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Steric bulk & solubility provide synthetic access & insight into non-symmetric perylenediimide syntheses

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Non-symmetric perylenediimides are valuable yet often synthetically challenging due to poor solubility. We compare synthetic strategies using sterically and electronically diverse amines, demonstrating that the first amine governs solubility and synthetic yields. In comparison with established molten imidazole methods, we developed higher yielding methods under milder conditions to achieve non-symmetric products.

Introduction

Perylenediimide (PDI) derivatives are aromatic chromophores with tuneable electronic properties, strong electronic coupling and notable electron-accepting capabilities—notably, the ability to undergo singlet fission.[1,2] These features, combined with high photochemical and thermal stability, render PDIs attractive building blocks for constructing monolayers, metal–organic frameworks and advanced polymer architectures.[3–6] However, the application of PDI derivatives is often limited by their poor solubility and the synthetic challenges associated with preparing non-symmetrically substituted PDIs in high yield. Conventional approaches require high temperatures with extended reaction times to overcome solubility issues, which often demand additional steps to prevent over-substitution to the symmetric product. Herein, we describe the synthesis of symmetric and non-symmetric PDI derivatives through a combination of amines chosen to balance functional utility with solubility. Our aim is to elucidate design principles to aid in the design of an accessible and tuneable synthetic approach to facilitate high-yield access to non-symmetric PDIs under mild-to-moderate intensity reaction conditions. Langhals *et al.* built upon prior work by Tröster by investigating the use of bulky amines with long alkyl chains or multiple aromatic substituents to disrupt PDI aggregation in solution; this approach led to increased solubility and decreased aggregation, which led to modulated fluorescence and decreased steric shielding.[7,8] However, the selected amines provided no synthetic handle for further application in synthetic use, wherein PDI structures could serve further purpose. Frischmann *et al.* synthesized non-symmetric PDIs by precluding the need for sequential imidization, through synthesis of a pre-substituted intermediate that could be converted into a perylene core.[9] However, such an approach does not enable non-symmetric substitution in good yield, even if it does enable the use of bulkier amines. Sengupta *et al.* expanded on the steric bulk strategy to disrupt aggregation by using bulky alkylamines to increase PDI solubility.[10] However, such alkyl groups remain a synthetic limitation due to their lack of additional functional groups for subsequent derivations or attachments. Nonetheless, higher solubility was achieved, but reaction conditions were aggressive and not apt for non-symmetric control: Bulkier amines with longer alkyl chains increased yield and solubility, while smaller amines required lower time and less harsh conditions (>80%).[11] Such an inverse relationship limits the applicability of this aggregation disruption method for non-symmetric PDI synthesis. Xue *et al.* developed another method leveraging a perylene mono-anhydride-diester (PMADE) in concert with constrained amine equivalents (moderate yields), which inspired later isolation of non-symmetric PDIs.[12]

The reported approach to non-symmetric PDI's involves stepwise opening and closing of the anhydride units on perylene-dianhydride (PDA), which provides access to non-symmetric imidization *via* selective 'opening' and 'closing' *via* anhydride to di-ester conversions. The corresponding perylene mono-anhydride/di-ester (PMADE) achieves an imidization yield as high as 73%.[13,14] More direct strategies have been reported, albeit with greatly impaired selectivity. One-pot reaction schemes with sequential addition of amines generally produce non-symmetric PDIs with ∼30%, for example in a 2015 report.[11] Other investigations have utilized an initial symmetric substitution, followed by step-wise removal and substitution of one amine (∼65%).[15,16] In this work, sequential imidization was selected for further investigation due to its high yield and ease of control of imidization.

