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Facile synthesis of chiral unsymmetric perylene tetracarboxylic diimides involving α-amino acids

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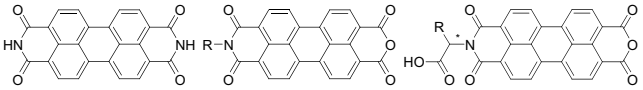
Abstract—A facile synthesis of chiral unsymmetric perylene tetracarboxylic diimides (PDIs) has been developed and the first two nonracemic chiral amphiphilic PDIs have been synthesized. The key building blocks, AB bifunctional 3,4,9,10-perylenetetracarboxylic-3,4-anhydride-9,10-imides, were prepared conveniently from enantiomerically pure α-amino acids, which were introduced as the steric and stereochemical controlling units. Such building blocks allow the incorporation of sterically and stereochemically controlled PDI moieties into both terminal and inner positions.

Perylene tetracarboxylic diimides (PDIs) have been attracting considerable attention as lightfast colorants,[1] highly efficient fluorophores,[2] the best n-type organic semiconductors[3] and versatile building blocks in self-assembly.[4] The parent PDI **1** has a rigid, planar π system. Due to strong π stacking interaction, **1** does not dissolve in any organic solvents. Therefore, solubilizing substituents are often required to improve the processability of PDIs. The imide nitrogen atoms are the preferred sites to attach solubilizing groups when retaining planarity of the PDI core is important. Symmetrically *N*,*N*′-disubstituted PDIs are easily accessible by the condensation of perylene tetracarboxylic dianhydride (PDA) with appropriate primary amines. However, in many instances, two N-substitution groups have to be installed in an unsymmetrical fashion, particularly when the PDI moieties are incorporated into complex molecular and supramolecular architectures, or into polymers as side groups. Counter-intuitively, unsymmetrically *N*,*N*′-disubstituted PDIs are not accessible via a step-wise condensation of PDA with two different primary amines by controlling the stoichiometric ratio.[1] They could be prepared by simultaneous condensation of PDA with a mixture of two primary amines. This strategy requires that the reactivity of two amines must be similar and it is frequently difficult to isolate the targeted unsymmetric PDI from the two undesired symmetric PDIs. A more efficient approach involves the 3,4,9,10-perylenetetracarboxylic-3,4-anhydride-9,10-imide **2** as the key intermediate. Variations of **2**, particularly those with symmetric secondary alkyl groups (swallow tails), have been widely integrated into donor–acceptor dyads and triads,[5] donor-bridge-acceptor molecules,[6] fluorescent sensors and light switches,[7] supramolecular assemblies[8] and PDI multichromophores[9] and PDI side chain polymers,[10] owing to the strong solubilizing power of swallow tails. Nonetheless, as monofunctional reagents, **2** only allows the introduction of PDI into terminal positions.



1 **2** **3**

In this Letter, we present a convenient method for the synthesis of AB bifunctional monoanhydride monoimides (**3s**), which allows selective functionalization at both termini. Thus, PDI moieties can be placed at both inner and terminal positions. By tuning R the π–π interaction between PDI cores can be tailored by steric means. This tunability is necessary to achieve a delicate balance between good solubility and the ability to form PDI stacks with extensive intermolecular π orbital overlap, which is crucial for various optoelectronic

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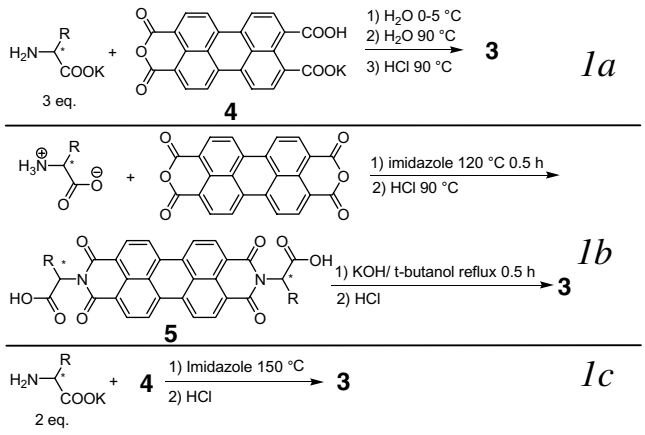


Scheme 1. All chirality centers are in *S* configuration. Compounds **3a**, **5a**: R = methyl, **3b**: R = 2-methylpropyl, **3c**: R = 1-methylethyl.

applications.[11] In addition, the configuration of the N-bound asymmetric center is controllable by using an optically pure α-amino acid as the starting material.

