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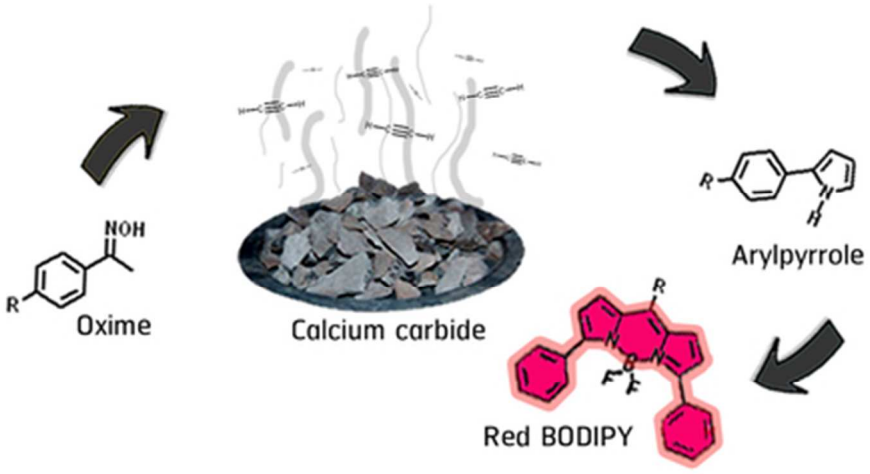

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Direct synthesis of aryl substituted pyrroles from calcium carbide: an underestimated chemical feedstock

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Received ooth January 2012,
Accepted ooth January 2012

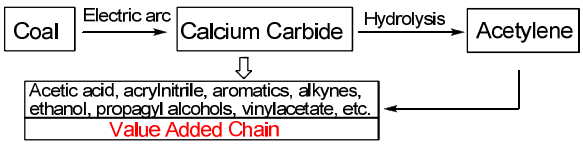
DOI: 10.1039/xoxxoooooox

www.rsc.org/

In this work, a novel synthetic methodology for preparation of aryl pyrroles directly from reactions of calcium carbide with oxime is reported. Various pyrrole derivatives are generated from the corresponding oximes in satisfactory yields (49-88%) under the optimized condition. The one-pot synthesis of aryl pyrrole from wildly available ketone is also successfully developed. A new near infrared fluorescent BODIPY dye containing phenyl substitution at the C-3 position is expediently prepared from the aryl pyrrole derived from this methodology. The key benefit of this methodology is the use of inexpensive and less hazardous primary chemical feedstock, calcium carbide, in wet solvent without any metal catalysts. This process offers a novel cost efficient synthesis of functionalized pyrrole.

Introduction

One of the key conversion routes along the value added chain in petrochemical industry is the formation of calcium carbide from electric arc furnace of coke and lime. The hydrolysis of calcium carbide gives acetylene gas as one of the major primary chemical feedstock for a more downstream chemical industry such as acetic acid, ethanol, aromatics, vinyl acetate, etc (Scheme 1).[1] Although acetylene gas is widely available and inexpensive, its highly flammable gaseous nature poses serious disadvantage in extra operation control and cost to prevent leakage and explosion. In light of industrial safety improvement without additional cost, a less hazardous and more economical starting material is highly desirable.[2] As a main source of acetylene gas, solid calcium carbide stands a good chance as a safer and cheaper alternative to acetylene gas for the production of acetylene-derived chemicals.



Scheme 1. Conversion of coal to commodity chemicals

In 2006, Zhang reported the use of calcium carbide as triplet C–C bond moiety for the synthesis of diarylethynes via Sonogarshira coupling reaction.[3] Following this work, our group and others recently developed methodologies for direct use of calcium carbide in the synthesis of C≡C containing compounds, such as diarylethynes,[4] poly(p-phenyleneethynylene)s (PPEs),[5] polyenynes,[6] propagylamine,[7] enaminones[8] and acetylenic alcohols.[9] All reported process relies on the slow release of calcium carbide into acetylene gas which then turns into corresponding anion (C_2^{2-} anion). Subsequently, the reactive intermediates act as either a coupling partner for metal catalyzed reaction or a nucleophile for carbonyl addition.