To demonstrate an optimal balance between the competitive factors of steric bulk, solubility and further synthetic

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utility—we herein synthesize a suite of non/symmetric PDIs to delineate the effects of amine structure, order of substitution and reaction method on yield and synthetic accessibility. This includes both symmetric and non-symmetric PDIs prepared for further synthetic applications. In this work, the influence of steric bulk and solubility on reaction yield was systematically investigated with eight (8) total alkyl and aryl amines to generate high-utility (*e.g.* brominated) PDIs—in principle useful for subsequent molecular assemblies or attachments. The findings herein demonstrate key principles and limitations of non-symmetric PDI synthesis, and such understanding may broaden the utility and applicability of non-symmetric PDI units. The reported methods were selected to contrast harsher conditions with more tailored parameters that might provide PDIs under more delicate conditions for future applications, likely requiring a wider array of functional amines (Fig. 1).

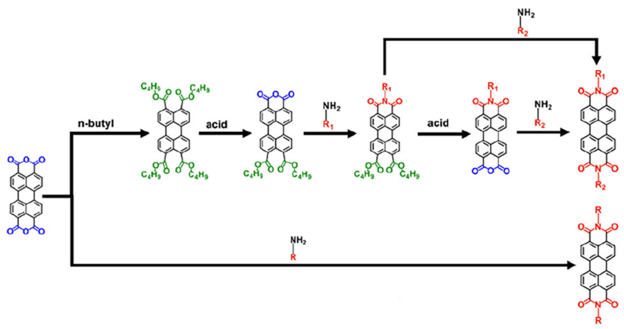
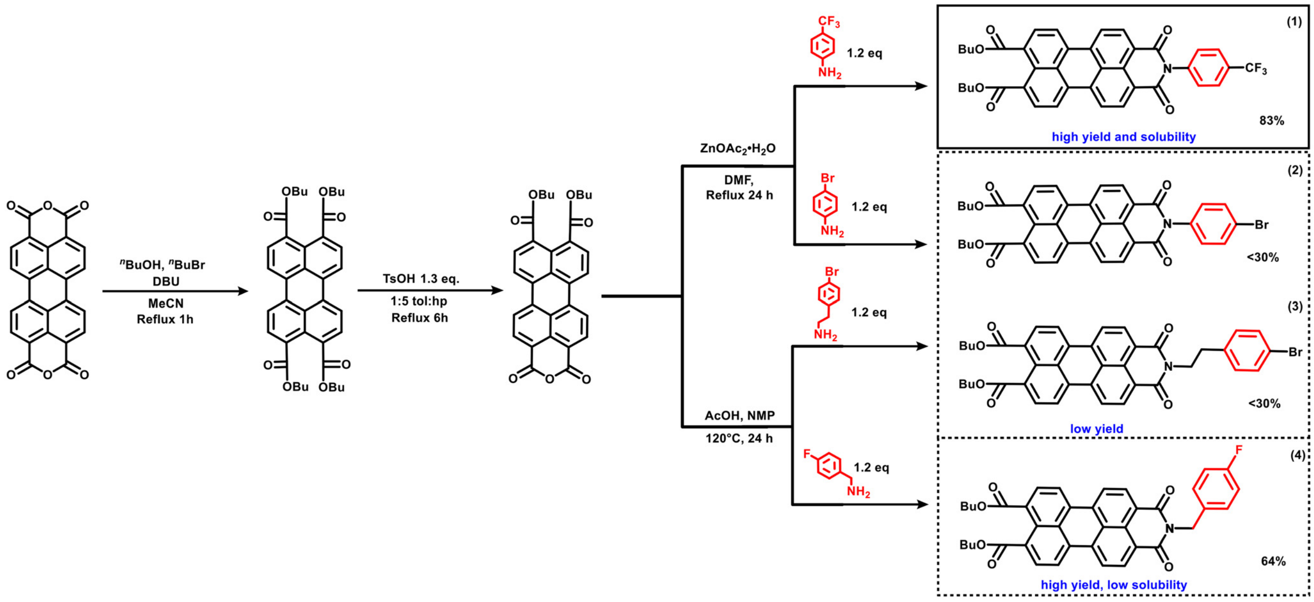


Fig. 1 Schematic of the conventional synthetic route involving 'opening and closing' symmetric synthons to generate asymmetric PDIs.

