Hz, 2H), 7.60 (d, J=7.5 Hz, 1H), 7.74–7.76 (m, 2H) ppm.

*3.2.2. 1-(4-Methylbenzoyl)-1H-pyrrole (**5b**).* Yellowish oil;[13] R_f 0.70 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=2.44 (s, 3H), 6.33 (t, J=2.5 Hz, 2H), 7.29 (dd, J=2.5, 4.0 Hz, 4H), 7.65 (d, J=8.5 Hz, 2H) ppm.

*3.2.3. 1-(2-Methoxybenzoyl)-1H-pyrrole (**5c**).* Yellowish oil; R_f 0.55 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=3.81 (s, 3H), 6.28 (t, J=2.5 Hz, 2H), 7.02–7.08 (m, 2H), 7.17 (s, 2H), 7.39 (dd, J=2.0, 8.0 Hz, 1H), 7.47–7.51 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ=55.78, 111.50, 113.06, 120.49, 120.61, 123.66, 129.22, 132.29, 156.79, 166.35 ppm.

*3.2.4. 1-(4-Fluorobenzoyl)-1H-pyrrole (**5d**).* Yellowish oil;[27] R_f 0.70 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.35 (t, J=2.5 Hz, 2H), 7.19 (t, J=8.5 Hz, 2H), 7.26 (t, J=2.5 Hz, 2H), 7.78 (dd, J=5.5, 8.5 Hz, 2H) ppm.

*3.2.5. 1-(2-Chlorobenzoyl)-1H-pyrrole (**5e**).* Yellowish oil;[15] R_f 0.60 (10% EtOAc in petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.33 (t, J=2.5 Hz, 2H), 7.12 (s, 2H), 7.37–7.40 (m, 1H), 7.45–7.50 (m, 3H) ppm.

3.3. General procedure for crossover reaction

A Schlenk reaction tube was charged with each amine (5.0 mmol), 2,5-dimethoxytetrahydrofuran (6.0 mmol), MgI_2 etherate (10% mmol), and acetonitrile (10 mL). The reaction mixture was stirred at 80 °C for several hours and then concentrated in vacuo. Flash column chromatography afforded the desired products. The ratio of each product was determined by column chromatography isolation or GC analysis.

Acknowledgements

Financial support from the Zhejiang Province Natural Science Foundation of China (Project Y4100692).

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.12.018.

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