Tetrahedron Letters 52 (2011) 2823–2825

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of large ring 3,4-alkylenedioxythiophenes (ADOT) derivatives via Mitsunobu reaction

Zhaochao Xu[a,b], Joo-Hee Kang[a], Fang Wang[a], Seung-Min Paek[c], Seong-Ju Hwang[a], Youngmee Kim[a], Sung-Jin Kim[a], Jin-Ho Choy[a,d,*], Juyoung Yoon[a,d,*]

[a] Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Republic of Korea
[b] State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, PR China
[c] Department of Chemistry and Green-Nano Materials Research Center, Kyungpook National University, Taegu 702-701, Korea
[d] Department of Bioinspired Science (WCU), Ewha Womans University, Seoul 120-750, Republic of Korea

ARTICLE INFO

Article history:
Received 19 February 2011
Accepted 11 March 2011
Available online 21 March 2011

ABSTRACT

Poly(3,4-ethylenedioxythiophene) (PEDOT) stands out for its optimized conductivity, stability, and high degree of transparency which has led to its successful commercialization. These excellent properties of PEDOT are mostly ascribed to the alkylenedioxy bridge across the 3- and 4-positions, and thus much effort has been dedicated to synthesizing 3,4-ethylenedioxythiophene (EDOT) analogs. However, only few homologous compounds were successfully synthesized, such as 3,4-propylenedioxythiophene (PrDOT) or 3,4-(1,4-butylenedioxy)thiophene (BuDOT). In this Letter, we use Mitsunobu reaction to synthesize a series of 3,4-alkylenedioxythiophenes (ADOTs) derivatives with 8- to 16-membered rings. The eight-membered compounds were obtained in high or excellent yield. We also found that the 9- to 16-membered EDOT analogs were obtained in relatively low yield because of the competitive reaction to make dimers. Our method provides an easy way to modify ethylenedioxythiophenes (EDOTs), and these obtained ADOTs compounds are promising building blocks for the synthesis of functional π-conjugated systems used in material chemistry.

Conjugated polymers that combine semiconducting properties with light harvesting abilities are used widely as materials in light-emitting diodes,[1] solar cells,[2] electrochromic devices,[3] field effect transistors,[4] and chemo- or bio-sensors.[5] Of these, poly(3,4-ethylenedioxythiophene) (PEDOT) has a unique combination of a moderate band gap and low oxidation potential, which gives PEDOT exceptional stability to the oxidized charged state resulting in high conductivity and good optical transparency in the visible spectral region.[6] Many applications of PEDOT have been rapidly developed based on these properties.[7] For example, PEDOT is a promising candidate for electrochromic applications, such as smart windows, variable reflectance mirrors, optical lenses, etc.[8] The color of PEDOT is deep blue-violet in its neutral state, which changes to pale blue upon doping owing to its small electronic band gap (E_g = 1.6 eV, 775 nm), low redox potential, and rapid response time, as well as facile fabrication in doped form.

The alkyl side chains not only enhance the ease of processing but also modify the electronic properties of the conjugated polymers. Appending a strong electron-donating alkylenedioxy bridge across the 3- and 4-positions can add electron density to the aromatic ring, drastically reduce both the monomer and polymer oxidation potentials, and alter the stability of the oxidized state and band gap. The potential of 3,4-ethylenedioxythiophene (EDOT) as a versatile building block for the synthesis of functional π-conjugated systems[9] has encouraged chemists to synthesize EDOT analogs,[10] such as 3,4-propylenedioxythiophene (PrDOT) or 3,4-(1,4-butylenedioxy)thiophene (BuDOT) (Fig. 1), and improve the synthetic route.[11] The most common and industrially applied synthesis route of EDOTs is the double Williamson etherification of 3,4-dihydroxy-2,5-thiophenedicarboxylic acid diethyl ester with 1,2-dihaloethanes under basic conditions as the key step.[6a,10] To increase the yields and functional groups as well as the stereochemistry tolerance, Reynolds and co-workers[12] and Bäuerle and co-workers[13] recently employed the Mitsunobu reaction[14] as a key step in the synthesis of a series of EDOT and PrDOT derivatives. However, the synthesis of 3,4-alkylenedioxythiophenes (ADOTs) with more than eight-membered rings is a challenge owing to their associated torsional, transannular, and large-angle strain. This Let-

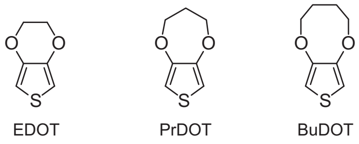


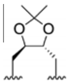
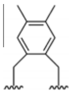
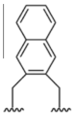
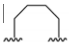
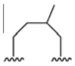
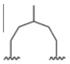
Figure 1. Structures of EDOT, PrDOT, and BuDOT.