Results and discussion

PMADE was imidized using 1.2 equivalents of $\mathbf{R_a}$(aryl-CF_3) and $Zn(OAc)_2$ refluxing in dimethyl formamide (DMF) (Scheme 1) (Fig. 2). The starting materials remained soluble throughout the reaction, although a precipitate developed during the reaction. The amine was non-symmetrically incorporated (83% average yield over 5 trials; 250 mg scale), and the identity of reasonably soluble product was confirmed by ^1H and ^{19}F NMR, IR and CI mass spectrometry. This imide was fully soluble under the conditions used to close the opposite-side anhydride for further substitution. The benzylamines $\mathbf{R_b}$(Bn-CF_3) and $\mathbf{R_c}$(Bn-F) were attempted under similar conditions, but the reaction color did not change dramatically, and the solution remained a slurry—resulting in poor yields of the target imides (<30%). *N*-methyl-2-pyrrolidone (NMP) with acetic acid were used in place of DMF and $Zn(OAc)_2$ to further solubilize $\mathbf{R_b}$(Bn-CF_3) and $\mathbf{R_c}$(Bn-F) and the reactions proceeded more readily, affording 83% and 63% yields, respectively. However, the product solubilities proved too limited to dissolve in the 1 : 5 toluene/heptane solvent mixture for anhydride closure, restricting further imidization. Separately, imidizations of PMADE with $\mathbf{R_d}$(aryl-Br) and $\mathbf{R_h}$(phenylethyl-Br) were attempted in DMF and NMP, respectively; despite appropriate solvating conditions, reaction yields proved exceptionally low (<10%); the isolated products did, however, exhibit suitable solubility for further use (in principle). However, the large discrepancy between yield percentages relative to the $\mathbf{R_a}$(aryl-CF_3) mono-substituted product precluded their use in further studies.

The amine $\mathbf{R_a}$(aryl-CF_3), in particular, enabled systematic exploration of the second imidization, as it proved the highest yield and most soluble intermediate after a mono-imidization. Subsequent imidization was performed with amines of varied



Scheme 1 Synthetic pathways used to perform initial mono-imidizations as key synthons to generate non-symmetric PDIs.

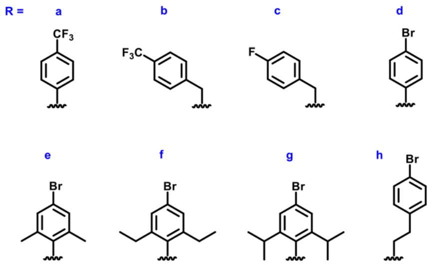


Fig. 2 The eight (8) substituted amines used herein in the study of non-symmetric PDI reaction efficiency and solubility.

steric bulk to investigate the steric influence on reaction efficiency. The bromoaniline moieties with 2,6-dimethyl (**e**), diethyl (**f**), or diisopropyl (**g**) groups ($\mathbf{R_e}$–**g**) were selected to nominally enhance solubility while retaining the *para*-bromo functionality as a synthetic handle for subsequent derivations. Alternately, $\mathbf{R_d}$(aryl-Br) and $\mathbf{R_h}$(phenylethyl-Br) were employed to contrast bulky aryl amines with an alkyl amine of similar steric profile. $\mathbf{R_{d-h}}$ were each added to the $\mathbf{R_a}$ intermediate (after ester to anhydride conversion) with alkyl and arylamines. Each imidization to the final PDI resulted in acceptable solubility and moderate yield of 75%, 47%, 48%, 52% and 98% (respectively). The addition of the di-isopropyl aniline was, notably, 30% less efficient than symmetric addition of the same amine in a prior symmetric PDI study, indicative of the challenge of non-symmetric PDI synthesis.[17]

The same four amines were directly added to the open ester form of the $\mathbf{R_a}$-substituted intermediate through reaction in a molten imidazole solution at 190 °C for 24 hours under dark conditions. After dilute acid treatment, vacuum filtration enabled isolation as previously reported.[7] Such harsh heating conditions contrasted the milder DMF/NMP reactions, thus providing comparison between mild and extreme conditions.

