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# Fast and efficient microwave-assisted synthesis of perylene bisimides

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**Abstract:** Perylene-3,4,9,10-tetracarboxylic acid bisimides have been widely studied as industrial pigments. Lately, these dyes have drawn considerable attention because of applications as photocatalysts and organic semi-conductors. Here, we report a novel method for fast and efficient synthesis of many different perylene bisimides, based on microwave-assisted reactions.

## Introduction

Perylene bisimides (PBIs) are robust and photostable dyes, with outstanding optical and electronic properties.<sup>[1]</sup> As a consequence, these compounds have been widely studied as pigments, fluorescence sensors, n-semiconductors in organic electronics, photovoltaics and bases for copolymers or oligomers, with important role in single junction devices.

The simple chemical structure of PBIs has different sites that can be exploited in order to tune the desired properties either in micro and macro scale. Indeed, the perylene core offers ten different positions (four ortho, four bay and two anhydride functions) that can be functionalized.

As anticipated, this chemistry is broad and many possibilities have been investigated since the first experiments of Kardos in 1913.<sup>[1a, 2]</sup>

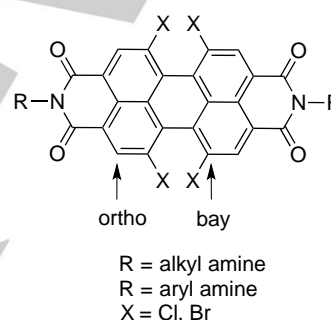
The pigment industry requires insoluble and high melting point PBI-based materials, although current work on PBIs for organic electronics and studies of photoinduced processes<sup>[3]</sup> and supramolecular organization generally require PBIs with reasonable solubility in common solvents.<sup>[2b]</sup>

A straightforward and simple route towards tuning the properties is the modification of PBIs at different positions. In fact, the introduction of a bulky alkyl or aryl substituent at the N-imide position highly increases the solubility in most of the organic solvents,<sup>[4]</sup> while carboxylates or quaternary ammonium cations are used for the formation of ionic bonds or to increase the solubility in water.<sup>[5]</sup>

Due to the importance of these dyes, many standard protocols have been devised to functionalize the imide position. Despite their wide range of applicability, the synthesis of these materials presents some limitations. Firstly, the condensation of Perylene

BisAnhydride (PBA) with aromatic amines and aminoacids require long reaction times, up to 48 hours at reflux in non common solvents, such as quinoline and imidazole.<sup>[2b, 4, 6]</sup>

Beside the harsh conditions, work up procedures represent another problem. Indeed, aromatic amines and aminoacids require long work-ups under strong conditions to get rid either of the unreacted anhydride and the side product, monoimide derivative. This does not occur for aliphatic amines, which give quantitative yields and need a simpler work-up to remove the excess of amines.



**Figure 1.** Chemical structures of some of the synthesized perylene bisimides derivatives.

Lastly, appropriate characterization of these molecules is an additional bottleneck of the procedure. Due to the poor solubility of both perylene bisimides and the related anhydride in deuterated solvents, NMR spectra are often not reported. In most cases, the purity of the compounds is assigned by IR, mass spectrometry and elemental analysis. Imide substitution is anyway not sufficient to modify the electronic properties of PBIs, such as absorption, fluorescence, and HOMO/LUMO energies, neither the supramolecular aggregation.<sup>[7]</sup> Tuning optical and electronic properties was achieved through the insertion of halogen moieties at bay positions of perylene bisanhydride. This route led to the synthesis of 1,6,7,12-tetrachloro- or 1,6,7,12-dibromo-perylene bisanhydride, that are useful precursors for nucleophilic substitutions and metal-catalysed reactions.<sup>[1a]</sup> Moreover, these halogenated compounds can further react with amines under acidic conditions to form bay-halogenated PBI derivatives.<sup>[8]</sup> Unfortunately, the abovementioned harsh reaction conditions are not compatible with halogenated PBAs thus compounds bearing aminoacids or anilines at imide positions are not reported in literature, up to date.

Consequently, a new and fast method for the synthesis of perylene bisimides with highly effective reactions appears to be instrumental, in order to produce a wider variety of these molecules in a more efficient way.