One of the highest value compounds that can be obtained from acetylene is 2-aryl pyrrole. It is a basic building block for pharmaceuticals,[10] and fluorescent dyes (BODIPY).[11] Current methods to prepare 2-aryl pyrrole involve either using unsubstituted pyrrole or ketoxime (Scheme 2). The first method involves a metal catalysed reaction to introduce the aryl group to C2-halogenated pyrroles.[12] In addition, direct C-H activation of pyrrole has recently been developed.[13] The drawbacks of these methods are the requirement of precious metal catalyst and additional protection/deprotection steps in some cases. Moreover, direct arylation of *N*-substituted pyrroles with aryl iodides in the presence of lithium *tert*-butoxide without the use of transition metal catalysts has also been reported.[14]

On the other hand, the readily and inexpensively available ketoxime can be converted to 2-aryl pyrrole in one step by a reaction with substituted alkynylcarbonyl compounds or acetylene gas. The former uses reagent metal catalyst such as Au and Ni to activate the triple bond.[15] The latter (so called Trofimov reaction) uses acetylene gas, bubbling into the reactor

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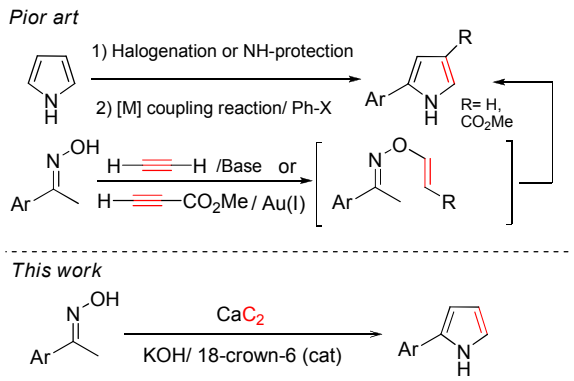
in the presence of a strong base.[16] The Trofimov reaction is a preferred method for 2-aryl pyrrole synthesis because metal is not required in the transformation and the product was directly obtained without additional deprotection step.



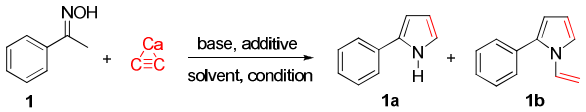
Scheme 2. Synthetic approach for 2-aryl pyrrole

In this study we proposed a novel process for direct transformation of calcium carbide into 2-aryl pyrroles (Scheme 2). This is not only an unprecedented application of calcium carbide as an electrophile precursor in a vinylation reaction to produce vinylic derivatives but also the first utilization in heterocycle synthesis. Our methods successfully overcome the challenge of poor solubility of calcium carbide in organic solvent and unpolarized nature of acetylenic triple bond to achieve excellent product yields. The developed method uses economical starting materials (ketoximes) and avoid handling of gaseous acetylene. The use of heavy metal is obliterated and overall process steps are significantly shortened. Therefore it can be considered as a convenient, safe, and more environmental conscious, green and sustainable process. Moreover, our process can be easily applied in large scale manufacturing in the chemical industries as well as for routine laboratory synthesis.

Results and Discussion

To design the reaction condition of the calcium carbide we realized the main problems which are a low solubility of calcium carbide and a poor electrophilic nature of acetylene gas which limited its application in organic synthesis. However, a previous work from Trofimov demonstrated that the use of superbase can promote the *O*-alkylation of oximes by acetylene gas.[16] Moreover, our work have shown that the use of wet polar aprotic solvent can slowly hydrolyze the calcium carbide into acetylene in situ.[4] Therefore, we began optimization study by reacting acetophenone oxime (**1**) with calcium carbide in the presence of base to provide the *NH*-2-aryl pyrrole (**1a**) along with *N*-vinyl pyrrole (**1b**) and the results are depicted in Table 1. Among several bases studied including KOH, NaOH and CsOH (Table 1, entries 1, 3-4), the best result were obtained with KOH, providing the desired pyrrole **1a** in 58% yield along with the over vinylation product **1b** in 3 % yield. Switching from DMSO to DMF result in no reaction (Table 1, entry 2). In order to drive the reaction forward the temperature was raised from 100 to 120 °C for 24 hour, however, the yield of the pyrrole **1a** decreased along with the increase of the over vinylation product **1b** (Table 1, entry 5). Therefore, controlling the temperature and the reaction are vital in the reaction condition (Table 1, entry 5). To increase the base strength, we therefore added a catalytic amount of 18-crown-6 as a catalyst (3% mol) in the reaction mixture. The yield of both pyrroles (**1a** and **1b**) increased to 65 and 8, respectively (Table 1, entry 6). It should be noted that under this condition, the crude NMR indicated that the oxime was completely consumed and no hydrolysis product (acetophenone) was detected in the reaction mixture. The slightly low yield of pyrrole **1a** is perhaps due to its air sensitivity and some decomposition may occur during the chromatographic purification.

