3,4-Alkylenedioxypyrroles: Functionalized Derivatives as Monomers for New Electron-Rich Conducting and Electroactive Polymers

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New functionalized derivatives of 3,4-ethylenedioxypyrrole (EDOP, **5a**) and 3,4-(1,3-propylenedioxy)-pyrrole (ProDOP, **5b**) as especially electron-rich monomers which yield highly electroactive and stable conducting polymers useful for a diverse set of applications have been synthesized. *N*-Alkylations of ProDOP were carried out to yield a variety of ProDOP derivatives having alkyl, sulfonatoalkoxy, glyme, and glyme alcohol pendant chains. Iodization of EDOP and ProDOP via iodo-decarboxylation afforded iodo-functionalized derivatives useful for subsequent aryl coupling chemistry. *N*-Protection and formylation of EDOP, followed by Knoevenagel condensation of the resultant 2-formyl-EDOP with aryl acetonitrile derivatives, led to 1-cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-thienyl)vinylene (**23**) (Th-CNV-EDOP) and 1-cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-(3,4-ethylenedioxythienyl)vinylene (**26**) (EDOT-CNV-EDOP). A 14-crown-4-ether **34** based dioxypyrrole was synthesized with a cavity potentially useful for lithium ion coordination and sensing in the resultant electroactive polymer. *C*-Alkylated ProDOPs (**43a**, **43b**, and **43c**) containing octyl, ethylhexyl, and dioctyl substituents appended to the central methylene of the propylene bridge, were prepared as monomers for potentially soluble π-conjugated polymers.

Introduction

Heterocycle-based conjugated polymers, such as polypyrrole, polythiophene, polyfuran, and others, have received significant attention due to the wide range of electrical, electrochemical, and optical properties they display.[1] The heteroatoms within the ring play an important role in controlling the properties of the polymers due to their intrinsic electron-donating or electron-withdrawing capabilities, along with other properties which include hydrogen-bonding and polarizability. As such, polyheterocyclic structures can be tuned for optimization of oxidative p-type doping, reductive n-type doping, and adjustment of the HOMO−LUMO energy levels which provide electronic transitions across a broad range of the electromagnetic spectrum. These polymers have been utilized in applications as semiconductors for field-effect transistors[2] and LEDs,[3] as conductors for electrostatic charge dissipation and EMI shielding, and as redox active materials for energy storage (batteries and supercapacitors) and electrochromic devices.[4] The structures of polyheterocycles are easily tailored by the nature and position of the heteroatom in the main chain ring, the ability to append a variety of substituents or fuse other rings onto the main chain, and the ability to control conjugation through electronic and steric interactions. This structural control has led to optimization of such properties as electronic conductivity, solution and melt processability, and stability of the conducting form of the polymers under a variety of environmental conditions.

As one of the many polyheterocycles investigated, poly(3,4-ethylenedioxythiophene) (PEDOT) stands out for its vastly improved redox and conductivity stability properties when compared to its parent, polythiophene.[5] Appending an akylenedioxy bridge across the 3- and 4-positions of the heterocycles adds electron density to the aromatic ring, reducing both the monomer and polymer oxidation potentials, which results in the formation of highly stable conducting states. The strong raising of the HOMO level of the conjugated π system also reduces the energy of the $\pi-\pi^*$ transition, resulting in a lower electronic band gap. This low band gap causes the majority of the electronic absorption of the doped state to be shifted into the near-infrared, and thus PEDOT is quite transmissive to visible light in its conducting state. Finally, the blocking of the 3- and 4-positions by the fused rings forces polymerization to the 2- and 5-positions, leading to a linear polymer chain with no $\alpha-\beta'$ coupling and fewer structural defects than most polyheterocycles. As the polymers are not branched or cross-linked, appropriately substituted derivatives can be prepared with relatively high molecular weight which are soluble and can be processed by common methods such as spin-

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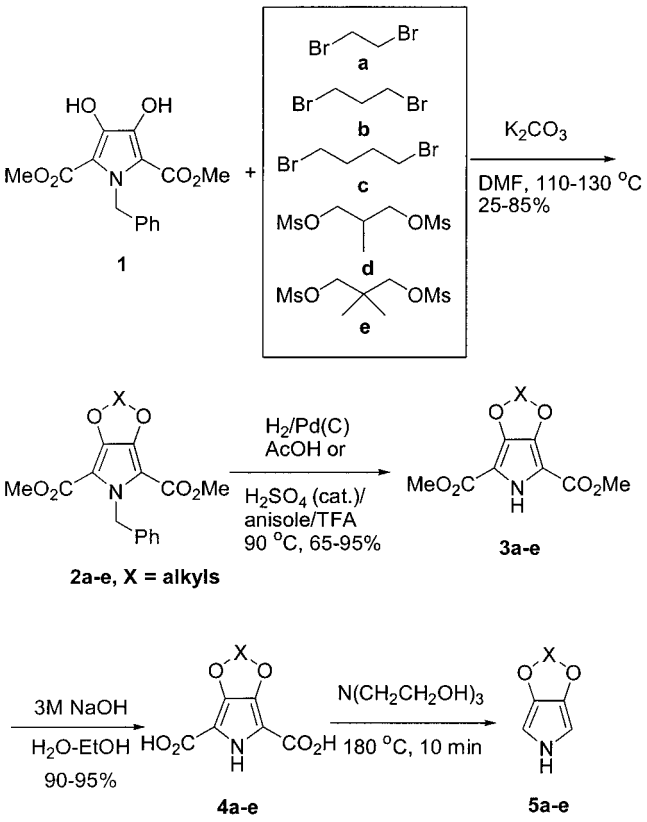
Scheme 1



coating and airbrush spraying.[5,6] The versatility of the synthetic methodology used to prepare EDOT has allowed us to extend this to a number of new derivatives including 3,4-(1,3-propylenedioxy)thiophene (ProDOT), 3,4-(1,4-butylenedioxy)thiophene (BuDOT), and a series of substituted monomers[7] which yield polymers with optimized electrochromic properties.

Combining the electron-rich character of polypyrroles with these 3,4-dioxy substitution concepts, we envisioned that 3,4-dioxypyrrole polymers might prove especially useful for the synthesis of very easily oxidized electroactive conjugated polymers. On the basis of the reported synthesis of 3,4-ethylenedioxypyrrole,[8] we reported on the synthesis of a small set of 3,4-alkylenedioxypyrroles (XDOPs) and the properties of their resultant polymers as potential electrochromic and biostable materials.[9−11] Similarly, Groenendaal et al.[12] studied the cyclic voltammetric switching of PEDOP and confirmed its extremely low oxidation potential. From these initial studies, we determined that the PXDOPs show unique electrochromic color changes, along with potentially useful conductivity and stability properties to warrant deeper investigation. Encouraged by these results, we expanded our study to a broad set of 3,4-alkylenedioxypyrrole derivatives which will provide a broad set of polymers having a range of properties. Here, we report on the synthesis of a variety of these new monomeric derivatives and demonstrate the breadth of chemistry possible within the synthesis of the 3,4-alkylenedioxypyrroles and their subsequent functionalization.

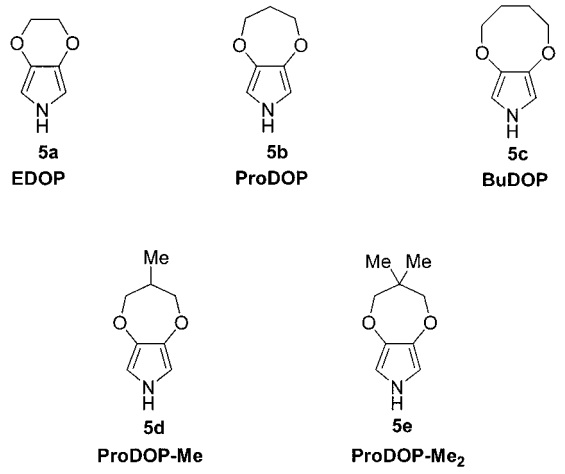


Figure 1. Structures of initial 3,4-alkylenedioxypyrroles synthesized.

Results and Discussion

The general synthetic route to the 3,4-alkylenedioxypyrroles is illustrated in Scheme 1, and the initial set of monomers prepared are shown in Figure 1.[9−11] These compounds (**5a**−**e**) were synthesized from the known intermediate dimethyl-*N*-benzyl-3,4-dihydroxypyrrole-2,5-dicarboxylate (**1**), in five steps in overall yields of 20−25%. This series of reactions (1,4-dioxane ring formation, benzyl group deprotection, hydrolysis, and decarboxylation) afforded the corresponding 3,4-ethylenedioxypyrrole (**5a**, EDOP),[8] 3,4-(1,3-propylenedioxy)pyrrole (**5b**, ProDOP), 3,4-(1,4-butylenedioxy)pyrrole (**5c**, BuDOP), 3,4-(2-methyl-1,3-propylenedioxy)pyrrole (**5d**, ProDOP-Me), and 3,4-(2,2-dimethyl-1,3-propylenedioxy)pyrrole (**5e**, ProDOP-Me_2) in moderate to good yields.[11]

With the parent monomers in hand, we investigated the *N*-alkylation of ProDOP with a variety of pendant substituents ranging from simple alkyl groups to glyme, glyme alcohol, and sulfonatoalkoxy derivatives as illustrated in Scheme 2. The ease of pyrrole functionalization provides new derivatives with a broad set of structural possibilities in a straightforward manner. Under the conditions used, ProDOP was easily *N*-alkylated in moderate to good yields of 40−85%. Increasing the polarity of the substituents suggests that the polymers derived from these monomers may ultimately prove useful as biocompatible substrates for cell growth[9,13,14] and, in the case of the sulfonate derivatized system, yield water soluble and self-dopable conducting polymers.[15] In general, these *N*-derivatized ProDOPs can be isolated by column chromatography or precipitation and subsequently stored as solids/liquids under argon in the freezer prior to polymerization.

