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Construction of Fluorescence-tunable Pyrido-Fused Benzimidazoles *via* Direct Intramolecular C-H amination under Transition-Metal-Free Conditions

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A novel methodology was discovered to construct multi-phenyl substituted pyrido-fused benzimidazole (PBI) core frameworks *via* direct oxidative intramolecular C-H amination of a-unsubstituted pyridinium salts under transition-metal free conditions. The resulting highly π-conjugated PBI derivatives exhibited highly tunable fluorescent emission not only in solution but also in the solid state.

Exploiting/ Exploring efficient methodologies for discovery of new fluorescent molecular frameworks has recently been the subject of growing interest.[1] The π-conjugated heteroaryl scaffolds have always been the key fluorescent core objects.[2] In particular, benzimidazolyl-based core scaffolds, especially pyrido-fused benzimidazole (PBI) and its derivatives, are prevalent in the fields of medical science[3] and advanced functional organic materials, such as organic light-emitting diodes (OLED), organic field effect transistors (FET) and fluorescent sensors.[4] It has reported that some of these complexes exhibited excellent solid fluorescence at least two times stronger than Alq3.[4h] However, there have been almost no systematic studies of the relationship between the structural and photophysical properties of PBI frameworks due to the limited structural diversity.

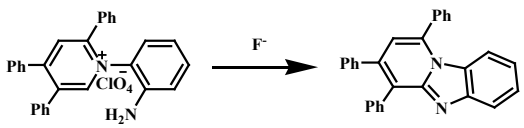
Accordingly, discovery of a new synthetic methodology to construct a chemical library of PBI core frameworks with tunable fluorescent emission is of great utility. Until now, several strategies had been explored to construct PBI frameworks, such as the reaction of substituted benzimidazoles with 1, 3-dicarbonyl compounds, 2-aminopyridine with either o-chloronitrobenzene, p-benzo-quinone, or 2-chlorocyclohexanone,a-pyrane thione derivatives with o-phenylenediamines as well as the photocyclization of (o-haloaryl)hetarylamines.[5] However, the reported synthetic routes has lengthy steps and rather low yields.

Recently, intramolecular C−H direct amination has received great attention as an effective way to construct N-heterocyclic compounds.[6] Zhu et al reported the synthesis of PBI compounds by using copper(II) and iron(III) as the co-catalyst.[7]

Although the yield is satisfactory, transtion metal catalyst needed high temperatures (100°C) and long reaction times. Moreover the formation of coupling products containing aryl halide groups requires use of an intermediate by introduction of protecting groups. On the other hand it is hard to construct as highly conjugated molecules, such as multi-phenyl substituted PBI derivatives. As is well known, the introduction of multi-phenyl group will not only improve the fluorescence intensity in solution due to the extension of the π-conjugation, but also induce strong solid-state fluorescence owing to the restriction of rotation of the peripheral phenyl rotors against the central stator.[8]

We have previously reported a novel chemodosimeter for fluoride ions.[9] In this case the "turn-on" fluorescence proved to originate from an unprecedented intramolecular cyclization of 2,4,5-triphenyl pyridinium salt to the corresponding PBI derivative shown in (Scheme 1).

Herein, we investigate the possibility of the above-mentioned transformation as a method to construct a chemical library of PBI core frameworks, and eventually realized a convenient synthesis of a series of multi-phenyl substituted PBI frameworks through direct oxidative intramolecular C-H amination under transition-metal free conditions.



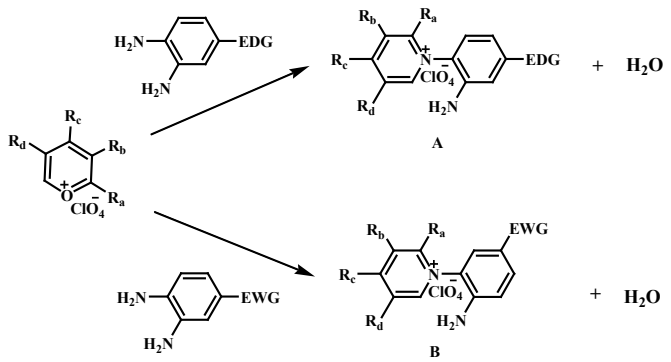
No fluorescence Blue fluorescence

Scheme 1 A novel reaction for the detection of fluoride ion.

