

# Synthesis of Isomerically Pure *anti*-Anthradithiophene Derivatives

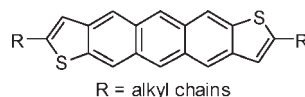
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## ABSTRACT



The regiospecific total synthesis and characterization of *anti*-isomers of 2,8-dialkylanthradithiophenes are described. The “*anti*” structure of the ADT derivatives is demonstrated by <sup>13</sup>C NMR as well as single crystal X-ray diffraction.

For decades, organic electronics have formed a hot topic in materials science.<sup>1</sup> A wide range of conjugated polymers is currently used as organic semiconductors.<sup>2</sup> However, the drawback of using polymers for optoelectronic applications is their low purity and difficult characterization inherent to their mass distribution. Consequently, the use of “small” organic molecules in electronic devices is an interesting alternative, since they are easier to produce with a high purity degree. In addition, they order much better in the solid state. Among the large variety of small molecules, linear fused (hetero)acenes have been preferentially used thanks to their high performances in electronic devices.<sup>1f,g</sup>

For example, pentacene has already demonstrated a charge carrier mobility ( $\mu$ ) of 1.5 up to 5 cm<sup>2</sup>/V·s in field-effect transistors (FET).<sup>3</sup> However, it is known for being poorly stable toward photoinduced degradation, especially in solution,<sup>4</sup> which is a weak point for solution processed organic electronic devices. Analogues of fused linear acenes including heteroatoms in their aromatic core, such as anthradithiophene (ADT) derivatives, have been described and have shown (i) a better stability toward photo-oxidation than their corresponding acenes and (ii) high charge carrier mobilities of about 0.4 to 6.0 cm<sup>2</sup>/V·s.<sup>5</sup> The use of

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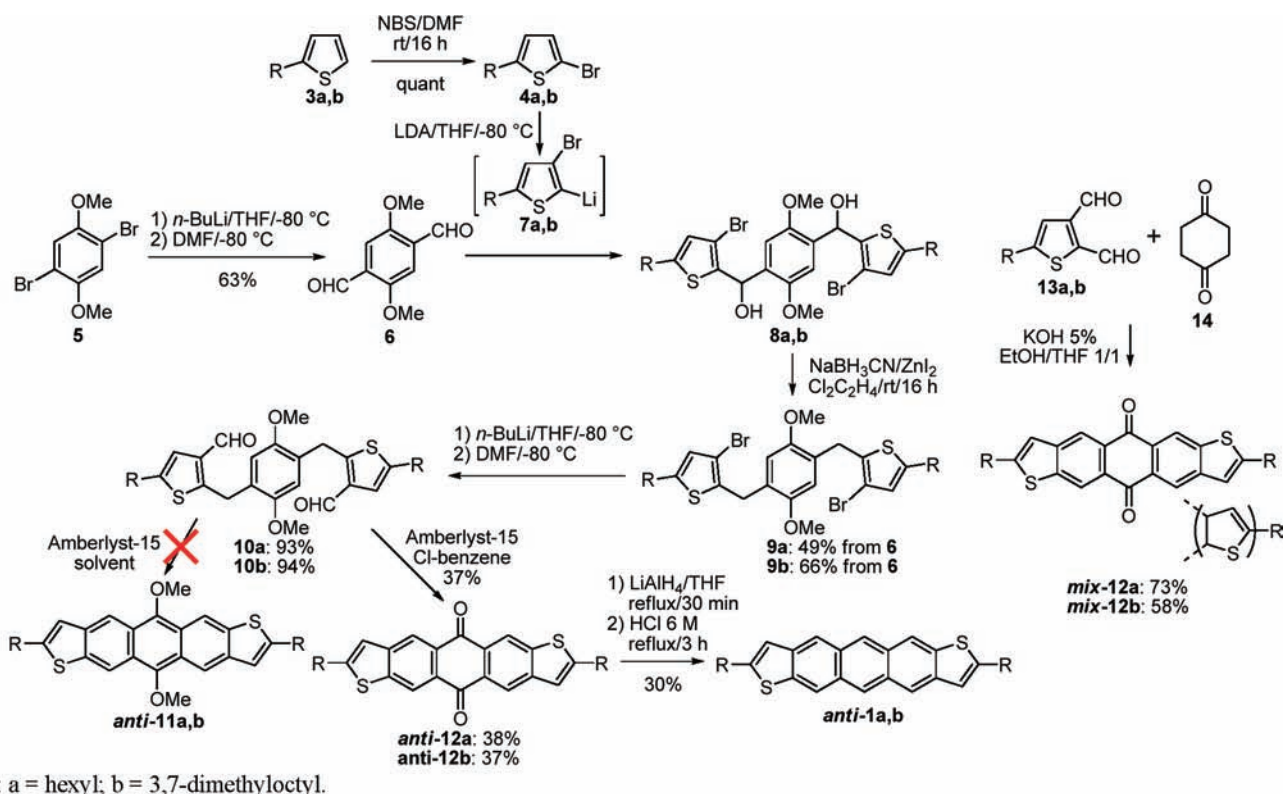
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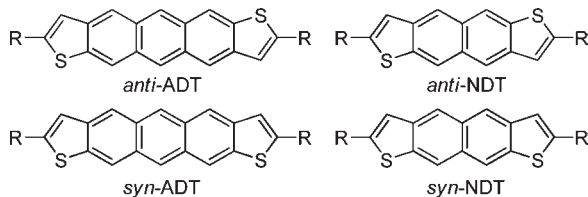
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**Scheme 1.** Synthesis of ADT *anti*-1a,b and Quinones *mix*-12a,b