Table 1. Effect of various parameters on the yield of aryl pyrroles



Entry[a]	Additive	Base [equiv.]	Solvent	Yield[b] **1a** [%]	Yield[b] **1b** [%]
1	-	KOH [1.5]	DMSO	58	3
2[c]	-	KOH [1.5]	DMF	0	0
3	-	NaOH [1.5]	DMSO	44	0
4	-	CsOH [1.5]	DMSO	48	0
5[d]	-	KOH [1.5]	DMSO	44	8
6	18-crown-6	KOH [1.5]	DMSO	65	8
7[e]	18-crown-6	KOH [3.0]	DMSO	32	12
8	-	KOH [1.5]	2%H_2O: DMSO	60	0
9	-	KOH [1.5]	10%H_2O :DMSO	32	0
10	18-crown-6	KOH [1.5]	2%H_2O: DMSO	73	0

[a]Acetophenone oxime (1 equiv.), CaC_2 (6 equiv.), 18-crown-6 (3 mol%) and solvent (0.074 mM) were heated at 100 °C in a sealed tube for 15 h. [b]Isolated yields after purified by column chromatography on neutral alumina. [c]Starting material was recovered in 50% yield. [d] The reaction was heated to 120°C. [e]Large excess (10 equiv.) of CaC_2 was added.

As mentioned above that all reactions were performed in the undried solvent. In order to increase the liberation of acetylene, we added small amount of water in to the reaction (Table 1, entry 8-10). The presence of water at 2% w/w with 18-crown-6 gave the best yield of the product **1a** (73%) and has been used as the optimized condition for further studies. Deliberate

