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3,4-Alkylenedioxy ring formation *via* double Mitsunobu reactions: an efficient route for the synthesis of 3,4-ethylenedioxythiophene (EDOT) and 3,4-propylenedioxythiophene (ProDOT) derivatives as monomers for electron-rich conducting polymers

Kyukwan Zong,[a] Luis Madrigal,[a] L. "Bert" Groenendaal[b] and John R. Reynolds*[a]

[a] *Department of Chemistry, Center for Macromolecular Science and Engineering, University of Florida, P.O. Box 117200, Gainesville, Florida 32611-7200, USA. E-mail: reynolds@chem.ufl.edu; Fax: 352-392-9741*

[b] *AGFA-Gevaert N.V, R&D Materials/Chemistry Department, Septestraat 27, B-2640, Mortsel, Belgium*

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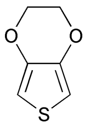
3,4-Alkylenedioxy ring functionalized thiophenes (XDOT's) have been synthesized by double Mitsunobu reactions to yield precursors to monomers for conjugated and electrically conducting polymers, including the commercially important 3,4-ethylenedioxythiophene (EDOT).

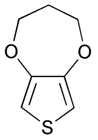
Heterocyclic conjugated polymers have received significant attention due to the wide range of electrical, electrochemical, and optical properties they display. The heteroatoms within the ring play an important role in controlling the properties of the polymers due to their intrinsic electron-donating or electron-withdrawing capabilities, polarizability, and possibility for hydrogen bonding.[1] These polymers have been utilized 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.[4,5]

Poly(3,4-ethylenedioxythiophene) (PEDOT) stands out for its optimized conductivity, stability and high degree of transparency which has led to its successful commercialization.[6] Appending an alkylenedioxy bridge across the 3- and 4-positions adds electron density to the aromatic ring, reducing both the monomer and polymer oxidation potentials, and leading to the formation of highly stable conducting polymers. The second homolog to EDOT (**1**), ProDOT (**2**) and derivatives, have recently emerged as important materials for potential use in stable and fast switching organic electrochromic devices.[7] With the rapid expansion of dioxythiophene chemistry, efficient and practical routes for the synthesis of a variety of monomer derivatives is needed.



1

EDOT



2

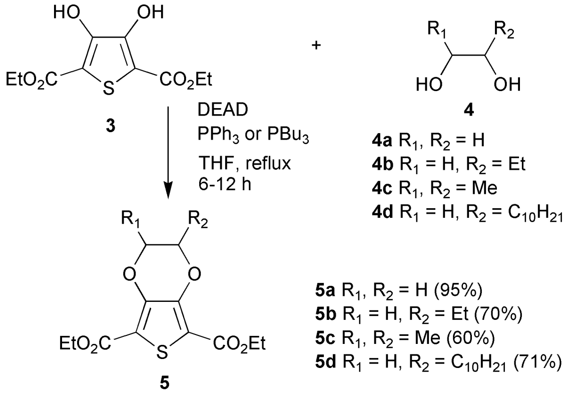
ProDOT

The most widely used synthetic route to dioxythiophenes involves double Williamson etherification. The method affords an efficient route for the synthesis of the parents EDOT (**1**) and ProDOT (**2**) but is limited in scope and employs environmentally undesirable dihaloalkanes or alkanedisulfonates. A trans-etherification route has been used as an alternative for the synthesis of alkyl substituted EDOT's and ProDOT's, but suffers from both limited substituents and uses the expensive (time intensive in preparation) starting material 3,4-dimethoxythiophene.[8]

Here, we report a new method for the synthesis of 3,4-alkylenedioxythiophenes that does not involve the use of dihaloalkanes. This method is not limited in the production of many substituted EDOT and ProDOT derivatives and provides monomers not accessible with previous known synthetic methods. The new method lies in the use of tandem Mitsunobu reactions of diethyl 3,4-dihydroxythiophene-2,5-dicarboxylate with various 1,2-diols or 1,3-diols. The Mitsunobu reaction is an important synthetic tool for converting alcohol stereochemistry under mild, essentially neutral conditions.[9]

As the original target of the work was to develop a new route to the commercial monomer EDOT (**1**), ethylene glycol was reacted under standard Mitsunobu conditions with the relatively acidic diol as outlined in Scheme 1.† Under these conditions [diethyl azodicarboxylate (DEAD), PPh_3, THF, RT] the reaction was slow and gave the desired product in moderate yield (30–40%) only with an extended reaction time (3 days). We found the reaction was highly facilitated by heating (THF reflux, $T = 66$ °C) to give the desired product (**5a**) in excellent yield in 12 h (95%).