Pyrylium salts, were prepared according to our previously reported work.[10] The key characteristic of pyrylium salts is the α -monosubstitution named α -active pyrylium salts, we designed and synthesized several functional organic molecules in our previous

work.[11] In order to access PBI frameworks, we first converted the active pyrylium salts into corresponding pyridinium salts with one active amino group neighboring the "α-active" C-H bonds. (Scheme 2).

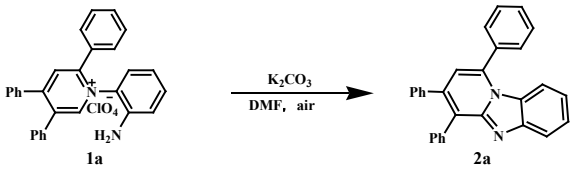
Different substitution (EWG/EDG) on O-phenylendiamines shows quite different activities. On the basis of substituents positioning effects, we finally got different type of pyridinium salts. For electron-withdrawing groups, such as NO_2 and Cl, the reaction activity of amino moiety on para-position is reduced, and type B pyridinium salts were obtained. In contrast, for electron-donating group, such as $-CH_3$ and OCH_3, the reaction activity of amino moiety on para-position is increased, therefore, type A pyridinium salt were obtained dominantly (Scheme 2), for both kind of pyridinium salt owing to the "α-active" C-H bond, which is electrophilic center, neighboring amino moiety act as nucleophile, easily attacked on the electrophilic activated center due to which we construct PBI frameworks.



Scheme 2 synthetic routes of pyridinium salts **A** with electron-donating group **(**EDG) and **B** with electron-drawing groups (EWG).

Pyridinium salt **1a** was chosen for optimizing the reaction conditions and the results were summarized in Table 1. It was found that the reaction could proceed in different solvents including non-polar solvent CH_2Cl_2, and polar solvents, such as CH_3CN, MeOH and DMF. However due to the poor solubility of pyridinium salts and base, the reaction in CH_2Cl_2 gave rather low yields (entry 11) while in DMF the reaction showed good yields. To activate the reaction, bases were used. Organic base triethylamine (TEA) and potassium tert-butoxide (KO_tBu) were tried, the resulting yields were low (entry 1 and 2), even with increasing the reaction time (entry 5 and 6). But inorganic base K_2CO_3 afforded good yields (entry 3). Increasing the amount of K_2CO_3 from 0.05 equiv.to 1 equiv, the yield increased correspondingly (entry 4). This result clearly indicated the role of base was not catalytic but stoichiometric. Furthermore, the reaction time increased from 2 hours to 12 hours gave rise to the excellent t yield (entry 8). Also observed that air (O_2) played a key role in this reaction, as no product could obtained under Argon atmosphere. Lastly the reaction temperature factor had minimal effect to improve the yields (entry 14).

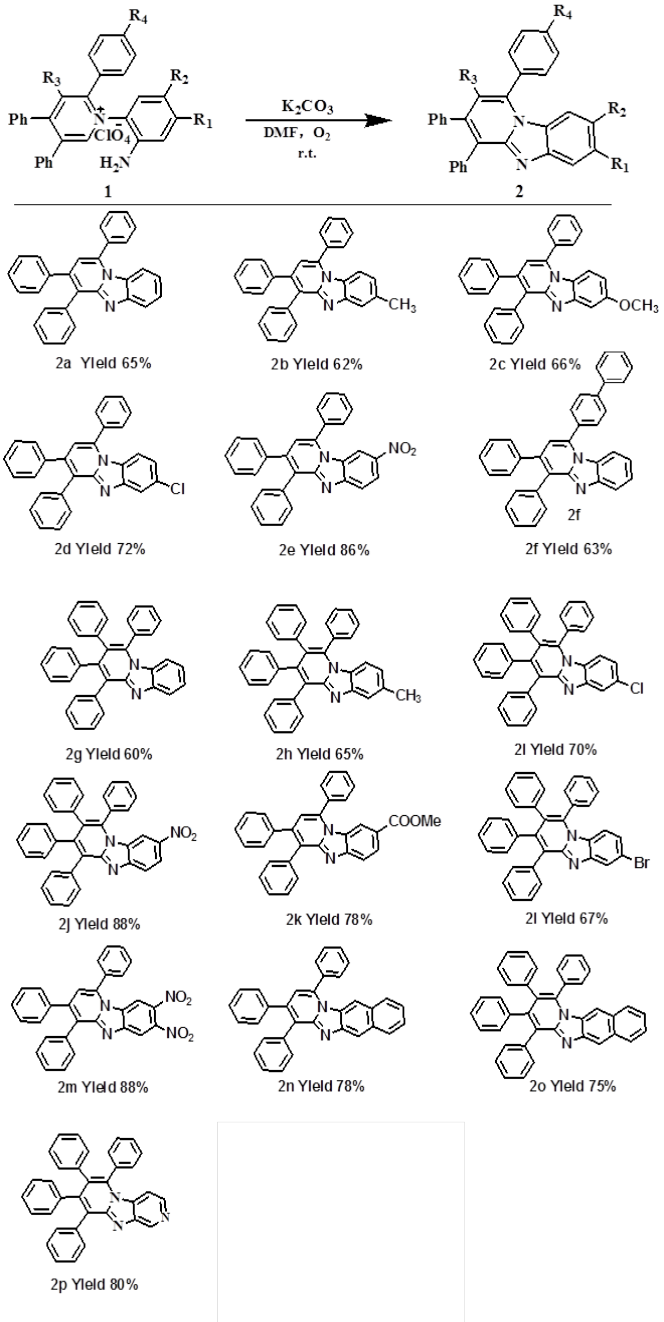
Table 1 Reaction optimization study for compound 2a.