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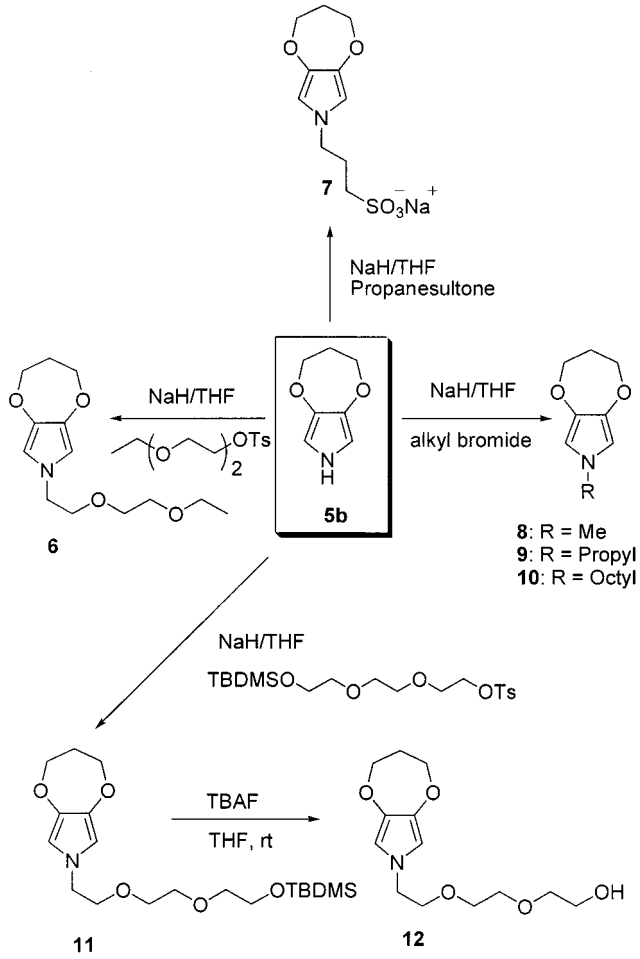
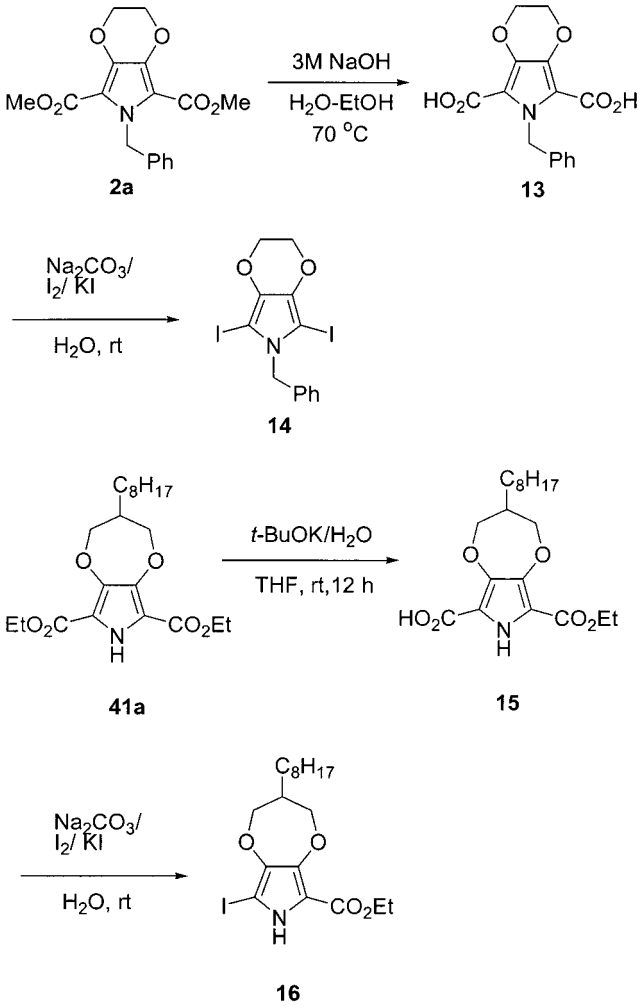
Scheme 2



Scheme 3



Next we considered the introduction of halides (bromide or iodide) at the 2- and 5-positions of the aromatic heterocycle in order to increase their utility in preparing multiaryl ring monomers via transition metal mediated coupling methods such as the Stille, Heck, and Suzuki reactions. Using the thiophene analogue EDOT as a comparison, multiaryl ring monomers have provided a broad set of polymers with a high degree of control of their redox and optical properties.[5] Bromination of EDOP was attempted under various conditions but was not successful due to the instability of EDOP. Bromination via bromine, NBS, and other reagents under standard conditions resulted in rapid and uncontrolled polymerization. We note that the highly electron-rich nature of EDOP, observable by the significantly lower oxidation potential for EDOP relative to pyrrole,[9−12] favors this polymerization. A series of *N*-protected EDOPs, derivatized with *t*-BOC, tosyl, silyl, and benzyl groups, was subsequently synthesized and subjected to standard bromination conditions. Surprisingly, the tosyl-protected EDOP was very sensitive to air and moisture, rendering the decomposed form. The *t*-BOC- and silyl-protected EDOP derivatives were fairly stable, though not enough to tolerate the subsequent oxidative reaction conditions. Finally, while the *N*-benzyl-protected EDOP was sufficiently stable to tolerate the bromination reaction conditions without significant decomposition, successful bromination could not be achieved. As an alternative, iodo-decarboxylation was examined on the *N*-benzyl-3,4-ethylenedioxypyrrole-2,5-dicarboxylic acid (**13**) using a literature procedure,[16] as shown in Scheme 3. The reaction proceeded smoothly to yield *N*-benzyl-2,5-diiodo-EDOP (**14**) in excellent yield which was sufficiently stable for further reaction. In an initial study employing **14**, transition metal mediated coupling with 2-trimethylstannyl-EDOT lead to the easily oxidized 2,5-bis(2-EDOT)EDOP. As will be illustrated later, the diester/diol derivative of 3,4-dioxypyrrole can also serve as an intermediate to *C*-alkylation derivatives. In this instance, diester **41a** (Scheme 3) could be selectively hydrolyzed[17] by treatment with excess potassium *tert*-butoxide/H_2O (1:1) to yield the mono-hydrolyzed product (**15**). Subsequent iodo-decarboxylation could be accomplished in the presence of the ester to yield the mono-iodo-compound **16**.

To obtain useful EDOP monomer derivatives, it is desirable to have *N*-protected EDOP on hand with the 2- and 5-positions open for further chemical transformations. Several protecting groups were examined, and the benzyl and *t*-BOC groups provided the most useful derivatives in terms of stability, ability for further reaction, and subsequent deprotection. As shown in Scheme 4, the benzyl protection of EDOP proceeded well in a 90% yield to provide *N*-benzyl-EDOP (**17**). In another route beginning with an EDOP precursor, the *N*-benzyl-

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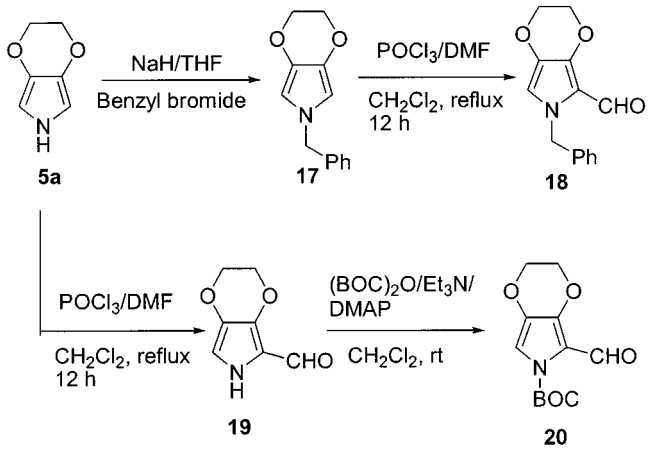
Scheme 4

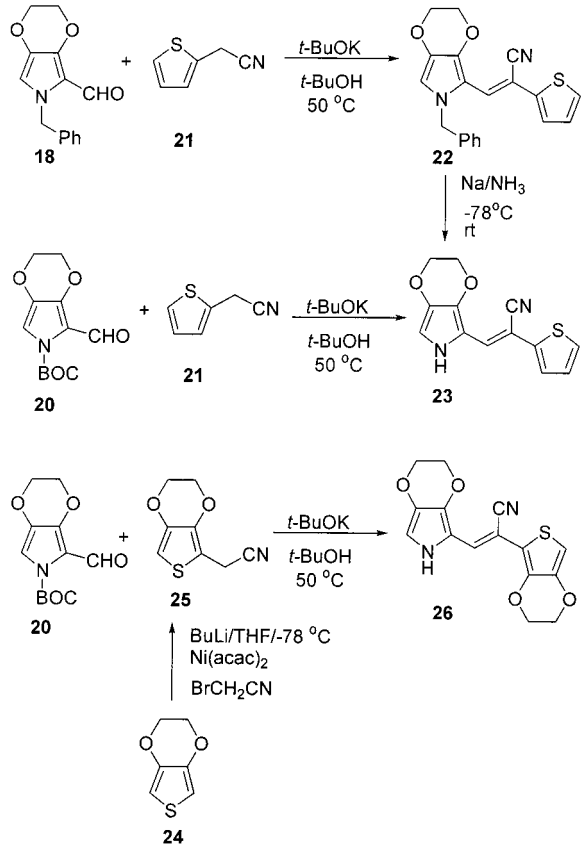


protected 2,5-diester derivative **2a** was hydrolyzed to diacid **13** and subsequently decarboxylated by heating in triethanolamine for a short period to yield *N*-benzyl-EDOP (**17**) in excellent yield. This latter route is preferred in the synthesis of **17** due to the lack of necessity for isolating EDOP (**5a**).