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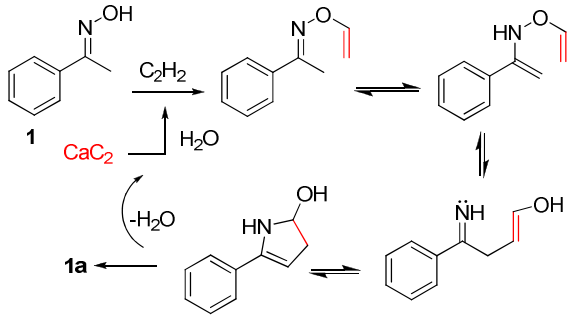
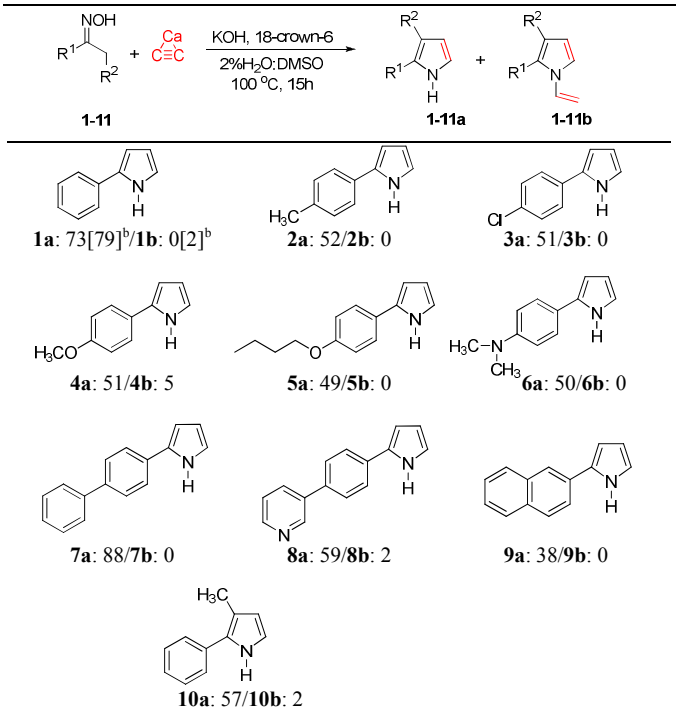
addition of water can suppress the formation of vinyl pyrrole and only trace amount were detected in crude ^{1}H NMR spectra. In the presence of water, the *N*-vinylation is sluggish due to the reduction of basic strength of the KOH in DMSO by the so called "leveling effect". However, too much added water (10%) gave significantly lower yield of **1a** perhaps due to the too fast hydrolysis of calcium carbide making acetylene escape from the system faster than react with the oxime, and also the leveling effect that lowering KOH/DMSO basic strength. Importantly, in comparison with the original Trofimov reaction, our reaction based on calcium carbide gave a comparable efficiency, offering an alternative synthesis of 2-aryl pyrroles that is both convenient and safer to perform. The proposed mechanism of the reaction between calcium carbide and oxime are presented in Scheme 3. The added water initially hydrolyzed calcium carbide to liberate the acetylene gas. The reaction then proceeded as in standard Trofimov reaction which involves the addition to acetylene followed by tautomerization to generate an enamine.[1c] Next, the enamine underwent a sigmatropic rearrangement to form an enol-imine intermediate. The desired aryl pyrrole **1a** was finally obtained following tautomerization-addition-dehydration sequence of the enol-imine intermediate.



Scheme 3. Proposed mechanism for the synthesis pyrrole **1a** from oxime **1**

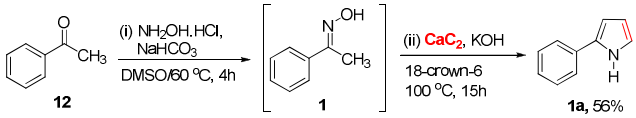
With the optimized condition in hands, we next expanded the scope of this reaction by subjecting a variety of oximes (**2-11**) into the reaction conditions (table 1). These oxime substrates were easily prepared from commercially available ketones using hydroxylamine hydrochloride and purified by recrystallization. A panel of acetophenone oximes (**2-6**) bearing methyl, chloride, methoxy, butoxyl and dimethyl amine were successfully transformed into the aryl pyrroles (**2a-6a**) in moderate yields along with small amount of over vinylation products (**2b-6b**) less than 6% yield. The oxime containing bicyclic structure such as **7-9** were also tested on the optimized condition and generated highly conjugated pyrroles **7a-9a** in fair to good yields. The scopes of the reaction also extend to prepare highly substituted pyrroles. Propiophenone oxime **10** were reacted with calcium carbide under the described condition to afford the 2,3-disubstituted pyrrole **10a** in 57% yield along with the corresponding vinylpyrrole **10b** in 2% yield.

Table 2 Substrate scope of oxime in the reaction with calcium carbide[a]



[a]Oxime (1 equiv), CaC_2 (6 equiv), 18-crown-6 (3mol%) in 2% water/DMSO (0.074 mM) were heated at 100°C in a sealed tube for 15 h and purified by column chromatography on neutral alumina. [b]GC yield from Trofimov reaction[16e]

Although oxime can be prepared easily, an additional oxime preparation step is still required. On the other hand, the use of ketone (the precursor of oxime) as the starting material is preferred because it allows a convenient one-pot preparation of 2-arylpyrroles. Here, we successfully developed such one-pot pyrrole synthesis directly from ketone, which combine combines oxime formation with Trofimov reaction, as shown in Scheme 5. The ketone **12** was reacted with hydroxylamine hydrochloride in DMSO at 60 ºC in the presence of a base ($NaHCO_3$). Addition of calcium carbide and catalytic amounts of 18-crown-6 into the reaction mixture led to the formation of aryl pyrrole (**1a**) in 56% yield as the sole product. This one-pot process is comparable to the two-step transformation in terms of isolated yield, but is shorter and more convenient to perform.