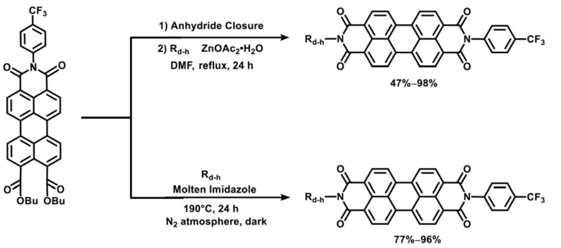
The molten imidazole conditions resulted in a less disparate set of reaction yields of the same corresponding non-symmetric PDIs where $\mathbf{R_{d-h}}$ yielded 96%, 92%, 93%, 76.5% and 94%.

The order of amide addition is of primary concern for the synthesis of non-symmetric PDIs. First imidization reactions with $\mathbf{R_a}$(**1**), or in some cases $\mathbf{R_b}$(**2**), exhibit high yields and good solubility of subsequent reactions. The first imidization was performed with the three other amines ($\mathbf{R_c}$, $\mathbf{R_d}$, $\mathbf{R_f}$), but in lower yields; additionally, subsequent reactions are dramatically hindered due to decreased solubility. For example, $\mathbf{R_c}$(**4**) is suitable for initial imidization, but the resulting product $\mathbf{R_c}$(**4**) PMADE exhibits dramatically decreased solubility, precluding further use. Thus, certain PDIs are synthetically viable only through selection of amines that *solubilize the non-symmetric PMADE intermediate*. Thus, an important design consideration is the identity of the solubilizing amine and its compatibility with the subsequent reaction conditions.

Across all studied PDIs, interconversion yields of anhydride-to-ester were consistently high (>95%). However, two amine addition methods proved more suitable for alkyl *vs.* aryl amines. Upon using conditions unfit for the amine, PMADE to PDI yields decreased by up to ~40% and some cases exhibited no detectable conversion for $\mathbf{R_h}$. Aryl amines performed best in DMF with $Zn(OAc)_2$ hydrate under reflux, whereas alkyl amines required more intense heating in NMP with glacial acetic acid. Solvent systems were selected due to their solubilizing ability of PDA and the amine (rather than product), which avoided high temperature or long reaction times. When insoluble, the effective concentration of the amine in solution was lowered and required higher temperature and longer reaction times to achieve the same yield. Simply stated, NMP proved ideal for aryl amines, and DMF proved optimal for alkyl amines. Zinc acetate functioned as a Lewis acidic catalyst, presumably activating the anhydrides to facilitate nucleophilic attack by the amines for more facile conversion while maintaining temperature at glacial acetic acid bp (150 °C).

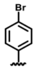
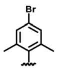
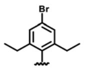
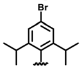
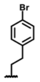
The yields of PMADE to PDI imidization from the anhydride method decreased significantly for sterically bulky amines (Scheme 2). While the alkyl amine $\mathbf{R_h}$(phenylethyl-Br) retained a high yield, those for aryl amines such as $\mathbf{R_d}$(aryl-Br) dropped by ~25%, with further decreases observed for more hindered analogues. Attempts to improve yields by modifying temperature, stoichiometry and duration proved unsuccessful. In such cases, the molten imidazole method offers a viable alternative, but this deviates from the desired outcome of milder conditions and often forces the synthesis of poorly soluble products unsuitable for further synthetic modifications.