With a stable *N*-benzyl EDOP in hand, we next explored the 2-formylation of **17** via the Vilsmeier−Haack method using a literature procedure.[18] The Vilsmeier−Haack reagent was prepared under standard conditions ($POCl_3$/DMF in CH_2Cl_2), and as shown in Scheme 4, direct treatment of **17** with this reagent followed by hydrolysis gave aldehyde **18** in moderate yield. In another route, also shown in Scheme 4, direct treatment of EDOP with the Vilsmeier−Haack reagent under similar conditions yielded the 2-formyl-EDOP (**19**) and subsequent *N*-protection by *t*-BOC gave **20** in good yield. These formylated EDOP derivatives are very useful for further chemical transformations such as Knoevenagel or Wittig type reactions which can be used to incorporate EDOP into more highly conjugated monomer systems.

Conjugated polymers containing alternating donor and acceptor units along the backbone have recently received significant attention due to their reduced electronic band gap and ability to be both p- and n-type doped.[19] In such polymers, we have utilized the cyanovinylene unit as an electron acceptor and reported the synthesis and electrochemical properties of polymer derivatives made from 1-cyano-2-(3,4-ethylenedioxythienyl)-1-(2-thienyl)vinylene (Th-CNV-EDOT) and 1-cyano-1,2-bis(2-(3,4-ethylenedioxythienyl)vinylene (EDOT-CNV-EDOT).[20] In this work, we note that by combining appropriate donors with the cyanovinylene acceptor we could design polymers with a systematic tuning of the electronic band gap from 1.1 to 1.6 eV.[21] Due to the high HOMO level of EDOP, we felt that this system might prove especially useful for closing the band gap further. The Knoevenagel condensation of *N*-benzyl EDOP-aldehyde **18** with 2-thienylacetonitrile afforded *N*-benzyl-protected 1-cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-thienyl)vinylene **22**, and subsequent deprotection using Na/NH_3 gave Th-CNV-EDOP

Scheme 5



(**23**) in moderate yield as shown in Scheme 5.[22] Within this route, the benzyl group deprotection was found to be difficult, and the most commonly used procedures (solvolysis and catalytic hydrogen transfer) were unsuccessful, requiring the use of Na/NH_3. To overcome this problem, the *t*-BOC-protected EDOP-aldehyde **20** was employed in the reaction. As illustrated in Scheme 5, the condensation proceeded smoothly to yield the desired product and interestingly occurred with concurrent deprotection. This concurrent condensation and deprotection allowed a simple one-pot reaction by treatment with excess base. It should be noted that the unprotected EDOP-aldehyde **19** did not undergo condensation under similar conditions. Extending this chemistry to an EDOT derivative, 2-(3,4-ethylenedioxythienyl)acetonitrile (**25**) was synthesized according to a known procedure[20] and condensation with **20** gave 1-cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-(3,4-ethylenedioxythienyl)vinylene (EDOP-CNV-EDOT) (**26**) in good yield.

In addition to the potentially useful electronic and optical properties provided by polyheterocycles, ionic interactions within the material also suggest their potential in ionic drug release[23] and as ion-sensing materials.[24] In this area, the possibility of fusing ion complexing groups directly onto conjugated polymer, such that they are in direct electronic communication with the π system, is one route in which high sensitivity sensing materials may be accessible.[25] In connection with the alkylene-

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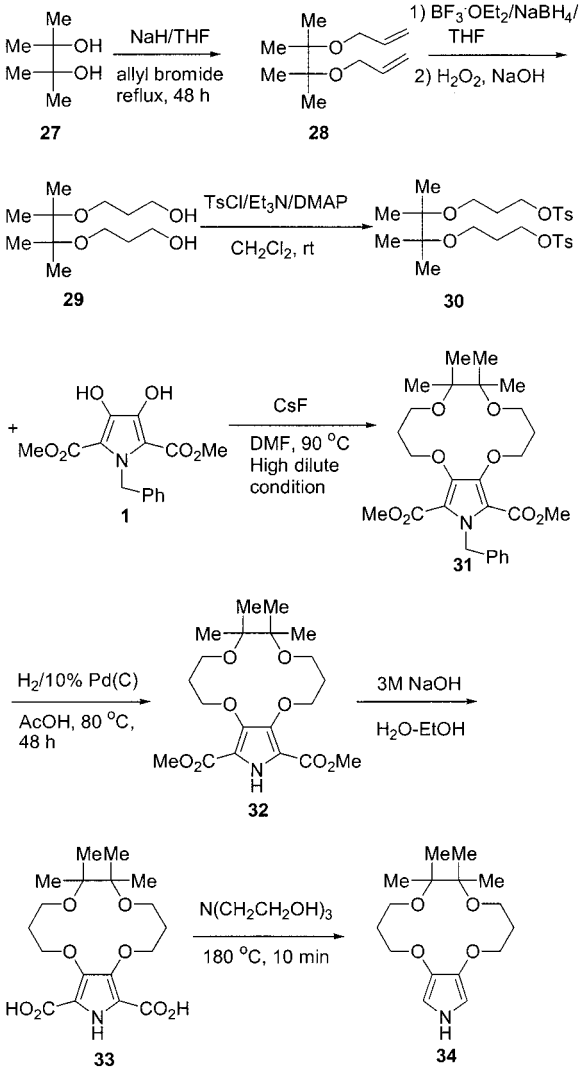
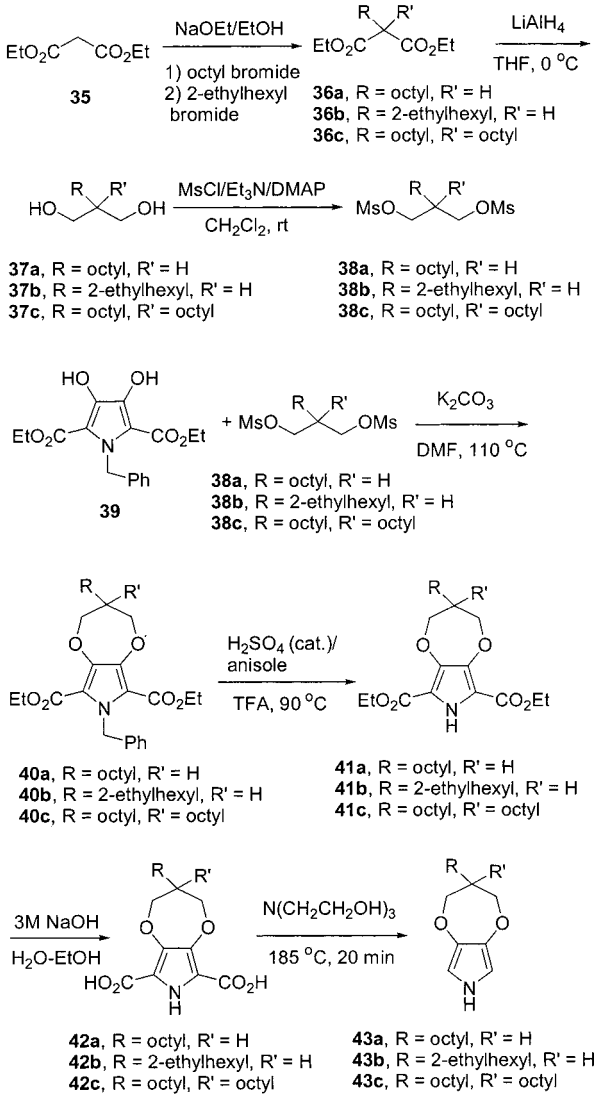
(25) Reddinger, J. L.; Reynolds, J. R. *Chem. Mater.* **1998**, *10*, 3.