Synthesis of **3a** with R = Methyl was initially attempted according to two general procedures established by Tröster[12] and Langhals[13] for **2s**, as shown in Scheme 1 (**1a** and **1b**). Compound **4** was synthesized according to a literature procedure.[12] Optically pure L-alanine was used as the amine source. It is known that both procedures produce a mixture of PDA, diimide and the aimed monoanhydride monoimide.[12,13] Compound **3a**, **5a** and PDA are similarly soluble in aqueous alkaline solution and poorly soluble in common organic solvents, which make it impractical to isolate **3a** efficiently. Thus, preparation efficiency of reactions was directly evaluated qualitatively using the combination of IR and UV–vis spectroscopy. Figure 1 illustrates the corresponding spectra of crude products. It is evident that procedure **1a** produces a large amount of PDA, as indicated by the significantly stronger anhydride bands in the IR spectrum and the intense UV–vis absorption peak at 548 nm. Although procedure **1b** is more efficient than **1a**, it has been reported that the yield of the monoimide monoanhydride by partial saponification is at most about 50% due to the random nature of the reaction.[13] The formation of PDA in procedure **1b** is unambiguously identified by a shoulder at 548 nm. As isolation of **3a** is difficult, it would be ideal if a more efficient procedure is available.

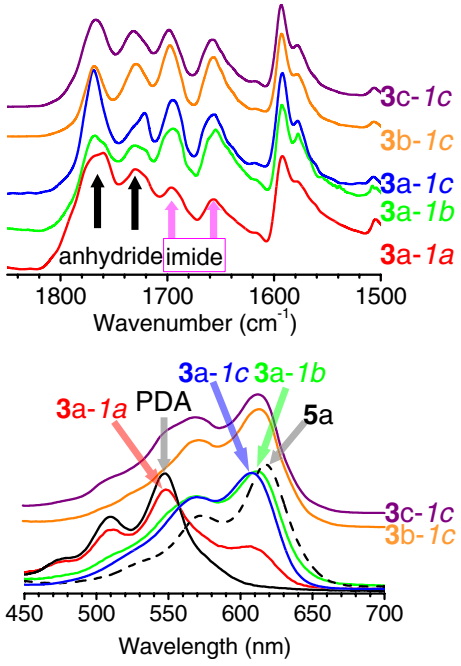
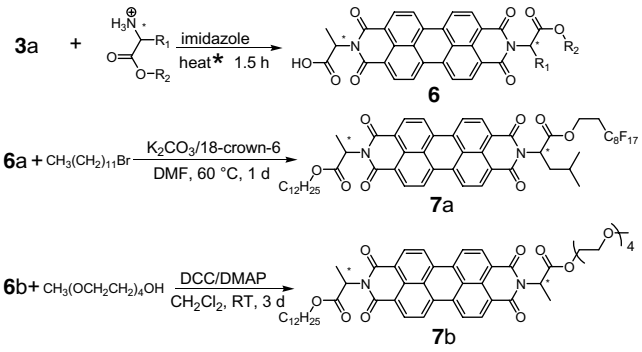


Figure 1. IR (top) and UV–vis (bottom, ~10^{-6} M in 96% sulfuric acid) spectra of **3s**.

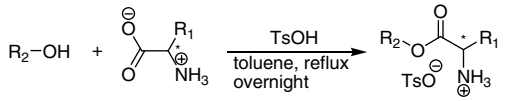
Procedure **1a** has been successfully applied to synthesize **2s** in yields greater than 85% from water-soluble primary amines with a primary alkyl group or its steric equivalent.[12] In our case, it is speculated that the steric hindrance caused by the methyl group in L-alanine slows down the nucleophilic attack of amino group to the anhydride group, so that competing basic hydrolysis of the anhydride group dominates the reaction, which produces the precursor of PDA. The yield of **3a** could be considerably improved if the hydrolysis reaction is suppressed. Therefore, in procedure **1c** the reaction was carried out in imidazole melt instead of water. The crude product is obtained in essentially quantitative yield. Gratifyingly, IR and UV spectra suggest that the crude product is mostly **3a** and contains no PDA, as indicated by the absence of a peak or shoulder at 548 nm. Moreover, the formation of **5a** is also reduced when compared with procedure **1b**, as indicated by the slightly blue-shifted UV absorption maxima.