Additionally, scalability of the molten imidazole method is limited to small-scale reactions due to the need for controlled, uniform and intense heating of the imidazole media. Although it tolerated moderate steric bulk better than the



Scheme 2 'Molten imidazole' *versus* 'closed anhydride' synthetic approach for second imidization; the anhydride method was performed following anhydride closure, and $\mathbf{R_h}$ was used in conjunction with the appropriate NMP conditions for imidization.

Table 1 Reaction yields for anhydride *versus* imidazole methods for second imidizations of the R_a – substituted intermediate

Amide	$\mathbf{R_d}$ 	$\mathbf{R_e}$ 	$\mathbf{R_f}$ 	$\mathbf{R_g}$ 	$\mathbf{R_h}$ 
Anhydride method (% yield)	75%	47%	48%	52%	98%
Molten imidazole (% yield)	96%	92%	93%	77%	94%

anhydride method, amines with isopropyl groups still exhibited diminished yields. Additionally, while the molten imidazole method generally produced higher yields, alkyl amines exhibited slightly higher yield under the milder, anhydride method. Table 1 summarizes average yields for selected amines using both methods.

Conclusion

The non-symmetric PDI syntheses reported herein—utilizing more soluble intermediate mono-imide intermediates—promote increased yields provided a judicious selection of the initial amine substituent. Initial, non-symmetric imidization with amines that *increase* PMADE (non-symmetric perylene-imide/ester) solubility results in tractable non-symmetric PDI syntheses. In contrast, initial non-symmetric imidization with amines that *decrease* intermediate PMADE solubility results in a synthetic 'dead-end' due to limited solubility. Furthermore, in the subsequent (second, *i.e.* non-symmetric) imidization, steric bulk modulates reaction yield, requiring harsh conditions to overcome steric inhibition. This contrasts past findings wherein alkyl chains increased the solubility of non-symmetric PDI intermediates—thus requiring compromise between additional, solubilizing alkyl bulk that either inhibits imidization or restricts available ring positions for further synthetic modification.[10] Alternatively, lower solubility intermediates can still be utilized by employing the harsher molten imidazole method—although this approach is generally restricted to smaller scales for safe laboratory operations. The molten imidazole method does dampen stark differences in reaction yields resulting from varying steric bulk. Overall, the findings herein provide a foundation for a more rational synthetic roadmap to a broader range of application-focused non-symmetric PMI/PDI intermediates and products, thus facilitating their future integration into more complex molecular and materials architectures—such as surfaces, nanocrystals and other hybrid molecular-materials assemblies.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: synthetic procedures and characterization through IR, GCMS (EI), and NMR spectra. See DOI: https://doi.org/10.1039/d6ob00321d.