Scheme 6



Scheme 7



dioxypyrrole chemistry discussed here and, toward this end, a 14-crown-4-ether derivatized dioxypyrrole was designed and synthesized as illustrated in Scheme 6 which may be potentially useful as a polymeric lithium sensor. Polymerization, redox switching, and ion dependent electrochemical results show this polymer to exhibit a strong electrochromic response which may yield ionochromic materials.[26]

To begin this synthesis, ditosylate **30** was prepared from pinacol (**27**) according to a literature procedure.[27] Diol **29** was synthesized through *O*-allylation, followed by hydroboration/oxidation and subsequent tosylation to yield **30** as a coupling partner to the dioxypyrrole **1**. The coupling reaction was performed by the procedure developed by Murashima and co-workers[28] with slight modifications. To achieve a good coupling yield, the traditional preparation method uses simultaneous injection of the two reactants by syringe to the refluxing reaction vessel. The procedure employed here avoids the use of these syringes by employing a Dean−Stark trap and was found to be convenient without any significant yield difference. Deprotection of the benzyl group by catalytic hydrogen transfer and hydrolysis gave the diacid **33** in good yield. Subsequent decarboxylation of **33** in hot triethanolamine gave the 14-crown-4-ether **34** in a 30% yield based on **1**.

The monomers described above were designed to be used in oxidative electrochemical polymerizations in which the resultant polymers deposit onto the electrode surfaces as insoluble redox active and conducting films. This method can be especially useful when preparing polymers for electrochemically based devices, but proves to be especially low in the bulk yield of polymer obtained based on the amount of monomer used. Ultimately, it is especially desirable to prepare monomer derivatives which can be polymerized using bulk synthesis conditions and which will yield solution processable polymers. As such, a high conversion of monomer to polymer is possible. This has been demonstrated for numerous conjugated polymer systems, especially those based on polythiophenes.[1] Toward this end, we have synthesized a series of modified ProDOP monomers having alkyl chains appended to the central methylene of the propylenedioxy moiety, as illustrated in Scheme 7.

Diethyl malonate was alkylated with octyl bromide and 2-ethylhexyl bromide to yield the mono- and dialkylated

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(27) Alston, D. R.; Stoddart, J. F.; Wolstenholme, J. B.; Allwood, B. L.; Williams, D. J. *Tetrahedron* **1985**, *41*, 2923.

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malonates **36a**, **36b**, and **36c**, respectively. After separation, reduction of the diesters with $LiAlH_4$ led to diols **37a**, **37b**, and **37c** which were converted into di-mesylates **38a**, **38b**, and **38c**, respectively. The alkylenedioxy ring formation reaction of *N*-benzyl-3,4-dihydroxypyrrole-2,5-dicarboxylate (**39**) with the dimesylates was performed according to the Merz procedure[8] to yield the cyclized products **40a**, **40b**, and **40c** in moderate to good yield, respectively. Utilizing the procedures employed for the preparation of the XDOP series (Scheme 1), the octyl- and ethylhexyl-derivatized ProDOPs **43a**, **43b**, and **43c** were synthesized. To date, we have shown that these monomers can undergo oxidative polymerization chemically and electrochemically to give rise to soluble polymers.[29]

Conclusions

The alkylenedioxypyrrole building block provides an immense flexibility for the synthesis of an entirely new family of electron-rich monomers for the synthesis of conducting polymers. *N*-Alkylation allows the incorporation of pendant substituents ranging from nonpolar hydrocarbon, through polar neutral species, to ionic species. ProDOPs substituted at the central methylene carbon of the alkylene bridge are easily synthesized. Having these two derivatization positions accessible while not affecting the polymerization position opens up a number of further possibilities, including those in which both *N*- and *C*-substitution is carried out on the same molecule. Utilizing various protecting groups at the 3,4-alkylenedioxypyrrole nitrogen allows chemistry to be successfully carried out at the 2-position. Our demonstration of successful halogenation and formylation on 3,4-ethylenedioxypyrrole serves as representative synthetic intermediates for more complex monomer syntheses. We have demonstrated the utility of these derivatives through the coupling of the diiodo molecules with 2-trimethylstannyl-EDOT and the formation of cyanovinylene-linked diheterocycle monomers using the formylated derivative. By controlling the chemistry of the fused dioxy ring system, we can also append ionically interacting systems such as the crown ether moiety demonstrated here. All of these derivatives are illustrative of the many other possibilities that the alkylenedioxypyrroles provide.

Experimental Section

General Procedure of *N*-Alkylation of ProDOP (6, 8−11). Sodium hydride (1.2 equiv free from mineral oil) was carefully added to a solution of ProDOP (1.0 equiv) in freshly distilled THF at 0 °C. After stirring for 1 h, alkylating reagents (1.2 equiv) were added, and the reaction mixtures were refluxed for 3−4 h. After cooling to room temperature, the THF was removed by rotary evaporator and aqueous NH_4Cl was carefully added. The aqueous solution was extracted with ether (3 times) and dried over $MgSO_4$. Purification by column chromatography on silica gel using hexane/ethyl acetate afforded the desired *N*-alkylated ProDOPs.

1-[2-(2-Ethoxyethoxy)ethyl]-3,4-(1,3-propylenedioxy)-pyrrole (6). After workup, the crude was purified by column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent to yield the product as a colorless oil (350 mg, 40%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.22 (s, 2H), 3.96 (m, 4H), 3.81 (t, J = 5.5 Hz, 2H), 3.67 (t, J = 5.5 Hz, 2H), 3.55 (m, 4H), 3.51 (q, J = 7.1 Hz, 2H), 2.11 (m, 2H), 1.20 (t, J = 7.1 Hz, 3H); FT-IR ($CDCl_3$) 3021, 2960, 1559, 1541 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{13}H_{22}NO_4$ 256.1548, found 256.1553.

3-[3,4-(1,3-Propylenedioxy)pyrrol-1-yl]propyl sodium-sulfonate (7). Sodium hydride (0.11 g, 4.70 mmol, washed by pentane) was carefully added to a solution of ProDOP (0.50 g, 3.60 mmol) in freshly distilled THF at 0 °C. After stirring for 1 h, 1,3-propanesultone (0.57 g, 4,70 mmol) was added, and the reaction mixtures were refluxed for 48 h. After the reaction was completed, the resulting solid was filtered and washed with acetone repeatedly to afford the product as a white powder (1.2 g, 85%); mp > 250 °C (decomp); ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.25 (s, 2H), 3.83 (m, 4H), 3.70 (t, J = 6.6 Hz, 2H), 2.33 (t, J = 7.1 Hz, 2H), 1.98 (m, 2H), 1.86 (pentet, J = 7.6 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 137.5, 105.4, 71.4, 48.1, 39.3, 34.8, 27.1; FT-IR ($CDCl_3$) 3022, 1545, 1419, 1366, 1216, 1185, 1060 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{10}H_{15}NO_5SNa$ 284.0568, found 284.0569.

***N*-Methyl-3,4-(1,3-propylenedioxy)pyrrole (8).** After workup, the crude was purified by column chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent to yield the product as a colorless oil (250 mg, 45%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.14 (s, 2H), 3.97 (m, 4H), 3.46 (s, 3H), 2.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.5, 106.5, 72.8, 34.2, 24.5; FT-IR ($CDCl_3$) 3021, 1460, 1371, 1216, 1056 cm^{-1}; HRMS (EI) (M^+) calcd for $C_8H_{11}NO_2$ 153.0789, found 153.0723.

***N*-Propyl-3,4-(1,3-propylenedioxy)pyrrole (9).** After workup, the crude was purified by column chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent to yield the product as a colorless oil (150 mg, 40%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.17 (s, 2H), 3.97 (m, 4H), 3.59 (t, J = 7.1 Hz, 2H), 2.12 (m, 2H), 1.71 (m, 2H), 0.87 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.6, 105.7, 72.3, 51.9, 35.2, 24.3, 11.1; FT-IR ($CDCl_3$) 3043 (s), 2989 (s), 1558 (s), 1423 (m), 1225 (s), 919 (s) cm^{-1}; HRMS (EI) (M^+) calcd for $C_{10}H_{15}NO_2$ 181.1102, found 181.1125.

***N*-Octyl-3,4-(1,3-propylenedioxy)pyrrole (10).** After workup, the crude was purified by column chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent to yield the product as a colorless oil (220 mg, 48%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.17 (s, 2H), 3.97 (m, 4H), 3.61 (t, J = 7.1 Hz, 2H), 2.12 (m, 2H), 1.62 (m, 2H), 1.20 (m, 10H), 0.87 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 105.7, 73.2, 72.4, 35.2, 33.1, 31.7, 29.3, 29.2, 29.1, 26.8, 22.6; FT-IR ($CDCl_3$) 3055, 2988, 1558, 1421, 1265, 909, 706 cm^{-1}; HRMS (EI) (M^+) calcd for $C_{15}H_{25}NO_2$ 251.1885, found 251.1901.

2-(2-{2-[3,4-(1,3-Propylenedioxy)pyrrol-1-yl]ethoxy}-ethoxy)ethanol (12). The semipurified product **11** was dissolved in THF, and tetrabutylammonium fluoride (1.0 M in THF) was added and stirred for 1 h at room temperature. After workup, the crude was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) as eluent to yield the product as a colorless oil (0.5 g, 55%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.25 (s, 2H), 3.96 (m, 4H), 3.80 (t, J = 4.9 Hz, 2H), 3.75−3.63 (m, 4H), 3.63−3.52 (m, 6H), 2.11 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 106.3, 72.5, 72.3, 71.1, 70.7, 70.4, 61.8, 50.1, 35.1; FT-IR ($CDCl_3$) 3448, 2930, 2872, 1557, 1460, 1413 cm^{-1}; HRMS (EI) (M^+) calcd for $C_{13}H_{21}NO_5$ 271.1419, found 271.1405. Anal. Calcd for $C_{13}H_{21}NO_5$: C, 57.55; H, 7.80; N, 5.16. Found: C, 57.28; H, 7.64; N, 5.05.