In order to define the scope and limitations of this new method, a more sterically hindered 1,2-butanediol (**4b**) was used and gave the product in moderate yields (up to 70%) under various conditions. When 2,3-butanediol (**4c**, isomer mixture) was employed, the product was obtained in relatively low yields (25–30%) after 2 days of reaction indicating that steric congestion slows the reaction. It has been shown that variation of reagents (azo compounds and phosphines) in the Mitsunobu method can affect the overall reaction.[9e] To our surprise, when tributylphosphine was employed in the reaction of **3** with **4c**, the reaction proceeded faster (12 h) and the yield was greatly improved (60%). Similarly, the reaction of **3** with **4a** in the presence of PBu_3 afforded the product in excellent yield (95%) after only 6 h reaction. Employing the long chain substituent ($C_{10}H_{21}$) in **4d** with PPh_3 did not hamper the reaction as a yield of 71% was attained after 12 h at 66 °C. While it is evident that the Mitsunobu reaction is somewhat sensitive to the degree of steric congestion of the alcohol employed (in fact tertiary



Scheme 1 Ethylenedioxythiophene derivative formation *via* Mitsunobu chemistry.

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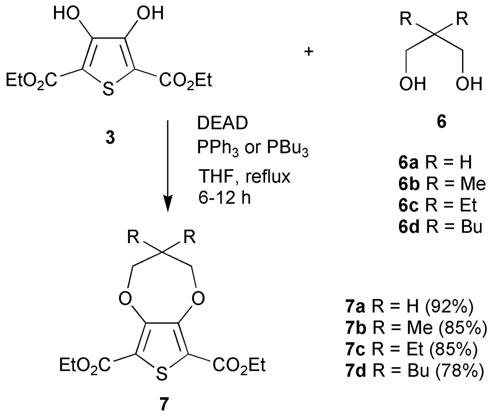
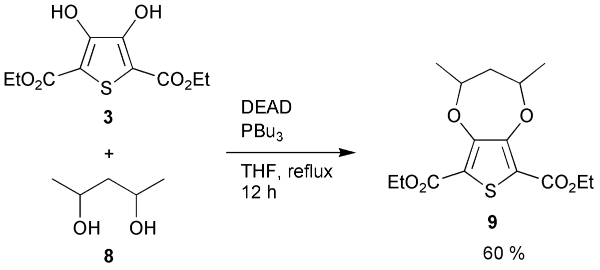
alcohols do not react), the route is generally applicable to the synthesis of a host of dioxane ring functionalized thiophenes.

The reaction was further explored by employing 1,3-alkanediols where the 7-membered dioxy ring is furnished by the reaction. The reaction of **3** with 1,3-propanediol (**6a**) proceeded smoothly under Mitsunobu conditions to give the corresponding product **7a** in excellent yield (92%) as shown in Scheme 2. Again, a systematic study was carried out to investigate the effect of increasing the steric environment of the diol employed in the reaction. Subjecting primary alcohols **6b, 6c,** and **6d** to the reaction conditions gave the product in high yields (*ca.* 80–85%). It should be noted that compounds **7b, 7c**, and **7d** have never been successfully prepared using the Williamson etherification route.



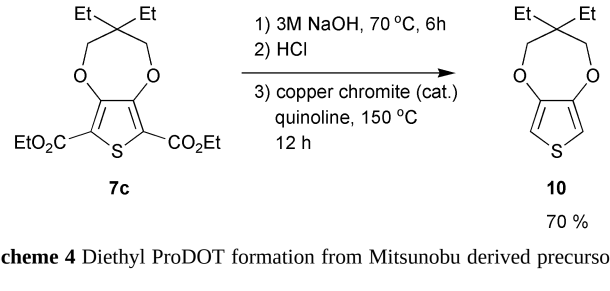
Scheme 2 Propylenedioxythiophene derivative formation *via* Mitsunobu chemistry.

Increasing the steric congestion further as shown in Scheme 3, subjection of 2,4-pentanediol (**8**, isomer mixture) to the Mitsunobu reaction gave the 1,3-dimethylProDOT (**9**) in 60% yield. With the above examples, it is demonstrated that the method developed here is useful for the synthesis EDOT and ProDOT derivatives with a wide variety of substituents.



Scheme 3 Sterically hindered ProDOT formation.

To confirm the usefulness of these intermediates in preparing new monomers for electroactive and conducting polymer formation, compound **7c** was hydrolysed and decarboxylated to yield 2,2′-diethyl substituted ProDOT (**10**) in 70% overall yield as shown in Scheme 4.



Scheme 4 Diethyl ProDOT formation from Mitsunobu derived precursor.