Procedure **1c** also works with other α-amino acids with different Rs. For instance, **3b** and **3c** have also been synthesized by using L-leucine and L-valine as the amine sources, respectively. Note that **3c** is always contaminated by PDA and its preparation is significantly more sensitive to moisture than **3b**, which is more sensitive than **3a**. Both can be rationalized by the increase of the steric hindrance toward nucleophilic attacks of the amino group to the anhydride group, while the competing hydrolysis due to trace amount of water is not affected.

The synthetic applicability of **3a** was demonstrated via the successful transformations at both the termini, which yields the first two nonracemic chiral amphiphilic PDIs. It is well-known that PDIs tend to aggregate into n-type semi-conducting molecular stacks. In the presence of chiral units, helical PDI stacks with preferred handedness were observed.[14] Introduction of amphiphilicity is expected to add one more dimension to the self-assembly of PDIs, as different morphologies such as micelles, vesicles, planar bilayers and nanotubes could be accessible. Although there are a few reports on amphiphilic unsymmetric PDIs,[15] nonracemic chiral amphiphilic unsymmetric PDIs have not been reported, probably limited by the accessibility of such compounds. However, the synthesis of such PDIs becomes straightforward when **3** is available, as depicted in Scheme 2. Besides the stacking interaction between PDI cores



Scheme 2. All chirality centers are in *S* configuration. Compounds **6a**, **7a**: R_1 = 2-methylpropyl, R_2 = 1*H*,1*H*,2*H*,2*H*-perfluorodecyl; **6b**, **7b**: R_1 = methyl, R_2 = dodecyl; *temp. **6a**: 120 °C; **6b**: 150 °C.



Scheme 3. All chirality centers are in *S* configuration. Amine source a: R_1 = 2-methylpropyl, R_2 = 1*H*,1*H*,2*H*,2*H*-perfluorodecyl Amine source b: R_1 = methyl, R_2 = dodecyl.

and helicity stemming from the molecular chirality, segregation of incompatible perfluorinated and perhydrogenated alkyl chains in **7a** and oligoethylene glycol and alkyl chains in **7b** may take place and influence the self-assembly behaviors profoundly. As delineated in Scheme 3, perfluorinated and tetraethylene glycol functionalized amine sources were prepared via acid catalyzed esterification. **6a** and **6b**[16] were isolated by column chromatography in 72% and 66%, respectively, assuming **3a** is pure. This implies that the yield of **3a** via procedure **1c** must be greater than 72%. Further functionalization of **6** is routine as shown in Scheme 2. Yields were 85% for **7a** and 50% for **7b**.[17] Both **7a** and **7b** are highly soluble in common organic solvents. Circular dichroism spectra shown in Figure 2 confirmed the optical active natures of **7a** and **7b**. Investigation on their self-assembly behaviors is in progress.

In conclusion, we have developed a convenient and efficient synthesis of AB bifunctional 3,4,9,10-perylene-tetracarboxylic-3,4-anhydride-9,10-imides. Steric and stereochemical control can be conveniently coded by using an enantiomerically pure α-amino acid with a tunable side group as the amine source. Such reagents are key building blocks for further development of sterically and stereochemically controlled unsymmetric PDIs in which the PDI moiety can be placed at both terminal and inner positions. Using such a building block, the first two nonracemic chiral amphiphilic PDIs were successfully synthesized.

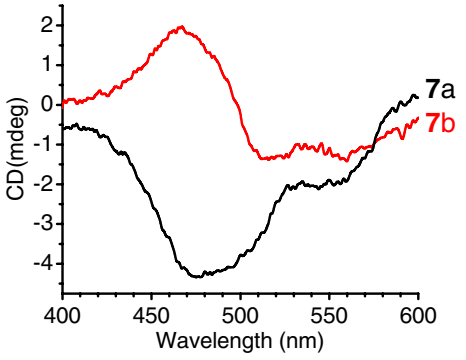


Figure 2. Circular dichroism spectra of **7a** and **7b** **7a**: 6×10^{-5} M in hexane; **7b**: 1.2×10^{-4} M in 1:3 THF/H_2O (v/v).