***N*-Benzyl-3,4-ethylenedioxypyrrole-2,5-dicarboxylic Acid (13).** The diester **2a** (10 g, 0.03 mol) was suspended in 3 M NaOH aqueous solution (150 mL), and ethanol (10−20 mL) was added as a cosolvent. The reaction mixture was stirred vigorously at 70−80 °C for 6 h. After cooling to 0 °C in an ice−water bath, the reaction mixture was carefully acidified with concentrated HCl. The resulting white precipitate was collected by filtration and washed with water twice to give the diacid as a white powder (8.6 g, 95%); mp 219 °C (decomp); ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.80 (br, 2H), 7.25 (m, 3H), 6.85 (m, 2H), 5.74 (s, 2H), 4.22 (s, 4H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.8, 140.6, 137.1, 129.1, 127.5, 126.7, 111.7, 65.8, 47.8; HRMS (FAB) (MH^+) calcd for $C_{15}H_{14}NO_6$ 304.0821, found 304.0820.

***N*-Benzyl-2,5-diiodo-3,4-ethylenedioxypyrrole (14) (Iodo-decarboxylation).** Diacid **13** (0.5 g, 1.65 mmol) was

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dissolved in an aqueous solution of sodium carbonate (7.7 g, 72.6 mmol) in 30 mL of water. A solution of iodine (0.92 g, 3.69 mmol) and potassium iodide (2.0 g, 12.11 mmol) in water was prepared. The solution of the diacid was slowly titrated by the solution of iodine and potassium iodide at room temperature. As the red-iodine color quickly disappeared in the process of reaction, a white precipitate was formed. After stirring for 30 min after the addition was completed, a white precipitate was collected by filtration and washed with water several times to remove inorganic compounds to yield *N*-benzyl-2,5-diiodo-3,4-ethylenedioxypyrrole **(14)** as a white powder (0.56 g, 85%): mp 154−155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 3H), 6.99 (m, 2H), 5.09 (s, 2H), 4.26 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 137.3, 128.5, 127.3, 126.4, 110.1, 66.5, 53.7; HRMS (FAB) (M^+) calcd for $C_{13}H_{11}NO_2I_2$ 466.8879, found 466.8805. Anal. Calcd for $C_{13}H_{11}NO_2I_2$: C, 33.43; H, 2.37, N, 3.00. Found: C, 34.17; H, 2.42; N, 2.94.

2-Ethoxycarbonyl-3,4-[2-(2-ethylhexyl)-1,3-propylenedioxy]pyrrole-5-carboxylic Acid (15). To a solution of diester **41a** (4.0 g, 10.11 mmol) in THF was added potassium *tert*-butoxide (4.5 g, 40.44 mmol) and H_2O (0.73 g, 40.44 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was stirred at room-temperature overnight. The THF was removed by rotary evaporator, and the residue was diluted with water, cooled by ice−water, and acidified with concentrated hydrochloric acid to yield a pale yellow precipitate. After filtering, the product was washed with water and vacuum-dried to yield a pale yellow solid as a mono-hydrolyzed compound. A pale yellow solid (3.3 g, 90%): mp 156−157 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.60 (br, 1H), 4.37 (q, J = 7.1 Hz, 2H), 4.28 (dd, J = 11.5, 2.7 Hz, 1H), 4.24 (dd, J = 11.5, 3.3 Hz, 1H), 4.05 (dd, J = 14.8, 6.6 Hz, 1H), 4.00 (dd, J = 14.8, 6.6 Hz, 1H), 2.30 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.40−1.20 (m, 11H), 0.87 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 159.6, 129.6, 112.3, 110.0, 101.4, 76.7, 76.2, 61.0, 40.2, 36.1, 32.9, 31.6, 28.7, 25.9, 23.1, 14.3, 14.0, 10.5; HRMS (FAB) (MH^+) calcd for $C_{19}H_{30}NO_6$ 368.2073, found 368.2070. Anal. Calcd for $C_{19}H_{29}NO_6$: C, 62.11; H, 7.96; N, 3.81. Found: C, 62.32; H, 7.57; N, 3.73.

Ethyl 2-Iodo-3,4-[2-(2-ethylhexyl)-1,3-propylenedioxy]-pyrrole-5-carboxylate (16). The procedure taken here is similar to that of compound **15**. A light yellow oil (0.3 g, 60%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (s, 1H), 4.34 (q, J = 6.5 Hz, 2H), 4.15 (dd, J = 11.5, 2.7 Hz, 1H), 4.10 (dd, J = 11.5, 3.3 Hz, 1H), 3.94 (dd, J = 12.1, 7.1 Hz, 1H), 3.82 (dd, J = 12.1, 7.1 Hz, 1H), 2.24 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.39−1.15 (m, 11H), 0.91−0.82 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 139.5, 128.7, 110.1, 76.3, 76.2, 60.3, 40.5, 36.2, 32.9, 31.7, 28.7, 25.9, 23.1, 14.5, 14.0, 10.5; FT-IR ($CDCl_3$) 3440, 2963, 2931, 2892, 1690, 1525 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{18}H_{29}NO_4I$ 450.1141, found 450.1104.

***N*-Benzyl-3,4-ethylenedioxypyrrole (17).** A solution of EDOP (1.0 g, 8.0 mmol) in THF was cooled to 0 °C, and mineral oil free sodium hydride (0.27 g, 12 mmol) was added. After stirring for 20 min, benzyl bromide (1.3 g, 8.0 mmol) in THF was added, and the reaction mixture was stirred for 6 h at room temperature. The reaction mixture was concentrated under reduced pressure, diluted with ether, carefully washed with water, and dried over $MgSO_4$. After being concentrated, the residue was purified by chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent to yield a white crystalline product (1.5 g, 90%): mp 69−70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (m, 3H), 7.10 (m, 2H), 6.10 (s, 2H), 4.83 (s, 2H), 4.18 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 128.5, 127.7, 127.1, 110.0, 101.7, 65.8, 53.9; FT-IR ($CDCl_3$) 3021, 2980, 2920, 1553, 1425, 1374, 1365 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{13}H_{14}NO_2$ 216.1024, found 216.1025. Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.30; H, 6.04; N, 6.46.

***N*-Benzyl-3,4-ethylenedioxypyrrole (17) from Decarboxylation.** A round-bottom flask was filled with triethanolamine and heated to 180 °C under argon with vigorous stirring. The diacid **13** (8.5 g, 28.0 mmol) was quickly added as one portion and vigorously stirred for 10 min. The reaction mixture was cooled to room temperature and poured into water. After extracting with methylene chloride (100 mL × 3), the combined organic layers were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (deactivated with triethylamine) using hexane/ethyl acetate (3:1) as eluent to yield a white crystalline product (5.4 g, 90%): mp 69−70 °C (identical to **17**).

***N*-Benzyl-2-formyl-3,4-ethylenedioxypyrrole (18).** Vilsmeier reagent was prepared by a procedure according to the literature.[18] $POCl_3$ (0.71 g, 4.65 mmol) was added to a DMF (0.34 g, 4.65 mmol) solution in methylene chloride (3.0 mL) at 0 °C, and the reaction mixture was allowed to come to room temperature. The solution was then slowly added to a solution of *N*-benzyl-3,4-ethylenedioxypyrrole (1.0 g, 4.65 mmol) in methylene chloride (5.0 mL) at 0 °C and allowed to come to room temperature. After stirring for 12 h, an excess of 3.0 M NaOH solution was added and stirred for 2 h in a hot water bath. The reaction mixture was extracted with methylene chloride (25 mL × 3), and the combined organic layers were dried over $MgSO_4$. Purification of the residue was accomplished by chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent to afford the product as a white solid (0.8 g, 70%): mp 75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.26 (m, 3H), 7.20 (m, 2H), 6.44 (s, 1H), 5.36 (s, 2H), 4.29 (m, 2H), 4.20 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 149.9, 137.6, 131.5, 128.6, 127.6, 127.4, 114.5, 114.1, 66.0, 65.2, 52.1; FT-IR ($CDCl_3$) 3021, 2825, 2720, 1646 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{14}H_{14}NO_3$ 244.0973, found 244.0983. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.00; H, 5.41; N, 5.74.

2-Formyl-3,4-ethylenedioxypyrrole (19). $POCl_3$ (1.67 g, 10.92 mmol) was added to a solution of DMF (0.84 g, 11.44 mmol) in methylene chloride (5.0 mL) at 0 °C and the reaction mixture allowed to come to room temperature. The reaction mixture was then slowly added to a solution of 3,4-ethylenedioxypyrrole (1.3 g, 10.40 mmol) in methylene chloride (5.0 mL) at 0 °C and allowed to come to room temperature. After stirring for 12 h, an excess of 3.0 M NaOH solution was added and stirred for 2 h in a hot water bath. The reaction mixture was extracted with methylene chloride (40 mL × 3), and the combined organic layers were dried over $MgSO_4$. Purification of the residue was accomplished by chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent to afford the product as a white solid (1.5 g, 65%): mp 147 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.43 (s, 1H), 9.02 (br, 1H), 6.62 (d, J = 3.8 Hz, 1H), 4.24 (m, 4H). Anal. Calcd for $C_7H_7NO_3$: C, 54.90; H, 4.61; N, 9.15. Found: C, 55.03; H, 4.48; N, 9.14.