Scheme 4. One-pot synthesis of 2-phenyl pyrrole **1a** from acetophenone **12**

To prove the scope of our methodology, we next synthesized 3-substituted BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) using the aryl pyrrole prepared by our

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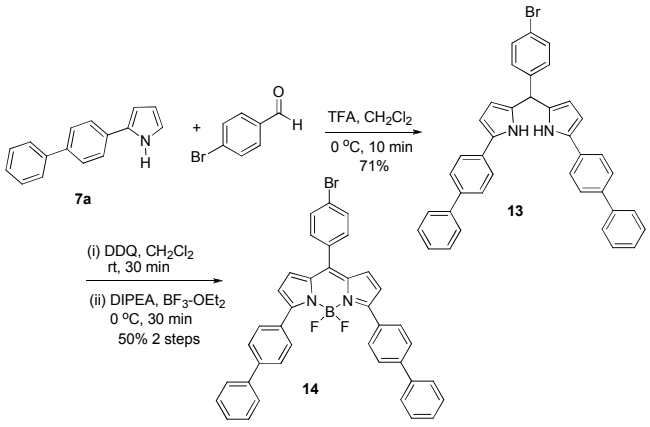
methods. Fluorescent BODIPY dyes are widely used as sensors, optoelectronic material, and imaging applications.[11b,17] In recent years, near infrared (NIR) dyes have attracted much interest for *in vivo* imaging applications[18] because it allows the bioimaging with the low interference from the tissue. The high penetration power and the low energy of the light also caused less cell damages. To make NIR BODIPY, the post structural modification of BODIBY scaffold by extension of π-conjugation such as alkenyl or aryl substitution at the 3-position is generally employed.[11b] The 3-alkenyl substituted BODIPY are obtained from Knoevenagel reaction of 3-methyl BODIPY.[11a] The preparation of 3-aryl substituted BODIPY usually involves metal-catalyzed cross coupling reaction of the halo-substituted BODIPY, which not only requires additional step but also causes the partial decomposition of BODIPY during the coupling reaction.[19]

With the readily accessible 2-aryl pyrroles in hands, we have the opportunity to perform a direct synthesis of BODIPY fluorophore containing aromatic substitutent at the C-3 position. Using the standard method,[20] the synthesis was accomplished via a two-step procedure presented in Scheme 6. Initially, a condensation of biphenyl-substituted pyrrole **7a** with 4-bromobenzaldehyde led to the formation of the dipyrrane **13** in 71% (Scheme 6). The oxidation of **13** using DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone) followed by a complexation with $BF_3{\cdot}OEt_2$ gave the desired BODIPY **14** with the biphenyl substitution at the C-3 position in 51% yield. The peripheral bromobenzene moiety at the C-5 position of **14** provides an opportunity for further probe attachment for fluorescence sensing applications. The absorption and emission spectra of the BODIPY **14** are shown in Figure **2**. The maximum absorption and emission wavelengths are at 582 and 623 nm, respectively. It is apparent that the conjugation extension of the BODIPY scaffold by installation of additional phenyl groups can shift both absorption and emission maxima into the far red region.



Scheme 5. The synthesis of BODIPY **14** from pyrrole **7a**

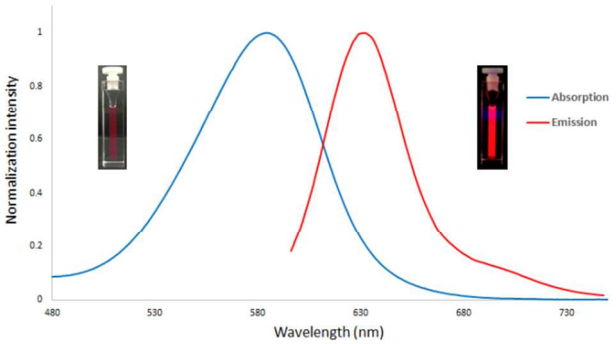


Fig. 1 UV-vis absorption and fluorescence emission spectra of BODIPY **14** in THF. λex = 582 nm.