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Supplementary data

Detailed experimental procedures and NMR spectra of final products are provided in the supplementary data. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.07.099.

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16. Spectroscopic data for **6a**:
^{1}H NMR (600 MHz, THF-d_8): δ 8.55–8.39 (m, 8H); 5.84–5.82 (m, 1H); 5.72 (q, $J = 7.2$ Hz, 1H); 4.54–4.43 (m, 2H); 2.68–2.62 (m, obscured by the water resonance); 2.29–2.14 (m, 2H); 1.71 (m, obscured by the solvent resonance); 1.07 (d, $J = 6.6$ Hz, 3H); 0.99 (d, $J = 6.6$ Hz, 3H). ^{19}F NMR (282 Hz, THF-d_8): δ −80.3, 3F; −112.6, 2F; −120.9 and −121.1, 6F; −121.9, 2F; −122.6, 2F; −125.4, 2F. HRMS (ESI): (M+*e*): Calcd for $C_{43}H_{27}F_{17}N_2O_8$ 1022.1496; found, 1022.1510.
Spectroscopic data for **6b**:
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.26–8.179 (m, 8H); 5.65 (q, $J = 6.9$ Hz, 1H); 5.75 (q, $J = 6.9$ Hz, 1H); 4.13-3.96 (m, 2H); 1.71–1.67 (m, 6H); 1.48–1.39 (m, 2H); 0.93–0.59 (m, 21H). HRMS (ESI): (M+*e*): Calcd for $C_{42}H_{42}N_2O_8$ 702.2941; found, 702.2961.
17. Spectroscopic data for **7a**:
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.58–8.31 (m, 8H); 5.85–5.83 (m, 1H); 5.79 (q, $J = 7.2$ Hz, 1H); 4.60–4.47 (m, 2H); 4.26–4.21 (m, 2H); 2.52 (q, $J = 18$ Hz, 2H); 2.32–2.13 (m, 2H); 2.29–2.14 (m, 2H); 1.78 (dd, $J_1 = 2.1$ Hz, $J_2 = 6.9$ Hz, 3H), 1.69–1.65 (m, 3H); 1.07 (d, $J = 6.6$ Hz, 3H); 0.99 (d, $J = 6.6$ Hz, 3H); 1.30–1.16 (m, 18H); 1.07 (d, $J = 6.6$ Hz, 3H), 0.99 (d, $J = 6.6$ Hz, 3H); 0.84 (t, $J = 6.6$ Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.24, 169.98, 162.84, 162.45, 134.51, 134.30, 131.70, 131.40, 129.31, 129.13, 126.03, 122.96, 122.92, 122.78, 65.72, 57.18, 52.10, 49.60, 38.03, 31.84, 30.45, 29.63, 29.57, 29.50, 29.48, 29.29, 29.17, 28.47, 25.91, 25.40, 23.02. ^{19}F NMR (282 MHz, $CDCl_3$): δ −79.5, 3F; −112.3, 2F; −120.6 and −120.8, 6F; −121.5, 2F; −122.2, 2F; −124.9, 2F. HRMS (M+*e*): Calcd for $C_{55}H_{51}F_{17}N_2O_8$ 1190.3374; found, 1190.3377.
Spectroscopic data for **7b**:
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70–8.61 (m, 8H); 5.84–5.75 (m, 2H); 4.40–4.15 (m, 4H); 3.75–3.66 (m, 2H); 3.62–3.50(m, 12H); 3.36 (s, 3H); 1.75 (d, $J = 6.9$ Hz, 6H); 1.63–1.60 (m, 2H); 1.24–1.14 (m, 18H); 0.87–0.83 (t, $J = 6.6$ Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.48, 170.43, 162.82, 162.72, 134.76, 134.72, 131.80, 129.48, 128.49, 123.33, 123.31, 123.22, 123.17, 72.09, 70.75, 70.73, 69.17, 65.91, 64.80, 59.22, 49.77, 49.68, 32.07, 29.85, 29.80, 29.72, 29.70, 29.53, 29.38, 28.66, 26.11, 22.86, 14.99, 14.31. HRMS (M+*e*): Calcd for $C_{51}H_{60}N_2O_{12}$ 892.4146; found, 892.4160.