***N*-BOC-2-Formyl-3,4-ethylenedioxypyrrole (20).** To a solution of aldehyde **19** (0.8 g, 5.2 mmol) in dichloromethane were added $(BOC)_2O$ (1.1 g, 5.2 mmol), triethylamine (1.1 g, 10.4 mmol), and 4-(dimethylamino)pyridine (DMAP) (61 mg, 0.5 mmol). The reaction mixture was stirred for 3 h and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate (3: 1) as eluent to yield a colorless crystalline product (1.2 g, 90%): mp 94−95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.24 (s, 1H), 6.88 (s, 1H), 4.38 (m, 2H), 4.22 (m, 2H), 1.60 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.9, 148.8, 143.2, 134.2, 116.6, 107.9, 85.1, 66.1, 64.9, 27.9; FT-IR ($CDCl_3$) 2930, 2859, 1653, 1544, 1460, 1380, 1322 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.90; H, 5.80; N, 5.73.

***N*-Benzyl-1-cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-thienyl)vinylene (22).** To a solution of the aldehyde **18** (0.60 g, 2.47 mmol) and 2-thiopheneacetonitrile (0.34 g, 2.72 mmol) in *tert*-butyl alcohol was added potassium *tert*-butoxide (0.61 g, 5.43 mmol) at room temperature. The reaction mixture was stirred for 3 h at 50 °C. After cooling to room temperature, The *tert*-butyl alcohol was removed by rotary evaporator and the residue was diluted with dichloromethane, washed with water, and dried over $MgSO_4$. The residue was purified by chromatography on silica gel using hexane/ethyl acetate (3: 1) as eluent to give the product as a yellow solid which was subjected to debenzylation in the next step. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (m, 3H), 7.19 (m, 2H), 7.13 (m, 2H), 6.99 (m, 1H), 6.96 (s, 1H), 6.44 (s, 1H), 4.97 (s, 2H), 4.35 (m, 2H), 4.27 (m, 2H).

1-Cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-thienyl)-vinylene (Th-CNV-EDOP) (23). A solution of compound **22** (0.9 g, 2.6 mmol) in THF was very slowly added to a solution of sodium (0.15 g. 6.5 mmol) in NH_3 (30 mL) at −78 °C. The reaction mixture was stirred for 3 h, and a 1.0 M NH_4Cl aqueous solution (20 mL) was carefully added. The stopper on the vessel was removed, and the reaction was allowed to come to ambient temperature. After evaporation of NH_3, the aqueous phase was extracted with dichloromethane and dried over $MgSO_4$. The residue was purified by chromatography on silica gel using hexane/ethyl acetate (3: 1) as eluent to yield a yellow crystalline product (0.45 g, 50%): mp 164−165 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (br, 1H), 7.30 (s, 1H), 7.16 (m, 2H), 7.02 (dd, J = 4.9, 3.8 Hz, 1H), 6.55 (d, J = 3.3 Hz, 1H), 4.30 (m, 2H), 4.22 (m, 2H); FT-IR ($CDCl_3$) 3460, 2989, 2930, 2202, 1575, 1538, 1343 cm^{-1}; HRMS (FAB) (M^+) calcd for $C_{13}H_{10}N_2O_2S$ 258.0463, found 258.0457. Anal. Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85. Found: C, 60.35; H, 3.89; N, 10.91.

1-Cyano-2-(2-(3,4-ethylenedioxypyrryl))-1-(2-(3,4-ethylenedioxythienyl)vinylene (EDOT-CNV-EDOP) (26). The procedure used was the same as that for compound **22**. However, it should be noted that the BOC group was removed in the process of the condensation which is advantageous over the previous procedure. A yellow crystalline product was obtained (1.20 g, 75%); mp 148 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (br, 1H), 7.34 (s, 1H), 6.49 (d, J = 3.8 Hz, 1H), 6.25 (s, 1H), 4.40−4.15 (m, 8H); FT-IR ($CDCl_3$) 3459, 2989, 2934, 2859, 2202, 1569, 1531, 1459, 1344 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{15}H_{13}N_2O_4S$ 317.0596, found 317.0601. Anal. Calcd for $C_{15}H_{12}N_2O_4S$: C, 56.95; H, 3.82, N, 8.86. Found: C, 56.44; H, 3.89; N, 8.61.

The known compounds **28**−**30** were synthesized by the procedure according to the literature.[27]

2,3-Diallyloxy-2,3-dimethylbutane (28). A clear oil (12.5 g, 85%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (m, 2H), 5.27 (m, 2H), 5.07 (m, 2H), 3.89 (m, 4H), 1.18 (s, 12H).

2,3-Bis(3-hydroxypropoxy)-2,3-dimethylbutane (29). A clear oil (8.2 g, 75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (m, 4H), 3.57 (m, 4H), 1.76 (m, 4H), 1.15 (s, 12H).

2,3-Bis(3-[*p*-toluenesulfonyloxy]propoxy)-2,3-dimethylbutane (30). Colorless crystals (8.9 g, 80%); mp 123−124 °C (lit.[27] 123−124 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.2 Hz, 4H), 7.31 (d, J = 8.2 Hz, 4H), 4.09 (t, J = 6.0 Hz, 4H), 3.35 (t, J = 6.0 Hz, 4H), 2.43 (s, 6H), 1.79 (pent, J = 6.0 Hz, 4H), 0.96 (s, 12H).

Dimethyl 14-Benzyl-6,6,7,7-tetramethyl-3,4,6,7,10,11-hexahydro-2*H*,9*H*,14*H*-[1,4,8,11]tetraoxacyclotetradecino-[2,3-*c*]pyrrole-13,15-dicarboxylate (31). Compound **31** was synthesized by a literature procedure with some modifications.[28] A large Dean−Stark trap was fitted into a two-neck round-bottom flask (1 L). The Dean−Stark trap was filled with a solution of diol **1** (5.0 g, 15.0 mmol) and ditosylate **30** (6.5 g, 12.0 mmol) in DMF (45 mL). Acetonitrile (450 mL) was added to the two-neck round-bottom flask followed by addition of CsF (9.1 g, 60.0 mmol). The reaction mixture was refluxed for 24 h under argon and cooled to room temperature. The solvent was removed by rotary evaporator and poured into water. The aqueous phase was washed with ether (150 mL × 3), and the combined organic layers were washed with water and dried over $MgSO_4$. The residue was purified by chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent to yield a colorless solid (2.71 g, 45%): mp 92−93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (m, 3H), 6.90 (m, 2H), 5.99 (s, 2H), 4.13 (t, J = 5.0 Hz, 4H), 3.80 (s, 6H), 3.77 (t, J = 5.5 Hz, 4H), 1.93 (pent, J = 5.5 Hz, 4H), 1.21 (s, 12H); FT-IR ($CDCl_3$) 3022, 2963, 1718, 1700, 1653, 1559, 1541, 1442 cm^{-1}; HRMS (FAB) (M^+) calcd for $C_{27}H_{37}NO_8$ 503.2519, found 503.2524. Anal. Calcd for $C_{27}H_{37}NO_8$: C, 64.40; H, 7.41; N, 2.78. Found: C, 64.22; H, 7.36; N, 2.67.

Dimethyl 6,6,7,7-Tetramethyl-3,4,6,7,10,11-hexahydro-2*H*,9*H*,14*H*-[1,4,8,11]tetraoxacyclotetradecino[2,3-*c*]pyrrole-13,15-dicarboxylate (32). To a solution of **31** (3.0 g, 5.64 mmol) in acetic acid (100 mL) was added carefully 10% Pd (C) (0.6 g) in one portion. The reaction flask was flushed with a hydrogen stream using a balloon containing hydrogen, and another hydrogen balloon was fitted onto the reaction flask. The reaction mixture was vigorously stirred for 48 h at 80−85 °C (it should be noted that new hydrogen balloons were added depending on the reaction scale). After cooling to room temperature, the reaction mixture was filtered through a Celite pad and concentrated under reduced pressure. Purification of the residue by chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent afforded **32** as a pale yellow solid (2.21 g, 95%): mp 106−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (br, 1H), 4.19 (t, J = 5.5 Hz, 4H), 3.88 (s, 6H), 3.76 (t, J = 6.0 Hz, 4H), 1.93 (pent, J = 5.5 Hz, 4H), 1.21 (s, 12H); FT-IR ($CDCl_3$) 3439, 3022, 2998, 2920, 1736, 1523, 1370, 1300 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{20}H_{32}NO_8$ 414.2127, found 414.2097. Anal. Calcd for $C_{20}H_{31}NO_8$: C, 58.10; H, 7.56; N, 3.39. Found: C, 58.88; H, 7.70; N, 3.20.

6,6,7,7-Tetramethyl-3,4,6,7,10,11-hexahydro-2*H*,9*H*,14*H*-[1,4,8,11]tetraoxacyclotetradecino[2,3-*c*]pyrrole-13,15-dicarboxylic Acid (33). The diester **32** (2.5 g, 6.1 mmol) was suspended in 3M NaOH (50 mL), and ethanol was added as a cosolvent (10 mL). The reaction mixture was stirred for 6 h at 60 °C and cooled to room temperature. The reaction mixture was extracted with ether to remove any unreacted starting material and byproducts, and the basic aqueous phase was cooled to 0 °C. Acidification by concentrated HCl afforded white solids after filtration (2.27 g, 97%). The resulting diacid was used in the next step without further purification.