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References

1 F. Würthner, Perylene Bisimide Dyes as Versatile Building Blocks for Functional Supramolecular Architectures, *Chem. Commun.*, 2004, (14), 1564–1579.
2 M. H. Farag and A. I. Krylov, Singlet Fission in Perylenediimide Dimers, *J. Phys. Chem. C*, 2018, **122**(45), 25753–25763.
3 C. Huang, S. Barlow and S. R. Marder, Perylene-3,4,9,10-Tetracarboxylic Acid Diimides: Synthesis, Physical Properties, and Use in Organic Electronics, *J. Org. Chem.*, 2011, **76**(8), 2386–2407.
4 P. I. Scheurle, A. Biewald, A. Mähringer, A. Hartschuh, D. D. Medina and T. Bein, A Novel Electrically Conductive Perylene Diimide-Based MOF-74 Series Featuring Luminescence and Redox Activity, *Small Struct.*, 2022, **3**(5), 2100195.
5 N. Fabre, R. Trojanowicz, L. Moreaud, C. Fiorini-Debuisschert, S. Vassant and F. Charra, Structure and Photonic Properties of a Perylenediimide Monolayer Assembled by the Langmuir–Blodgett Technique, *Langmuir*, 2023, **39**(50), 18252–18262, DOI: 10.1021/acs.langmuir.3c02038.
6 L. Wang, M. Hu, X. Liu, Y. Zhang, Y. Liu, Z. Yuan, X. Zhao, Y. Hu and Y. Chen, Fused Perylene Diimide-Based Polymeric Acceptors for All-Polymer Solar Cells with High Open-Circuit Voltage, *J. Mater. Chem. C*, 2023, **11**(8), 2977–2983.
7 H. Langhals, R. Ismael and O. Yürük, Persistent Fluorescence of Perylene Dyes by Steric Inhibition of Aggregation, *Tetrahedron*, 2000, **56**(30), 5435–5441.
8 H. Tröster, Untersuchungen Zur Protonierung von Perylen-3,4,9,10-Tetracarbonsäurealkalisalzen, *Dyes Pigm.*, 1983, **4**(3), 171–177.
9 P. D. Frischmann and F. Würthner, Synthesis of a Non-Aggregating Bay-Unsubstituted Perylene Bisimide Dye with Latent Bromo Groups for C–C Cross Coupling, *Org. Lett.*, 2013, **15**(18), 4674–4677.
10 S. Sengupta, R. K. Dubey, R. W. M. Hoek, S. P. P. van Eeden, D. D. Gunbaş, F. C. Grozema, E. J. R. Sudhölter and W. F. Jager, Synthesis of Regioisomerically Pure 1,7-Dibromoperylene-3,4,9,10-Tetracarboxylic Acid Derivatives, *J. Org. Chem.*, 2014, **79**(14), 6655–6662.
11 J. E. A. Webb, K. Chen, S. K. K. Prasad, J. P. Wojciechowski, A. Falber, P. Thordarson and J. M. Hodgkiss, Quantifying Highly Efficient Incoherent Energy Transfer in Perylene-Based Multichromophore Arrays, *Phys. Chem. Chem. Phys.*, 2016, **18**(3), 1712–1719.
12 C. Xue, R. Sun, R. Annab, D. Abadi and S. Jin, Perylene Monoanhydride Diester: A Versatile Intermediate for the Synthesis of Unsymmetrically Substituted Perylene

Tetracarboxylic Derivatives, *Tetrahedron Lett.*, 2009, **50**, 853–856.

13 R. Summart, P. Thaichana, J. Supan, P. Meepowpan, T. R. Lee and W. Tuntiwechapikul, Superiority of an Asymmetric Perylene Diimide in Terms of Hydrosolubility, G-Quadruplex Binding, Cellular Uptake, and Telomerase Inhibition in Prostate Cancer Cells, *ACS Omega*, 2020, **5**(46), 29733–29745.

14 R. Williams, A Highly Soluble Asymmetric Perylene-Bis (Dicarboximide)-Acceptor System Incorporating a Methylene Bridged Methoxybenzene-Donor: Solvent Dependence of Charge Transfer Interactions, *Turk. J. Chem.*, 2009, **33**(6), 727–737.

15 "Helter-Skelter-Like" Perylene Polyisocyanopeptides – Schwartz – 2009 – Chemistry – A European Journal – Wiley Online Library. https://chemistry-europe.onlinelibrary.wiley.com/doi/epdf/10.1002/chem.200801746.

16 J. Tao, J. Zhang, Y. Song, J. Liu and H.-J. Xu, Two Asymmetrical Perylene Diimide Derivatives: Synthesis, Optical-Electrochemical Properties and Morphologies of Self-Assembly, *J. Solid State Chem.*, 2022, **305**, 122665.

17 R. K. Dubey, N. Westerveld, F. C. Grozema, E. J. R. Sudhölter and W. F. Jager, Facile Synthesis of Pure 1,6,7,12-Tetrachloroperylene-3,4,9,10-Tetracarboxy Bisanhydride and Bisimide, *Org. Lett.*, 2015, **17**(8), 1882–1885.