ADT in FETs has been extensively explored, but the reported studies have always relied on the use of a mixture of *syn*-/*anti*-ADT isomers (Figure 1).<sup>5b,6</sup> Takimiya et al. have recently proposed the synthesis of isomeric *syn*- and *anti*-linear naphthodithiophene (NDT) derivatives (Figure 1).



**Figure 1.** Structures of *anti*-/*syn*-isomers of anthradithiophene (ADT) and naphthodithiophene (NDT) derivatives.

They have demonstrated that the centrosymmetric (= *anti*-) isomer exhibits a higher charge carrier mobility  $\mu$ , up to  $1.50 \text{ cm}^2/\text{V}\cdot\text{s}$ , than its axisymmetric counterpart (= *syn*-) isomer that reaches at best  $\mu = 0.06 \text{ cm}^2/\text{V}\cdot\text{s}$ .<sup>7</sup> Lately, Anthony et al. have reported the synthesis and the separation by fractional recrystallization of the *syn*-/*anti*-isomer

mixture of ADT amides and their use in polymer solar cells.<sup>8</sup> They have shown that the efficiency is higher for bulk-heterojunctions based on poly(3-hexylthiophene) solar cells incorporating the *syn*-ADT amide isomer. In this context, we investigated the total synthesis of isomerically pure *anti*-ADT derivatives. Alkyl chains were attached on positions 2 and 8 of the ADT skeleton in order to fulfill solubility requirements to perform structural characterizations.

ADT *anti*-1a,b derivatives were prepared as presented in Scheme 1. The synthetic strategy was inspired by the work of Wex et al. in which the preparation of a single isomer of thienobisbenzothiophene is described.<sup>9</sup>

Starting materials **4a,b** and **6** were prepared following synthetic procedures previously described: synthons **4a,b** were obtained in quantitative yields by bromination of 2-alkylthiophenes **3a,b** using *N*-bromosuccinimide<sup>10</sup> and 2,5-dimethoxyterephthalaldehyde (**6**) was synthesized in 63% yield by lithiation of compound **5** with *n*-BuLi followed by reaction of the corresponding dilithiated species with DMF.<sup>11</sup> Intermediates **7a,b** were generated *in situ* from **4a,b** via a halogen dance reaction using LDA<sup>12</sup> and were subsequently quenched with compound **6** to