Materials and methods

All chemicals were obtained from commercial suppliers (Sigma Aldrich), and were used without further purification. All solvents were used directly without drying, except for dimethyl sulfoxide (DMSO), which was dried over 4 Å molecular sieves. Calcium carbide was ground before use. Analytical thin-layer chromatography (TLC) was performed on Kieselgel F254 pre-coated plastic TLC plates from EM Science. Visualization was performed with a 254 nm ultraviolet lamp. Column chromatography was carried out with aluminium oxide (90 active neutral, 70-230 mesh) from Merck and silica gel (60, 230-400 mesh) from ICN Silitech. The ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 or Bruker Avance 400 for ^1H (400 MHz) and Bruker Avance 400 for ^{13}C (100 MHz) in $CDCl_3$ or $(CD_3)_2SO$ solution. Mass spectra were performed by Micromass Quattro micro TM API and triple quadrupole GC/MS from Agilent technologies. The UV-visible absorption spectra were obtained from Varian Cary 50 UV-Vis spectrometer and the fluorescence emission spectra were recorded on the Varian Cary Eclipse spectrofluorometer.

General procedure for synthesis 2-arylpyrroles

A mixture of calcium carbide (6.0 equiv), ketone oxime (1.0 equiv), potassium hydroxide (1.5 equiv) and 18-crown-6 (3.0 mol%) was suspended in 10 mL of (50:1) DMSO/H_2O in a sealed tube. The reaction mixture was stirred at 100 ºC overnight. The reaction was cooled to room temperature and diluted by dropwise addition of H_2O (10 mL). The reaction mixture was filtered and extracted solution into ether (5 × 30 mL). The combined extracts were washed with brine (2 x 30 mL), dried over $MgSO_4$ and evaporated under reduced pressure to give the crude product, which was further purified by column chromatography on alumina (eluted with ethyl acetate / hexanes = 1: 3) to afford the desired compound.

General procedure for one-pot synthesis of 2-phenylpyrrole (1a)

Hydroxylamine hydrochloride (0.83 mmol, 57 mg) was dissolved in DMSO (10 mL) in a sealed tube with a magnetic stirrer bar, and then $NaHCO_3$ (0.83 mmol, 93 mg) and acetophenone (0.83 mmol, 100 mg) were added. The reaction mixture was stirred at 60 °C for 4 h. After the completion of reaction, calcium carbide (4.98 mmol, 319 mg), potassium hydroxide (1.25 mmol, 70 mg) and 18-crown-6 were

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added and the mixture was heated to 100 °C for overnight. The reaction was cooled to room temperature and diluted by dropwise addition of H_2O (10 mL). The reaction mixture was filtered and extracted solution into ether (5 × 30 mL). The combined extracts were washed with brine (2 x 30 mL), dried over $MgSO_4$ and evaporated under reduced pressure to give the crude product, which was further purified by column chromatography on alumina (eluted with ethyl acetate / hexanes = 1: 3) to afford the corresponding 2-phenylpyrrole as a purple solid (66 mg, 56% yield).

2-Phenylpyrrole (1a)[21] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.45 (br, 1H, NH), 7.36 (d, *J*=8.0 Hz, 2H, Ar-H), 7.36 (t, *J*=8.0 Hz, 2H, Ar-H), 7.11 (1H, d, *J*=8.0 Hz, Ar-H), 6.87 (s,1H, CH), 6.53 (s, 1H, CH), 6.31 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 132.8, 132.2, 128.9, 126.2, 123.7, 118.9, 110.1, 106.0. ESI-MS calculated for $C_{10}H_9N$: 143.07, found at 143.01

2-*p*-Tolylpyrrole (2a)[12c] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.41 (br, 1H, NH), 7.37 (d, *J*=8.0 Hz, 2H, Ar-H), 7.17 (d, *J*=8.0 Hz, 2H, Ar-H), 6.84 (s, 1H, CH), 6.47 (s, 1H, CH), 6.28 (s, 1H, CH), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 135.9, 132.3, 130.1, 129.5, 123.9, 118.4, 110.0, 105.4, 21.1. ; GC-Ms : m/z: 157.1