Entry	Base	Equiv	Solvent	T(℃)	Time(h)	Yield
1	TEA	0.05	DMF	25	2	10
2	KO_tBu	0.05	DMF	25	2	5
3	K_2CO_3	0.05	DMF	25	2	15
4	K_2CO_3	1	DMF	25	2	35
5	TEA	0.05	DMF	25	12	17
6	KO_tBu	0.05	DMF	25	12	5
7	K_2CO_3	0.05	DMF	25	12	15
8	**K_2CO_3**	**1**	**DMF**	**25**	**12**	**65**
9	K_2CO_3	5	DMF	25	2	55
10	K_2CO_3	5	MeOH	25	2	22
11	K_2CO_3	5	DCM[c]	25	2	5
12	K_2CO_3	5	CH_3CN	25	2	18
13	KOH	5	DMF	25	2	32
14	K_2CO_3	1	DMF	60	6	64

With the optimized conditions, we have prepared PBI derivatives with different substituents to examine the reaction scope. For starting substrates, at present, just three "α-active"pyrylium salts were chosen with the purpose to introduce multiple phenyl groups into final products. In contrast for diamine substrates, the reaction showed good universality. Using aryl diamine derivatives with different substituents, satisfactory yields of PBI compunds were achieved (Scheme 3). Furthermore, it was observed that substrates (**2e**, **2j** and **2m**) with NO_2 group afforded good yields and substrates (**2b** and **2c**) with -CH_3 and -OCH_3 groups gave rise to relatively low yields. These results indicated the properties of substituents on diamine had some effect on the final product yields, higher yields obtained from the aryl diamines with electron-withdrawing groups, lower yields were from the aryl diamines with electron-donating group. Halide groups (substrates **2d**, **2i** and **2**l), such as Cl and Br were readily introduced into the final product, which is an extral advantage for further coupling modifications, this is not easy approach through conventional transtion-metal catalized coupling process. The formation of coupling products containing aryl halide groups have to requires excess strategies or the intermediate introduction of protective groups. For obtaining more highly conjugated products, also tried to introduce naphthlene and pyrene moieties into the system. Starting from naphthalene diamines, 2n and 2o were synthesized in good yields. If the starting material changed with pyrene diamine corresponding pyridinium salt could not obtain, it might be owing to the steric hindrance and electronic cloud effects.

Scheme 3 Synthetic routes of the synthesized targeted compounds.



A single crystal of PBI with nitro-substitution (**2e**) was obtained by slow diffusion method with solvents system of hexane and CH_2Cl_2 solution of **2e** (Figure 1). In this study we have observed the position of NO_2 group is attached on C9 instead of C8, which provide further proof of the formation of type B pyridinium salts on the basis of the substituent positioning effects. And the peripheral phenyl groups exhibit non-planar with pyridine center just like propeller. In the solid state, this restriction of the rotation of phenyl rotors against the cental stator may induce strong fluorescence.