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provide the diols **8a,b**. These were then reduced without further purification into compounds **9a** (49% from **6**) and **9b** (66% from **6**) using NaBH<sub>3</sub>CN and ZnI<sub>2</sub>.<sup>9</sup> The exact positions of the bromine atoms were confirmed by HMBC 2D-NMR (Figure SI6) as well as single crystal XRD structure determination (Figure SII). Compounds **10a,b** were obtained in good yields (**10a**: 93% and **10b**: 94%) by formylation of dibrominated derivatives **9a,b** using *n*-BuLi, followed by reaction of the organolithium intermediates with DMF. The next step was performed using Amberlyst acidic resin as a cyclization/aromatization agent.<sup>9</sup> Surprisingly, the initially expected *anti*-**11a,b** ADT derivatives were not achieved from the cyclization step since *anti*-**12a,b** quinones were always isolated. Several experimental conditions, listed in Table 1, have been tested on the hexyl derivative **10a** in order to optimize the reaction yield. The first conditions applied were the ones described by Wex et al. (entry 1). In our case, no reaction was observed since the starting compound **10a** was quantitatively recovered even after 64 h of reaction time. The use of toluene instead of benzene (entry 2) led to the formation of the quinone *anti*-**12a** in 23% yield. Reaction in *p*-xylene, which possesses a higher boiling point than benzene and toluene, was found to be unsuccessful since degradation of the reaction mixture was observed (entry 3). Using a different cyclization/aromatization agent from Amberlyst-15, *i.e.* *p*-toluenesulfonic acid (*p*-TSA)<sup>13a</sup> (entry 4) or Amberlyst-36<sup>13b</sup> (entry 5), resulted in the degradation of the reaction mixture (with *p*-TSA) and in recovery of the starting material (with Amberlyst-36). It is rational to suppose that the cyclization/aromatization process might involve charged intermediates. Thus, an effect on the reaction is expected by changing the solvent polarity. Indeed, the reaction in nonpolar decane (entry 6) led to the formation of the quinone *anti*-**12a** in 6% yield whereas the use of polar chlorobenzene (entry 7) provided the compound *anti*-**12a** in 38% yield. The two conditions which gave the best results (entries 2 and 7) were repeated on the derivative **10b** bearing 3,7-dimethyloctyl chains instead of hexyl chains. Similar observations were made since quinone *anti*-**12b** was obtained in 22% and 37% yield, using toluene and chlorobenzene as reaction solvents, respectively.

At first glance, the yields of 22–37% obtained for the synthesis of products *anti*-**12a,b** seem rather low. However, taking into account that four reactions are involved, cyclization, aromatization, cleavage of the methoxy groups, and oxidation (Figure SI31), the observed yields appear appreciable. In order to confirm the selective formation of isomerically pure quinones *anti*-**12a,b** by spectroscopic characterizations, the synthesis of *syn*-/*anti*-isomers

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(13) (a) *p*-TSA = lower molecular weight analogue of Amberlyst resins; (b) Capacity of Amberlyst-15 = 4.70 equiv/kg; Amberlyst-36 = 5.40 equiv/kg.