In conclusion, we have demonstrated that the reaction of **3** with various 1,2 or 1,3-diols under mild Mitsunobu conditions gives the corresponding cyclized products in good to excellent yields. The new method yields monomer precursors with a variety of substituents on the dioxane ring which are otherwise difficult to be introduced and avoids the use of environmentally unfavorable dihaloalkanes. In connection with this study, the investigation of optically active and further functionalized dioxythiophenes, along with dioxypyrroles, is in progress.

Notes and references

† *Experimental procedure*: In a typical procedure, to a solution of **3** (1.0 equiv.), diol (1.0 equiv.), and PBu_3 (2.0 equiv.) in dry THF was dropwise added diethyl azodicarboxylate (2.4 equiv.) under argon at room temperature. The reaction mixture was stirred for 1 h and stirred at reflux for 6–12 h. The reaction was cooled and THF was removed by a rotary evaporator. The residue was diluted with ether and stood for crystallization of tributylphosphine oxide for 12 h. Tributylphosphine oxide was filtered off and the filtrate was concentrated. Purification of the residue by chromatography on silica gel using hexane/ethyl acetate (3 : 1) as an eluent afforded the desired product. All compounds were fully characterized by ^1H NMR, ^{13}C NMR, HRMS, and elemental analysis. Results for previously unreported compounds are as follows.

Spectroscopic data of selected compounds: **5b**: a colorless solid; mp 130 °C; ^{1}HNMR (300 MHz, $CDCl_3$) δ 4.58 (dd, J = 12.0, 2.0 Hz, 1H), 4.53 (q, J = 7.0 Hz, 4H), 4.38 (m, 1H), 4.23 (dd, J = 12.0, 7.6 Hz, 1H), 2.10–1.85 (m, 2H), 1.55 (t, J = 7.0 Hz, 3H), 1.54 (t, J = 7.0 Hz, 3H), 1.31 (t, J = 7.3 Hz, 3H); HRMS (FAB) calcd for $C_{14}H_{18}O_6S$ (MH^+) 315.0902, found 315.0902; Anal. Calcd for $C_{14}H_{18}O_6S$: C, 53.49; H, 5.77; S, 10.20. Found: C, 53.53; H, 5.80; S, 10.21%. **5c**: a colorless solid; mp 105 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.45 (q, J = 6.6 Hz, 2H), 4.32 (q, J = 7.1 Hz, 4H), 1.38 (d, J = 7.0 Hz, 6H), 1.37 (t, J = 7.1 Hz, 6H); HRMS (FAB) calcd for $C_{14}H_{18}O_6S$ (MH^+) 315.0902, found 315.0902; Anal. Calcd for $C_{14}H_{18}O_6S$: C, 53.49; H, 5.77; S, 10.20. Found: C, 53.43; H, 5.72; S, 10.22%. **5d**: a colorless solid; mp 89–90 °C; ^{1}HNMR (300 MHz, $CDCl_3$) δ 4.40 (m, 1H), 4.33 (q, J = 7.0 Hz, 4H), 4.29 (m, 1H), 4.03 (dd, J = 11.3, 7.6 Hz, 1H), 1.58 (t, J = 7.2 Hz, 2H), 1.36 (t, J = 6.8 Hz, 6H), 1.23–130 (m, 16H), 0.86 (t, J = 6.7 Hz, 4H). **7c**: a colorless solid; mp 100 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.20 (q, J = 7.1 Hz, 4H), 4.15 (s, 4H), 1.42 (q, J = 7.5 Hz, 4H), 1.35 (t, J = 7.1 Hz, 6H), 0.85 (t, J = 7.5 Hz, 6H); HRMS (FAB) calcd for $C_{17}H_{24}O_6S$ (MH^+) 357.1372, found 357.1372; Anal. Calcd for $C_{17}H_{24}O_6S$: C, 57.28; H, 6.79; S, 9.00. Found: C, 57.20; H, 6.78; S, 9.02%. **9**: a colorless thick oil; ^1H NMR (300 MHz, $CDCl_3$) δ 4.70–4.50 (m, 1H), 4.41–4.21 (m, 4H), 4.22–4.12 (m, 1H), 2.22–1.95 (m, 2H), 1.46 9d, J = 6.3 Hz, 3H), 1.43 (d, J = 6.3 Hz, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H); HRMS (FAB) calcd for $C_{15}H_{20}O_6S$ (MH^+) 329.1059, found 329.1059; Anal. Calcd for $C_{15}H_{20}O_6S$: C, 54.86; H, 6.14; S, 9.76. Found: C, 54.80; H, 6.17; S, 9.80%.

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