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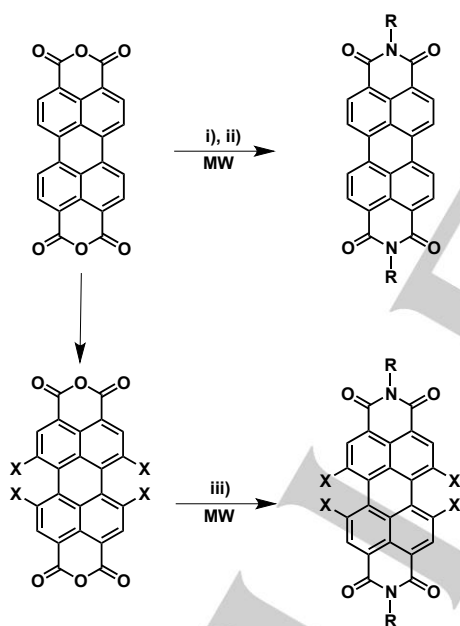
Microwave-assisted synthesis has attracted the organic chemists, since it guarantees accelerations of the reactions, higher yields under milder reaction conditions and higher product purities.<sup>[9]</sup>

Herein, we report an innovative and efficient microwave assisted synthesis of perylene bisimides. A large variety of amines, bearing different moieties, has been reacted with PBA in high yield and short reaction times, using dimethylformamide (DMF) as the solvent.

## Results and Discussion

Reactions were run in a dedicated microwave reactor in pressure-resistant, tightly sealed quartz tubes. The procedure consisted of 5 cycles of irradiation at 60 W for 10 min., with cooling intervals of 2 min. The microwave maximum temperature was set at 200°C.

The final products were characterized by <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, MALDI-MS, FT-IR, UV-Vis absorption and fluorescence spectroscopies. <sup>13</sup>C-NMR analysis was not possible for all compounds, due to their poor solubility in standard deuterated solvents.



**Figure 2.** General scheme of imidation reaction. i) Reagents and conditions for alkylamines and aminoacids: DMF, R-NH<sub>2</sub> 2 equiv., 50 min. irradiation, T<sub>max</sub> 200°C, 50 W. ii) Reagents and conditions for aromatic amines: DMF, R-NH<sub>2</sub> 4 equiv., Et<sub>3</sub>N, 50 min, T<sub>max</sub> 200°C, 80 W. iii) Reagents and conditions for bay-halogenated PDA with amines: DMF, R-NH<sub>2</sub> 2 equiv., acetic acid, 10 min, T<sub>max</sub> 200°C, 50 W.

Several standards methods for the synthesis of PBIs have been previously described.<sup>[2b, 4, 6]</sup> A first procedure involves heating PBA with the appropriate amine in the presence of dicyclohexylcarbodiimide (DCC), using water as separating reagent at 220-240 °C and a small amount of quinoline as

solvent, providing nearly quantitative yield after 18 hours. The work up consists of treating the suspension several times with methanol in order to remove quinoline, then with an aqueous solution of K<sub>2</sub>CO<sub>3</sub> to dissolve unreacted PBA and finally crystallizing the imide derivative from toluene.<sup>[2b, 4]</sup>

In order to prepare the carboxylated PBIs, an alternative strategy was exploited. PBA was heated in imidazole at 140 °C in the presence of the appropriate aminoacid for 10 hours, under argon. The crude was washed with ethanol and then precipitated with an aqueous solution of HCl.<sup>[6]</sup> Both methods require a large excess of amines.

In addition, we synthesized several perylene derivatives (1-17) as reported in Table 1. Several amines were used for our synthesis in order to set up a valid method for a wide variety of the PBIs, including alkyl amines (1, 2, 3, 4, 6, 8), amino alcohols (4, 8), heteroaryl amines (7), aminoacids (9-11). In addition, we managed to functionalize bay-halogenated PBIs with some of the latter amines (12-17).

In this method, the reactions take place in a range of 6-10 min. for halogenated PBIs (12-17), up to 2 hours for some other amines (7-8). The appropriate amine is used in stoichiometric amount (1-6, 9-17) or in a slight excess (7-8). DMF is the elected solvent for all the reactions. We developed two different work-up procedures depending on the nature of the amine. The products of unchanged amines (1-8, 12-17) were suspended in 50 mL of