6,6,7,7-Tetramethyl-3,4,6,7,10,11-hexahydro-2*H*,9*H*,14*H*-[1,4,8,11]tetraoxacyclotetradecino[2,3-*c*]pyrrole (34). The decarboxylation procedure is similar to that of compound **17**. A light brown solid (1.50 g, 73%); mp 48−50 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.09 (br, 1H), 6.27 (d, J = 3.3 Hz, 2H), 4.04 (t, J = 5.5 Hz, 4H), 3.76 (t, J = 6.0 Hz, 4H), 1.90 (pentet, J = 5.5 Hz, 4H), 1.18 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 113.0, 102.9, 80.6, 69.9, 59.2, 31.0, 21.5; FT-IR ($CDCl_3$) 3487, 3021, 1653, 1579, 1542, 1227 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{16}H_{28}NO_4$ 298.2018, found 298.2012. Anal. Calcd for $C_{16}H_{27}NO_4$: C, 64.62; H, 9.15, N, 4.71. Found: C, 64.47; H, 8.98; N, 4.50.

Diethyl 2-(2-ethylhexyl)malonate (36b). To a solution of NaOEt in ethanol was added diethyl malonate (20.0 g, 0.13 mol) and 2-ethylhexyl bromide (25.1 g, 0.13 mol) at room temperature. The reaction mixture was stirred for 6 h, and the ethanol was removed by rotary evaporator. Dilute HCl solution was added and extracted with ether (100 mL × 3). The combined ether layers were dried over $MgSO_4$, concentrated, and purified by distillation under reduced pressure (125−126 °C, 3.0 mmHg, lit.[30] 126−127 °C, 3.0 mmHg) to give **36b** as a clear oil (17.7 g, 50%): ^{1}H NMR (300 MHz, $CDCl_3$) 4.20 (q, J = 7.1 Hz, 4H), 3.41 (t, J = 7.7 Hz, 1H), 1.84 (m, 2H), 1.40−1.15 (m, 15H), 0.95−0.80 (m, 6H).

Diethyl 2-Octylmalonate (36a). A clear oil (15.4 g, 45%); bp 128−130 °C (3.0 mmHg)(lit.,[31] 110−123 °C, 0.9−1.0 mmHg); ^{1}H NMR (300 MHz, $CDCl_3$) 4.20 (q, J = 7.1 Hz, 4H), 3.30 (t, J = 7.1 Hz, 1H), 1.87 (m, 2H), 1.30−1.10 (m, 15H), 0.87 (t, J = 7.1 Hz, 6H).

Diethyl 2,2-Dioctylmalonate (36c). A clear oil (17.2 g, 38%); bp 155−156 °C (3.0 mmHg)(lit.,[32] 200 °C, 0.1 kPa); ^{1}H NMR (300 MHz, $CDCl_3$) 4.20 (q, J = 7.1 Hz, 4H), 1.85 (m, 4H), 1.38−1.07 (m, 30H), 0.86 (t, J = 6.6 Hz, 6H).

2-(2-Ethylhexyl)-1,3-propanediol (37b). To a solution of the diester **36b** (10.0 g, 36.7 mmol) in dry ether was added $LiAlH_4$ (2.8 g, 73.4 mmol) at 0 °C. The reaction mixture was stirred for 6 h at room temperature, and water (ca. 10 mL) was carefully added. The reaction mixture was stirred for 1 h and allowed to stand to settle the salts. A clear ether layer was carefully decanted, and the combined layers were dried over $MgSO_4$. Purification of the crude product by chromatog-

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raphy on silica gel using hexane/ethyl acetate (2:1) as eluent afforded diol **37b** as a clear oil (4.8 g, 70%): ^{1}H NMR (300 MHz, $CDCl_3$) 3.80 (dd, J = 10.4, 3.8 Hz, 2H), 3.61 (dd, J = 10.4, 8.2 Hz, 2H), 2.65 (s, 2H), 1.84 (m, 1H), 1.38−1.20 (m, 9H), 1.20−1.08 (m, 2H), 0.90 (t, J = 6.6 Hz, 3H), 0.83 (t, J = 7.7 Hz, 3H).

2-Octyl-1,3-propanediol (37a). A colorless crystal (5.2 g, 75%) (lit.[31]); mp 45−46 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 3.83 (dd, J = 10.4, 3.3 Hz, 2H), 3.66 (dd, J = 11.0, 7.7 Hz, 2H), 2.42 (s, 2H), 1.78 (m, 1H), 1.40−1.20 (m, 14H), 0.88 (t, J = 6.6 Hz, 3H).

2,2-Dioctyl-1,3-propanediol (37c). A clear oil (6.5 g, 65%)-(lit.[32]); ^{1}H NMR (300 MHz, $CDCl_3$) 3.56 (d, J = 4.4, 4H), 2.50 (s, 2H), 1.40−1.15 (m, 28H), 0.88 (t, J = 6.6 Hz, 6H).

General Procedure for the Preparation of Ditosylates 38a, 38b, and 38c. To a solution of the diol (1.0 equiv) and toluenesulfonyl chloride (2.0 equiv) in dichloromethane was dropwise added a solution of triethylamine (2.5 equiv) and 4-(dimethylamino)pyridine (0.1 mol %) in dichloromethane at room temperature. The reaction mixture was stirred for 3 h and concentrated under reduced pressure. The residue was dissolved in ether, washed with water several times, and dried over $MgSO_4$. The solvent was removed, and the residue was used in the next step without further purification after vacuum-drying.

Diethyl *N*-Benzyl-3,4-dihydroxypyrrole-2,5-dicarboxylate(39). The preparation of **39** is similar to that of **1**. Colorless crystals (hot methanol, 80%); mp 146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.81 (s, 2H), 7.23 (m, 3H), 6.91 (m, 2H), 5.78 (s, 2H), 4.32 (q, J = 7.1 Hz, 4H), 1.25 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 139.8, 139.3, 128.6, 127.1, 125.7, 111.2, 61.4, 49.5, 14.4. Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.75; N, 4.20. Found: C, 61.00; H, 5.75; N, 4.21.

General Procedure for the Preparation of Diethyl *N*-Benzyl-3,4-(2-alkyl-1,3-propylenedioxy)pyrrole-2,5-dicarboxylates (40a, 40b, and 40c). To a mixture of diethyl *N*-benzyl-3,4-dihydroxypyrrole-2,5-dicarboxylate (**39**) (7.5 g, 22.6 mmol) and ditosylate **38a** (7.8 g, 22.6 mmol) in dry DMF was added potassium carbonate (15.6 g, 0.1 mol) at room temperature. The reaction mixture was stirred for 12 h at 110 °C under argon. After cooling to room temperature, the reaction mixture was poured into ice water and extracted with ether. The combined ether layers were dried over $MgSO_4$ and concentrated by rotary evaporator. Purification by chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent afforded the product as pale yellow oil.

Diethyl *N*-Benzyl-3,4-(2-octyl-1,3-propylenedioxy)pyrrole-2,5-dicarboxylate (40a). A pale yellow oil (8.2 g, 75%); ^{1}H NMR (300 MHz, $CDCl_3$) 7.20 (m, 3H), 6.90 (m, 2H), 5.90 (s, 2H), 4.26 (q, J = 7.1 Hz, 4H), 4.21 (dd, J = 8.2, 3.3 Hz, 2H), 3.98 (dd, J = 12.1, 6.6 Hz, 2H), 2.22 (m, 1H), 1.50−1.20 (m, 14H), 1.26 (t, J = 7.1 Hz, 6H), 0.88 (t, J = 6.6 Hz, 3H).

Diethyl *N*-Benzyl-3,4-[2-(2-ethylhexyl)-1,3-propylenedioxy]pyrrole-2,5-dicarboxylate (40b). A pale yellow oil (7.80 g, 71%); ^{1}H NMR (300 MHz, $CDCl_3$) 7.21 (m, 3H), 6.91 (m, 2H), 5.90 (s, 2H), 4.26 (q, J = 7.1 Hz, 4H), 4.22 (dd, J = 11.5, 2.7 Hz, 2H), 3.88 (dd, J = 11.5, 7.1 Hz, 2H), 2.35 (m, 1H), 1.40−1.23 (m, 11H), 1.26 (t, J = 7.1 Hz, 6H), 0.90 (t, J = 6.0 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 142.6, 139.2, 128.2, 126.7, 126.1, 114.0, 75.9, 75.8, 60.4, 48.8, 40.0, 36.3, 32.9, 32.3, 28.7, 26.0, 23.0, 14.1, 13.9, 10.5.