**Table 1.** Optimization of the Cyclization Step Conditions on **10a**

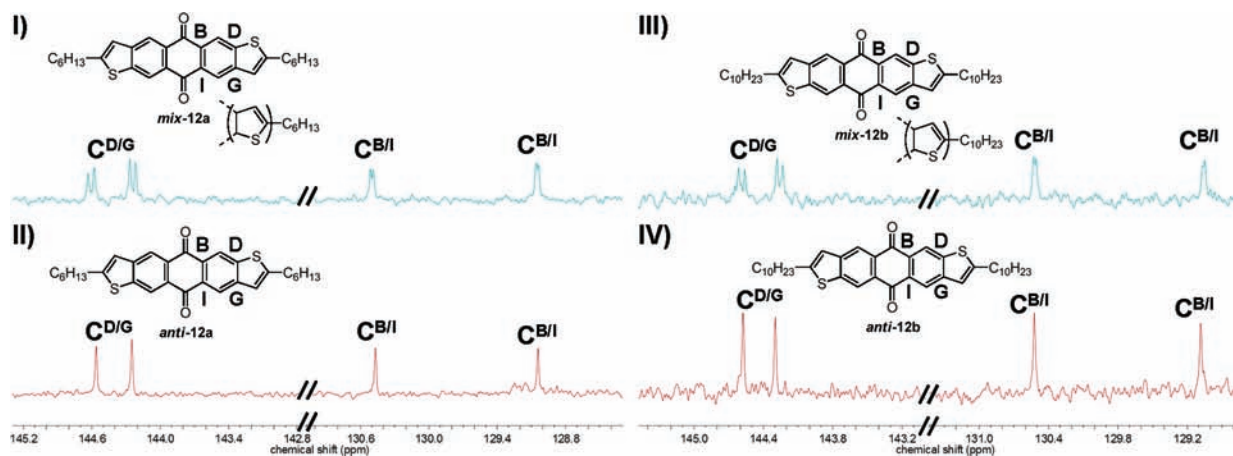
entry	C/A agent	solvent	temp (°C)	time (h)	yield of <i>anti</i> - <b>12a</b> (%)
1	A15	benzene	80	64	no reaction
2	A15	toluene	110	64	23
3	A15	<i>p</i> -xylene	140	64	degradation
4	<i>p</i> -TSA	toluene	110	64	degradation
5	A36	toluene	110	64	no reaction
6	A15	decane	130	64	6
7	A15	Cl-benzene	130	29	38

mixtures of quinones *mix*-**12a,b**, in 73% (*mix*-**12a**) and in 58% (*mix*-**12b**) yields, was carried out by condensation of 5-alkylthiophene-2,3-carboxaldehyde **13a,b** with cyclohexane-1,4-dione **14** in the presence of 5% KOH<sub>aq</sub> solution (Scheme 1).<sup>6b</sup>

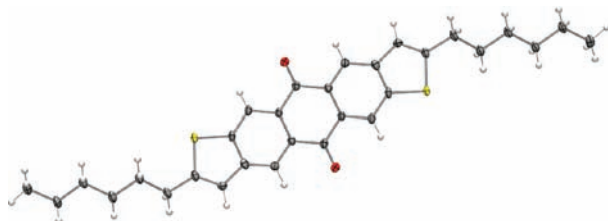
<sup>1</sup>H NMR and UV–visible measurements did not afford any information on the synthesis of isomerically pure quinones *anti*-**12a,b** since their <sup>1</sup>H NMR and absorption spectra are identical to those of *mix*-**12a,b** (Figures SI3,5,7,9,23–26). On the contrary, the presence of single *anti*-quinone isomers was established using <sup>13</sup>C NMR spectroscopy where slight changes were observed for quaternary carbons C<sup>B</sup>, C<sup>D</sup>, C<sup>I</sup>, and C<sup>G</sup> located in the aromatic region (Figure 2). For the pure isomers *anti*-**12a,b** these carbon atoms appear as single peaks at  $\delta = 129.0, 130.5$  ppm for C<sup>B/I</sup> and at  $\delta = 144.4, 144.6$  ppm for C<sup>D/G</sup> whereas twin peaks are observed in the <sup>13</sup>C NMR spectra of *mix*-**12a,b** indicating the presence of an isomer mixture (Figure 2). This observation shows that single *anti*-isomers were formed for compounds *anti*-**12a,b**, and it was also confirmed by X-ray diffraction measurement performed on a crystalline splinter of *anti*-**12a** (crystals were grown by slow evaporation of CH<sub>2</sub>Cl<sub>2</sub> solution at room temperature, Figure 3). A slight amount of disorder (8.2%) is present in the orientation of the thiophene rings, as it is often the case for thiophene systems with unsubstituted position 3.<sup>14</sup> The disorder is also identical on either side of the molecule, in agreement with the crystallographic symmetry.