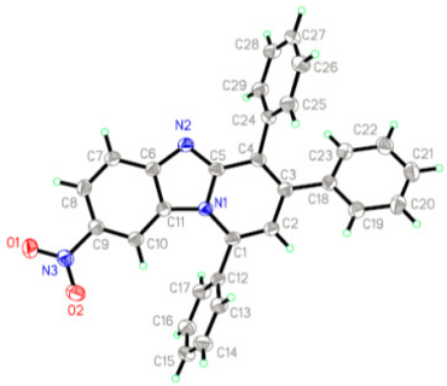
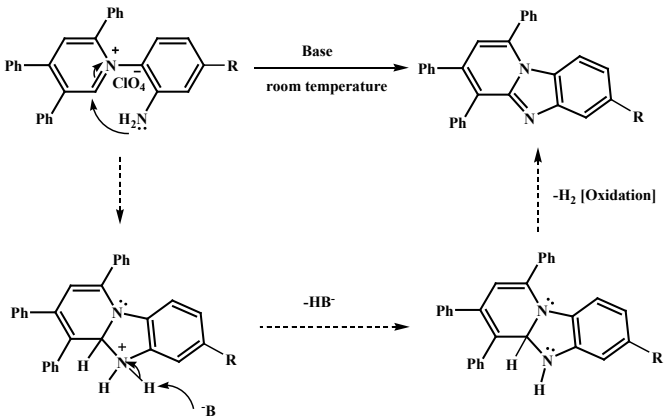


Fig. 1 X-ray single crystal of **5a**

On the basis of results, a possible reaction mechanism was proposed shown in Scheme 4. The amino group attacked on the sp^2 hybridized Carbon of pyridinium salt moiety which acts as an highly electrophilic center, and obtained a metastable ring, deprotonating occurs by base formed new five member ring. **R** substituent group has controlled the reactivity of the compound, when **R** is electron withdrawing group then the deprotonating step is become easier than the **R** is as electron donating group due to the withdrawing effects. However compounds bearing electron withdrawing group afforded good yield as compare to the electron donating group. Further we have observed that in the presence of air (or O_2), dehydrogenation occurred and formed final PBI products with five member aromatic ring.



Scheme 4. The Proposed mechanism for synthetic targeted compounds.

As expected the multi-phenyl substituted PBI derivatives exhibit excellent optical performance shown in Figure 2. PBI derivatives exhibited tunable fluorescence with the change of substituents not only in solution but also in the solid state （from blue to yellow-green fluorescence). With the extension of π-conjugation (**2o**) or introduction of electron withdrawing group (**2j**), the fluorescence spectra changed to longer wavelength with compound containing a

pyridine moiety (**2p**) showed intense blue fluorescence. The good fluorescent performance of PBIs in solution as well as in the solid has great potential in sensing and optoelectronic fields.

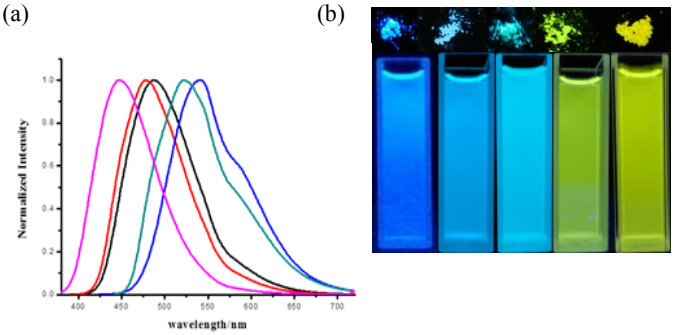


Figure. 2 (a) Normalized fluorescence spectra of PBIs in $CH_3CN(1\times10^{-5}M)$. (b) Fluorescence images of different PBIs in CH_3CN, from left to right: **2p, 2d, 2b, 2o, 2j.** (c)Solid-state fluorescence images of different PBIs, from left to right: **2p, 2d, 2b, 2o, 2j.**

In summary, constructed a new and mild synthetic route to multi-phenyl subtituted PBI compounds via efficient intramolecular C-H amination. The reaction proceeds well under room temperature with air and the absence of the use of a transition metal catalyst. This reaction exhibited good universality for substrates, especially for the introduction of halide groups, which is not easy approach by conventional transtion-metal catalyzed coupling processes. Furthermore the introduction of multiple phenyl or other aromatic groups impart good fluorescence performance to obtained PBIs. Further work will focus on the detailed exploration of these fluorescent properties and potential applications as OLEDs, sensors and π-gels etc. .

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Notes and references

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Electronic Supplementary Information (ESI) available: details of experimental procedures, characterization of pyridinium salts and PBIs including ^{1}H NMR, ^{13}C NMR and HR-MS. See DOI: 10.1039/b000000x/

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