2-(4-Chlorophenyl)pyrrole (3a)[12c] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.84 (br, 1H, NH), 7.40 (d, *J*=8.6 Hz, 2H, Ar-H), 7.33 (d, *J*=8.5 Hz, 2H, Ar-H), 6.88 (s, 1H, CH), 6.52 (d, *J*=5.6 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 131.8, 131.3, 131.0, 129.0, 125.0, 119.2, 110.4, 106.5.; GC-Ms : m/z: 177.1

2-(4-Methoxyphenyl)pyrrole (4a)[13c] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.24 (br, 1H, NH), 7.30 (d, *J*=8.4 Hz, 2H, Ar-H), 6.82 (d, *J*=8.5 Hz, 2H, Ar-H), 6.72 (s, 1H, CH), 6.32 (s, 1H, CH), 6.19 (s, 1H, CH), 3.73 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 158.3, 132.2, 126.0, 125.3, 118.2, 114.4, 109.9, 104.9, 55.35.; GC-Ms : m/z: 173.1

2-(4-Butoxyphenyl)pyrrole (5a) : ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.33 (br, 1H, NH), 7.39 (d, *J*=8.6 Hz, 2H, Ar-H), 6.90 (d, *J*=8.3 Hz, 2H, Ar-H), 6.83 (s, 1H, CH), 6.40 (s, 1H, CH), 6.27 (s, 1H, CH), 3.97 (t, *J*=6.5 Hz, 2H, OCH_2), 1.82-1.73 (m, 2H, CH_2), 1.50 (q, *J*=8.0 Hz, 2H, CH_2), 0.98 (t, *J*=7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 157.9, 132.3, 130.6, 125.8, 125.3, 118.1, 115.0, 109.9, 104.8, 67.8, 31.4, 19.3, 13.3.; GC-Ms : m/z: 215.2

***N,N*-Dimethyl-4-(pyrrol-2-yl)aniline (6a)**[12d] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.31 (br, 1H, NH), 7.37 (d, *J*=8.7 Hz, 2H, Ar-H), 6.80 (s, 1H, CH). 6.77 (d, *J*=8.5 Hz, 2H, Ar-H), 6.36 (s, 1H, CH), 6.28 (s, 1H, CH), 2.97 (s, 6H, N-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 149.3, 132.9, 125.1, 125.1, 122.0, 117.5, 113.0, 109.7, 103.9, 40.6.; GC-Ms: m/z: 186.2

2-(Biphenyl-4-yl)pyrrole (7a)[12c] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.48 (br, 1H, NH), 7.62 (d, *J*=8.3 Hz, 4H, Ar-H), 7.55 (d, *J*=8.4 Hz, 2H, Ar-H), 7.45 (t, *J*=7.6 Hz, 2H, Ar-H), 7.34 (t, *J*=7.4 Hz, 1H, Ar-H), 6.90 (s, 1H, CH), 6.58 (s, 1H, CH), 6.32 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 140.7, 138.9, 131.8, 128.8, 127.5, 127.2, 126.8, 124.2, 118.9, 110.3, 106.2.; GC-Ms : m/z: 219.1

3-(4-(Pyrrol-2-yl)phenyl)pyridine (8a) : ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 9.40 (br, 1H, NH), 8.94 (s, 1H,), 8.85 (1H, d, *J*=5.2 Hz), 8.58 (1H, s), 8.41 (1H, d, *J*=4.6 Hz) 7.96 (1H, d, *J*=8.0 Hz), 7.81 (1H, d, *J*=9.2 Hz), 7.30 (2H, d, *J*=4.0 Hz), 6.93 (1H, d, *J*=1.9 Hz), 6.59 (1H, d, *J*=1.1 Hz), 6.31 (1H, d, *J*=2.4 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 152.5, 149.2, 147.1, 146.1, 144.7, 133.7, 133.2, 131.6, 129.4, 128.4, 123.9, 123.4, 120.4, 110.3, 107.4.