<sup>13</sup>C NMR spectroscopy indicates that the product contains only the *anti*-**12a,b** isomer and the formation of the *syn*-product is impossible from the geometry of the starting compound **9a,b**, which was independently confirmed (Figures SII,6). Therefore, the observed disorder is not a result of the presence of a mixture of *syn*- and *anti*-isomers, but 8.2% of the molecules are simply flipped over in the lattice. The impact of the molecular shape on entering it into the lattice in the wrong way is minimal. The effect is also minimal from the energy point of view: the sulfur side

(14) As an example, we searched the Crystal Structure Database (v5.31, with four updates) for unsubstituted benzo[*b*]thiophenes in the 3-position. Molecules substituted asymmetrically on the benzo[*b*]thiophene benzene ring were removed from the resulting set. This yields 76 benzo[*b*]thiophenes which can in principle display this type of disorder. Of these 76, 43 are disordered (57%).



**Figure 2.** Comparison of selected window of  $^{13}\text{C}$  NMR spectra of (I) *mix-12a*, (II) *anti-12a*, (III) *mix-12b*, and (IV) *anti-12b*.



**Figure 3.** Single crystal XRD image of *anti-12a*. Displacement ellipsoids at the 50% level (The structure has overlap between 3 of the 5 rings in a stairway-like arrangement. The intermolecular distance amounts to 3.56 Å. Neighboring ADT are shifted up or down by half of this intermolecular distance, leading to staggered columns. The hexyl chains can be found in layers between the anthradithiophene layers). The .cif file is available as Supporting Information.

of the ring exchanges an edge-to-edge CH–S interaction in the major orientation for interactions with the hexyl chains in the minor orientation.

Finally, quinones *anti-12a,b* were reduced into ADT *anti-1a,b* in 30% yields using  $\text{LiAlH}_4$ . Although both products present poor solubility in common organic solvents, their  $^1\text{H}$  NMR spectra have been recorded (Figures SI21,22). Comparison of the  $^1\text{H}$  NMR spectra of ADT *anti-1a,b* with those of their quinone precursors *anti-12a,b* (Figures SI3,5) shows the presence of an extra signal in the aromatic region at  $\delta = 6.14$  ppm which is assigned to the protons in positions 5,11 of the ADT core. After reduction, signals for protons  $\text{H}^{\text{a,b}}$  ( $\delta = 8.76$  and  $8.62$  ppm for *anti-12a*;

$\delta = 8.72$  and  $8.58$  ppm for *anti-12b*) and  $\text{H}^{\text{c}}$  ( $\delta = 7.23$  and  $7.21$  ppm for *anti-12a,b* respectively) are shifted to higher fields ( $\delta(\text{H}^{\text{a,b}}) = 7.79$  and  $7.68$  ppm;  $\delta(\text{H}^{\text{c}}) = 6.99$  ppm) for *anti-1a,b*. The synthesis of ADT *anti-1a,b* was also confirmed by (i) mass spectrometry by the observation of  $m/z$  ratios at 458.2108 for **1a** and at 570.3368 for **1b** (Figures SI29,30) and (ii) optical measurements since absorption spectra of compounds *anti-1a,b* present typical ADT spectral profiles showing three waves beyond 410 nm: 424, 452, and 483 nm for **1a** and 425, 452, and 483 nm for **1b** (Figures SI27,28).<sup>6d</sup>

In conclusion, we have reported the first total synthesis of pure *anti*-isomers of anthradithiophene derivatives using a six-step synthetic pathway. The *anti*-configuration of the ADT compounds has been unambiguously proven by  $^{13}\text{C}$  NMR and X-ray diffraction experiments on their quinone precursors. This synthetic work, which can be regarded as a first milestone in ADT chemistry, offers an opportunity for further physical studies on the property performance of *anti*-ADT compared to the *syn*-/*anti*-ADT mixture in electronic devices such as field effect transistors.

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**Supporting Information Available.** Experimental procedures, optical and NMR spectra and XRD data in CIF format for **9a** and *anti-12a*. This material is free of charge via the Internet at <http://pubs.acs.org>.