**Table 1.** Summary of the synthesized PBI derivatives

PBI	Starting anhydride	Amine	Yield %
1	PBA	N,N-dimethylethylenediamine	99
2	PBA	(2-methoxyethyl)amine	99
3	PBA	1-(3-aminopropyl)imidazole	99
4	PBA	2-(2-aminoethoxy)ethanol	99
5	PBA	4-amino-1-butanol	92
6	PBA	octylamine	87
7	PBA	4-aminopyridine	45
8	PBA	dopamine	43
9	PBA	5-amino-isophthalic acid	87
10	PBA	glycine	42
11	PBA	β-alanine	64
12	PBA-4Br	N,N-dimethylethylenediamine	80
13	PBA-4Br	(2-methoxyethyl)amine	87
14	PBA-4Br	1-(3-aminopropyl)imidazole	95
15	PBA-4Cl	N,N-dimethylethylenediamine	
16	PBA-4Cl	(2-methoxyethyl)amine	85
17	PBA-4Cl	1-(3-aminopropyl)imidazole	95

10% KOH aqueous solution and stirred for 2 hours. The precipitate was filtered and washed thoroughly with water until neutralization of the filtrate. On the other hand, products of aminoacids (**9-12**) were dissolved in basic solution at pH 10 and filtered. The solution was then acidified with concentrated HCl to pH 1, filtered and washed until neutralization.

The starting PBA is insoluble in common deuterated solvents and is not detected in the NMR spectra. Consequently, reactions were monitored by IR spectroscopy to check the absence of unreacted anhydride. All the final compounds exhibited strong peaks at 1690 and 1650  $\text{cm}^{-1}$  related to the C=O stretching of imide groups, while typical peaks related to C=O stretching of anhydride at 1765  $\text{cm}^{-1}$  and 1730  $\text{cm}^{-1}$  were not detected, in accordance with data reported in literature.<sup>[10]</sup>

Moreover, we observed that the presence of unreacted PBA in the crude affected the solubility of the final compounds. In fact, the addition of a small amount of PBA to a PBI solution caused precipitation of the latter, especially for those bearing amino acid groups (**9-12**). This experimental evidence confirmed the hypothesis that traces of the perylene anhydride in solution facilitate the aggregation of the PBIs. Thus, appropriate work-up procedures appeared instrumental to obtain the final compounds in high purity and to collect characterization data of derivatives such as PBIs **4**, **5**, **7**, **11**, not reported in the literature up to date.<sup>[11]</sup>

This study highlights that the main factors influencing the reactions were the steric hindrance and the polarity of amines.<sup>[12]</sup> In the experiments, the steric bulkiness at the  $\alpha$ -carbon influenced the outcome of the reaction. Amines with a small linear structure (**1-6**, **12-17**) gave higher yields in shorter time. To compensate the lower reactivity of some reagents (**7**, **8**), the number of cycles of irradiation was increased and both conditions and work-up procedures were slightly modified as reported in the Experimental Section.

In addition, aminoacids reacted faster than nonpolar amines. On similar steric hindrance, derivative **9** was obtained in shorter time and higher yields than compound **7**. Indeed, the presence of carboxylic groups on the isophthalic amine promoted the reaction, enhancing the polarity.

On the other hand, the basicity of the amine does not particularly influence the outcome of reactions. Indeed, weak nucleophiles, such as isophthalic amine and 4-aminopyridine, showed reaction rates comparable to the ones of stronger nucleophiles, such as dopamine and  $\beta$ -alanine.

Bay-halogenated PBIs are very reactive species due to the higher solubility of the related anhydride in DMF. Reactions took place in only 6-10 min, with all the tested amines, without detectable substitution at bay-positions. The yields were comparable to not-bay-halogenated PBIs, almost quantitative.

## Conclusions

A fast and versatile microwave-assisted method for the synthesis of a broad library of perylene bisimide derivatives has been developed. Imidation reactions of the perylene bisanhydride (PBA) were performed using a large variety of

amines, such as alkyl amines (**1**, **2**, **3**, **4**, **6**), amino alcohols (**4**, **8**), heteroaryl amines (**7**) and aminoacids (**9-11**). This strategy turned out to be compatible also with bay-halogenated PBAs, functionalizing selectively the imide position without affecting the aromatic core. Different efficient work-up procedures gave highly pure products in short times. Despite of mild conditions, weak nucleophiles like aromatic amines and aminoacids efficiently provided functionalized perylene bisimides, with some novel entries not previously reported in the literature.

## Experimental Section

### General Information.

All solvents used were of reagent quality and purchased commercially. All purchased starting materials were used without further purification. The microwave reactor used for this study (CEM Discover) was purchased from CEM Corp. NMR spectra were recorded on 400 MHz instruments and referenced to the solvent. All spectra were recorded at 298 K.