2-(Naphthalen-2-yl)pyrrole (9a)[12c] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.61 (br, 1H, NH), 7.85 (s, 1H, Ar-H), 7.84-7.78 (m, 3H, Ar-H), 7.67 (dd, *J*=8.4,1.6, 2H, Ar-H), 7.52-7.36 (m, 2H, Ar-H), 6.93 (s, 1H, CH), 6.66 (s, 1H, CH), 6.35 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 133.8, 132.2, 132.1, 130.2, 128.6, 127.8, 127.7, 126.5, 125.4, 123.3, 121.1, 119.2, 110.3, 106.7.; GC-Ms : m/z: 193.2

3-Methyl-2-phenylpyrrole (10a)[22] **:** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.15 (br, 1H, NH), 7.46-7.32 (m, 5H, Ar-H), 7.26 (s, 1H, CH), 6.78 (s, 1H, CH), 6.16 (s, 1H, CH), 2.29 (s, 3H, CH_3).; ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 133.8, 128.7, 126.4, 126.0, 123.0, 117.3, 116.2, 112.2, 12.5.; GC-Ms : m/z: 156.1

Synthesis of BODIPY 14

4-Bromobenzaldehyde (0.28 mmol, 52 mg) and 2-(biphenyl-4-yl)pyrrole **(7a)** (0.558, 122 mg) was dissolved in dichloromethane (30 mL) in round bottomed flask with a magnetic stirrer bar. The reaction mixture was stirred at room temperature for 5 minutes then a few drops of trifluoroacetic acid was added, and the reaction was stirred for another 5 minutes. The reaction was washed with water (3 x 30 mL), dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel (dichloromethane / hexanes = 1:2) gave compound **13** as a dark red solid (240 mg, 71% yield). The intermediate **13** (0.196 mmol, 119 mg) and DDQ (0.196 mmol, 45 mg) was dissolved in dichloromethane (10 mL) in a round bottomed flask with a magnetic stirrer bar under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 30 minutes. Then *N,N*-diisopropylethylamine (1.97 mmol, 0.34 mL) and boron trifluoride diethyl etherate (2.36 mmol, 0.30 mL) were added at 0 ºC and the mixture was stirred for 30 minutes. The reaction was washed with saturated $NaHCO_3$ (3 x 30 mL), brine (3 x 30 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (dichloromethane / hexanes = 1:2) to give the product as a red solid (129 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.00 (d, J=8.4 Hz, 4H, Ar-H), 7.73-7.61 (m, 10H, Ar-H), 7.52-7.42 (m, 6H, Ar-H), 7.37 (d, *J*=7.4 Hz, 2H, Ar-H), 6.89 (d, *J*=4.4 Hz, 2H, CH), 6.72 (d, *J*=4.2 Hz, 2H, CH).; ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 142.4, 140.5, 136.4, 133.3, 132.0, 131.7, 131.4, 130.5, 130.0, 130.0, 129.9, 128.8, 127.6, 127.2, 127.0, 124.7, 121.2. HRMS (ESI) calculated for $[M+Na]^+$: 673.1238, found at 673.1232.

Conclusions

In summary, a practical synthesis of 2-arylpyrroles from calcium carbide and oximes was successfully developed. The reaction was carried out in wet solvent without the use of toxic metal. Moreover, the process was extended to prepare 2-arylpyrroles in one-pot manner starting from acetophenone and hydroxylamine. The resulting aryl pyrroles prove to be an excellent building block for NIR-BODIPY fluorophores. These novel synthetic methods provide an opportunity to position calcium carbide as a sustainable and cost efficient carbon source in modern chemical industries.

ARTICLE View Article Online DOI: 10.1039/C4GC01615G Journal Name

Acknowledgements

This study is financially supported by the Thailand Research Fund (TRF-RSA5780055) and Nanotechnology Center (NANOTEC), NSTDA, Ministry of Science and Technology, Thailand, through its program of Center of Excellence Network. This work is part of the Project for Establishment of Comprehensive Center for Innovative Food, Health Products and Agriculture supported by the Thai Government Stimulus Package 2 (TKK2555, SP2), the Higher Education Research Promotion and National Research University Project of Thailand, Office of the Higher Education Commission (AM1006A-56) and the Ratchadaphiseksomphot Endowment Fund of Chulalongkorn University (RES560530126-AM).

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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