Diethyl *N*-Benzyl-3,4-(2,2-dioctyl-1,3-propylenedioxy)-pyrrole-2,5-dicarboxylate (40c). A pale yellow oil (5.60 g, 25%); ^{1}H NMR (300 MHz, $CDCl_3$) 7.20 (m, 3H), 6.85 (m, 2H), 5.89 (s, 2H), 4.24 (q, J = 7.1 Hz, 4H), 3.90 (s, 4H), 1.50−1.10 (m, 34H), 0.87 (t, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 143.3, 137.7, 128.6, 127.1, 126.5, 114.2, 79.4, 61.0, 49.5, 44.4, 32.5, 32.4, 31.0, 30.0, 29.9, 23.5, 23.3, 14.6, 14.5; FT-IR ($CDCl_3$) 3023, 2965, 1716, 1437, 1365, 1291 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{36}H_{56}NO_6$ 598.4107, found 598.4114. Anal. Calcd for $C_{36}H_{55}NO_6$: C, 72.33; H, 9.27; N, 2.34. Found: C, 72.19; H, 9.41; N, 2.14.

Debenzylation of 40a, 40b, and 40c. A reaction mixture of **40a** (5.0 g, 10.3 mmol), anisole (1.5 g, 13.4 mmol), and H_2SO_4 (0.7 g, 7.0 mmol) in trifluroacetic acid was refluxed for 0.5 h at 90 °C. After cooling to room temperature, the trifluroacetic acid was removed by rotary evaporator, and the residue was neutralized by aqueous saturated sodium bicarbonate. The aqueous phase was extracted with ether (3 × 100 mL), and the combined ether layers were dried over $MgSO_4$. Purification by chromatography on silica gel using hexane/ethyl acetate (3:1) as eluent afforded the product.

Diethyl 3,4-(2-Octyl-1,3-propylenedioxy)pyrrole-2,5-dicarboxylate (41a). A pale yellow oil (2.80 g, 72%); ^{1}H NMR (300 MHz, $CDCl_3$) 8.70 (br, 1H), 4.32 (q, J = 7.1, 4H), 4.15 (dd, J = 11.5, 3.3 Hz, 2H), 4.05 (dd, J = 12.1, 6.6 Hz, 2H), 2.18 (m, 1H), 1.45−1.20 (m, 14 H), 1.35 (t, J = 7.1 Hz, 6H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 141.7, 110.7, 75.6, 60.7, 42.4, 31.8, 29.6, 29.4, 29.2, 28.0, 27.0, 22.5, 14.3, 13.9; FT-IR ($CDCl_3$) 3446, 3022, 2980, 1700, 1653, 1526, 1459 cm^{-1}.

Diethyl 3,4-[2-(2-Ethylhexyl)-1,3-propylenedioxy]pyrrole-2,5-dicarboxylate (41b). A pale yellow oil (2.53 g, 70%); ^{1}H NMR (300 MHz, $CDCl_3$) 8.65 (br, 1H), 4.37 (q, J = 7.1, 4H), 4.24 (dd, J = 12.1, 3.3 Hz, 2H), 3.97 (dd, J = 12.1, 7.1 Hz, 2H), 2.30 (m, 1H), 1.36 (t, J = 7.1 Hz, 6H), 1.40−1.22 (m, 11 H), 0.91−0.83 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 140.9, 110.0, 75.3, 75.2, 59.9, 39.4, 35.4, 32.1, 31.4, 27.9, 25.2, 22.2, 13.6, 13.2, 9.7.

Diethyl 3,4-(2,2-Dioctyl-1,3-propylenedioxy)pyrrole-2,5-dicarboxylate (41c). A pale yellow oil (3.50 g, 65%); ^{1}H NMR (300 MHz, $CDCl_3$) 8.61 (s, 1H), 4.33 (q, J = 7.1, 4H), 3.94 (s, 4H), 1.35 (t, J = 7.1 Hz, 6H), 1.45−1.18 (m, 28H), 0.87 (t, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 142.0, 110.5, 79.2, 60.7, 43.8, 31.8, 30.4, 29.4, 29.2, 22.7, 22.6, 22.5, 14.3, 13.9; FT-IR ($CDCl_3$) 3444, 2932, 2858, 1701, 1530, 1483, 1276 cm^{-1}; HRMS (FAB) calcd for $C_{29}H_{49}NO_6$ (MH^+) 508.3638, found 508.3641.

Hydrolysis of 41a, 41b, and 41c. The procedure used is the same as that used for the preparation of compound **13**.

3,4-(2-Octyl-1,3-propylenedioxy)pyrrole-2,5-dicarboxylic Acid (42a). A white powder (2.50 g, 92%); mp 165−167 °C; ^{1}H NMR (300 MHz, DMSO-d_6) 10.70 (br, 1H), 4.02 (dd, J = 11.5, 2.7, 2H), 3.91 (dd, J = 12.1, 6.0 Hz, 2H), 2.05 (m, 1H), 1.40−1.20 (m, 14H), 0.84 (t, J = 7.1, 3H); HRMS (FAB) (MH^+) calcd for $C_{17}H_{26}NO_6$ 340.1760, found 340.1735. Anal. Calcd for $C_{17}H_{25}NO_6$: C, 60.16; H, 7.42; N, 4.13. Found: C, 60.54; H, 7.67; N, 4.10.

3,4-[2-(2-Ethylhexyl)-1,3-propylenedioxy]pyrrole-2,5-dicarboxylic Acid (42b). A white powder (2.20 g, 85%); mp 164−165 °C; ^{1}H NMR (300 MHz, DMSO-d_6) 10.70 (br, 1H), 4.02 (dd, J = 12.0, 2.7, 2H), 3.85 (dd, J = 12.0, 6.0 Hz, 2H), 2.10 (m, 1H), 1.40−1.17 (m, 11H), 0.89 (t, J = 7.1 Hz, 3H), 0.86 (t, J = 6.6, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.3, 140.6, 111.0, 74.8, 74.8, 39.5, 34.9, 32.1, 30.6, 27.8, 25.1, 22.2, 13.6, 10.1; HRMS (FAB) (MH^+) calcd for $C_{17}H_{26}NO_6$ 340.1760, found 340.1735. Anal. Calcd for $C_{17}H_{25}NO_6$: C, 60.16; H, 7.42; N, 4.13. Found: C, 60.07; H, 7.56; N, 3.98.

3,4-(2,2-Dioctyl-1,3-propylenedioxy)pyrrole-2,5-dicarboxylic Acid (42c). A white powder (2.5 g, 85%); mp 125−127 °C; ^{1}H NMR (300 MHz, DMSO-d_6) 10.70 (s, 1H), 3.78 (s, 4H), 1.50−1.02 (m, 28H), 0.84 (t, J = 7.1, 6H); FT-IR ($CDCl_3$) 3280, 2928, 1700, 1653, 1093; HRMS (FAB) (MH^+) calcd for $C_{25}H_{41}NO_6$ 452.3012, found 542.2987. Anal. Calcd for $C_{25}H_{41}NO_6$: C, 66.49; H, 9.15; N, 3.10. Found: C, 66.42; H, 9.28; N, 2.98.

Decarboxylation of the Diacids 42a, 42b, and 42c. The procedure used here is the same as that for the preparation of *N*-benzyl-3,4-ethylenedioxypyrrole (**17**).

3,4-(2-Octyl-1,3-propylenedioxy)pyrrole (43a). An off-white solid (1.20 g, 85%); mp 79−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (br, 1H), 6.28 (d, J = 3.3 Hz, 2H), 4.01 (dd, J = 11.5, 2.2, 2H), 3.85 (dd, J = 11.6, 6.6 Hz, 2H), 2.05 (m, 1H), 1.50−1.20 (m, 14H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 103.1, 76.7, 43.6, 31.8, 29.8, 29.4, 29.2, 27.4, 27.1, 22.5, 13.9; FT-IR ($CDCl_3$) 3489, 3021, 2963, 2931, 1653, 1545, 1495, 1380 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{15}H_{26}NO_2$ 252.1963, found 252.1963. Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.02; N, 5.57. Found: C, 71.76; H, 9.94; N, 5.19.

3,4-[2-(2-Ethylhexyl)-1,3-propylenedioxy]pyrrole (43b). A pale yellow oil (0.50 g, 40%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (br, 1H), 6.30 (d, J = 3.3 Hz, 2H), 4.01 (dd, J = 12.1, 2.7, 2H), 3.76 (dd, J = 11.5, 6.6 Hz, 2H), 2.15 (m, 1H), 1.40−1.20 (m, 11H), 0.89 (t, J = 6.0 Hz, 3H), 0.86 (t, J = 7.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 113.9, 103.1, 76.5, 76.4, 41.3, 36.2, 33.0, 31.2, 28.7, 26.1, 23.9, 23.1, 14.0, 10.5; FT-IR ($CDCl_3$) 3490, 2962, 2931, 1543, 1459, 1322 cm^{-1}; HRMS (FAB) (MH^+) calcd for $C_{15}H_{26}NO_2$ 252.1963, found 252.1965. Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.02; N, 5.57. Found: C, 71.44; H, 9.98; N, 5.21.

3,4-(2,2-Dioctyl-1,3-propylenedioxy)pyrrole (43c). A pale brown oil. Full characterization was not successful due to its high instability. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (br, 1H), 6.30 (d, J = 3.3 Hz, 2H), 3.89 (s, 4H), 1.50−1.00 (m, 28H), 0.85 (t, J = 7.1 Hz, 6H).

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Supporting Information Available: ^{1}H NMR Spectra of **6**, **7**, **8**, **9**, **10**, **13**, **14**, **16**, **22**, **26**, **32**, **37a**, **37b**, **37c**, **40a**, **40b**, **40c**, **41a**, **41b**, and **41c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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