$^1\text{H}$  NMR spectral data are reported as follows: chemical shift in parts per million on the  $\delta$  scale, integration, multiplicity, coupling constants (Hz), and assignments.  $^{13}\text{C}$  NMR spectral data are reported as follows: chemical shifts in parts per million on the  $\delta$  scale and carbon environments determined from DEPT spectra. All spectra were referenced to their respective solvent residual peaks. The 1,6,7,12-tetrabromo-perylene bisanhydride and 1,6,7,12-tetrachloro-perylene bisanhydride were prepared according to literature.<sup>[13]</sup>

### Synthesis of perylene bisimides with alkylamine. General Procedure. (1-6)

100 mg of perylene-3,4,9,10-tetracarboxylic bisanhydride were suspended in dry DMF (5 mL) with 2 equiv. of the corresponding amine in a pressure tight microwave tube.

The suspension was sonicated for few minutes before heating under microwave irradiation at 50W for 10 min. 5 cycles. Max T was set at 200 °C.

After cooling the colour turned to dark red and the mixture appeared more homogenous.

50 mL of NaOH 1 M were added to the starting material and stirred for 20 min. The precipitate was filtered washing abundantly with water until pH neutralization and dried in vacuum pump.

### Synthesis of perylene bisimides with aromatic amines. General Procedure. (7-8)

100 mg of perylene-3,4,9,10-tetracarboxylic bisanhydride were suspended in dry DMF (5 mL) with 4 equiv. of the corresponding amine and 50  $\mu\text{L}$  of  $\text{Et}_3\text{N}$  in a pressure tight microwave tube.

The suspension was sonicated for few minutes before heating under microwave irradiation at 80 W for 10 min. 10 cycles. Max T was set at 200 °C.

After cooling the colour turned to dark red and the mixture appeared more homogenous.

To the mixture 50 mL of KOH 10% aq. solution was added and solution was stirred for 2h. The precipitate was isolated through

filtration and washed with abundant water until pH neutralization and dried in vacuum pump.

#### Synthesis of perylene bisimides with aminoacids. General Procedure. (9-11)

100 mg of perylene-3,4,9,10-tetracarboxylic bisanhydride were suspended in dry DMF (5 mL) with 4 equiv. of the corresponding amine and 50  $\mu$ L of Et<sub>3</sub>N in a pressure tight microwave tube. The suspension was sonicated for few minutes before heating under microwave irradiation at 50 W for 10 min, 5 cycles. Max T was set at 200 °C.

After cooling the colour turned to dark red and the mixture appeared more homogenous.

To the mixture 50 mL of pH 8 aq. solution was added and stirred for 2 hours. The precipitated unreacted anhydride was filtered off. The filtrate was then acidified with HCl 5 % and the precipitated was filtered, washed with water and then dried in vacuum pump.

#### Synthesis of halogenated perylene bisimides with alkylamine. General procedure. (12-17)

100 mg of tetrachlorinated or tetrabrominated perylene-3,4,9,10-tetracarboxylic bisanhydride were suspended in dry DMF (5 mL) with 2 equiv. of the corresponding amine and 1 mL of acetic acid in a pressure tight microwave tube.

The suspension was sonicated for few minutes before heating under microwave irradiation at 60W for 10 min. Max T was set at 200 °C.

After cooling the colour turned to dark red-black and the mixture appeared more homogenous.

50 mL of NaOH 1 M were added to the starting material and stirred for 20 min. The precipitate was filtered, washing abundantly with water until pH neutralization and dried in vacuum pump.

#### Acknowledgements

This work was supported by the University of Trieste, Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei

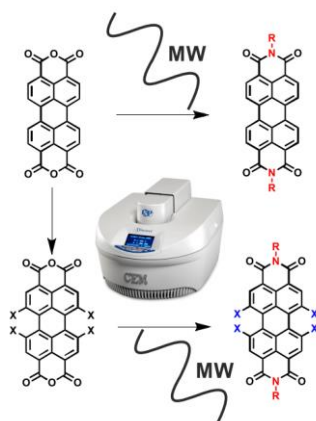
Materiali (INSTM), Ministero dell'Università e della Ricerca (MIUR) (FIRB prot. RBAP11ETKA and Cofin. Prot. 2010N3T9M4).

Keywords: Microwave irradiation • perylene bisimides • aminoacids • amines • condensation

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## SHORT COMMUNICATION

Perylene Bisimides (PBIs) are dyes which can be used in a wide variety of applications. Much effort has been devoted on the synthesis of these materials. Herein, we present the successful synthesis of different PBIs derivatives with the use of microwave irradiation. The products are collected in very good yields, in short time and with high purity.



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