---

* Corresponding authors. Fax: +82 2 3277 3419.
E-mail addresses: jhchoy@ewha.ac.kr, jyoon@ewha.ac.kr (J. Yoon).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.03.062

Table 1
Mitsunobu reaction of **1** with 1,*n*-alkyl diols to large ring 3,4-alkylenedioxythiophenes (ADOTs)

Entry	R	Product	Yield[a] (%)	Mp (°C)
1		**2a**; **3a**; **4a**	78; 82; 66	80; >250; ~[b]
2		**2b**; **3b**; **4b**	86; 82; 73	146; >250; ~[b]
3		**2c**; **3c**; **4c**	97; 69; 44	148; >250; 116
4		**2d**; **3d**; **4d**	92; 85; 75	169; >250; 201
5		**2e**	61	78–79
6		**2f**	55	72–73
7		**2g**	37	68–69
8		**2h**; **3h**; **2h**$_{\mathbf{d}}$	43; 74; 23	44–45; >250; 133–134
9	$(CH_2)_6$	**2i**; **2i**$_{\mathbf{d}}$	25; 31	54–55; 137–138
10	$(CH_2)_7$	**2j**	28	62–63
11	$(CH_2)_8$	**2k**; **2k**$_{\mathbf{d}}$	28; 29	65–66; 134–135
12	$(CH_2)_9$	**2l**; **2l**$_{\mathbf{d}}$	27; 36	87–88; 139–140
13	$(CH_2)_{10}$	**2m**; **2m**$_{\mathbf{d}}$	24; 34	64–65; 115–116
14	$(CH_2)_{12}$	**2n**; **2n**$_{\mathbf{d}}$	26; 34	74–75; 122–123
15	$C_2H_4OC_2H_4$	**2o**[c]	74	
16	$(C_2H_4OC_2H_4)_2$	**2p**[c]	78	
17	$(C_2H_4OC_2H_4)_3$	**2q**[c]	79	
18	$(C_2H_4OC_2H_4)_4$	**2r**[c]	67	

[a] Isolated yields.
[b] Pale yellow oil.
[c] Reported in another paper.[17]

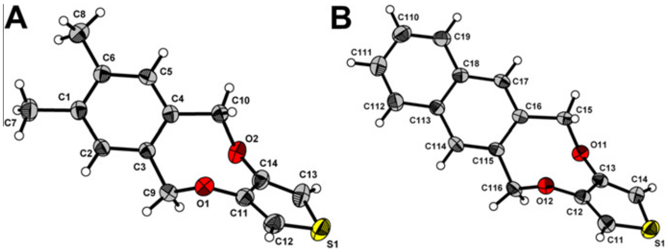


Figure 2. Crystal structures of **4c** (a) and **4d** (b).

ter reports the first large ring ADOTs with 8- to 16-membered rings synthesized by the Mitsunobu reaction.

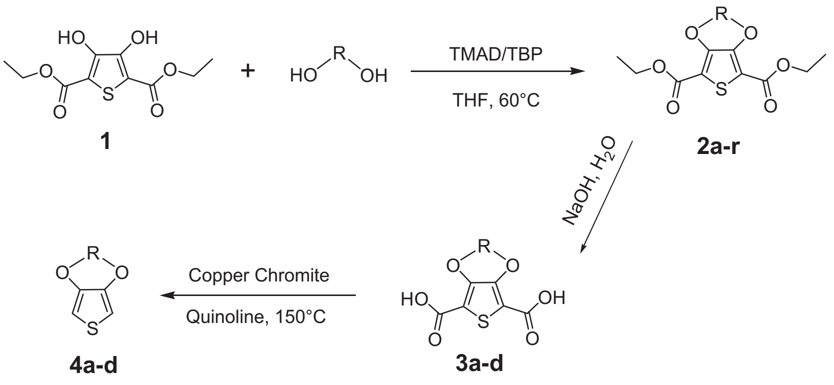
The Mitsunobu reaction allows the conversion of primary and secondary alcohols with nucleophiles into a range of functional groups, such as esters, using a redox combination of trialkyl or triarylphosphine and a dialkyl azodicarboxylate.[14,15] In Reynolds[12] and Bäuerle's[13] studies, the key step was the Mitsunobu reaction between diols and 3,4-dihydroxy-2,5-thiophenedicarboxylic acid diethyl ester **1** using DEAD/TPP[12] and DIAD/TBP,[13] respectively. However, the utilization scope of Mitsunobu reaction is limited by the steric congestion of alcohols and the acidity of nucleophiles (pK_a <13). To overcome these drawbacks, Tsunoda et al developed a versatile Mitsunobu reagent system of *N*,*N*,*N*′,*N*′-tetramethylazodicarboxamide (TMAD) and tributylphosphine (TBP) applicable to nucleophiles with a pK_a up to 13.5 and different steric environments.[16] In the present study, the TMAD/TBP system was introduced to the syntheses of ADOTs (Scheme 1) and a series of large ring derivatives were prepared, which are summarized in Table 1.

The eight-membered compounds **2a–f** were obtained in high or excellent yield. These were then saponified in NaOH/H_2O followed by decarboxylation with copper chromite in quinoline to yield the final monomers **4a–d**. When the rigidity of the rings and molecular weight were increased, the melting points increased and crystalline solids could be obtained. Figure 2 shows the crystal structures of compounds **4c** and **4d**. The reaction can still be performed with long chain linear diols (1,*n*-alkyl diols, *n* = 5–12). However, the resulting 9- to 16-membered EDOT analogs **2h–n** were obtained in low yield because of the competitive reaction to make dimers **2(h–n)**$_{\mathbf{d}}$ (Scheme 2). Monomers **2h–n** and dimers **2(h–n)**$_{\mathbf{d}}$ have similar ^{1}H NMR and ^{13}C NMR spectra but they can be differentiated by their melting points or MS (see Supplementary data). The dimer compounds have higher melting points than the monomer compounds (Table 1, entries 8–14). Interestingly, the reaction of ethylene glycol derivatives with compound **1** only produces monomer products **2o–r** without dimers. This might be due to the reaction of intermediate phosphonium[18] with the ethylene bridged oxygen of diols, which insures monomer ring closure. The detailed experimental procedures and characterization data are available in the Supplementary data.

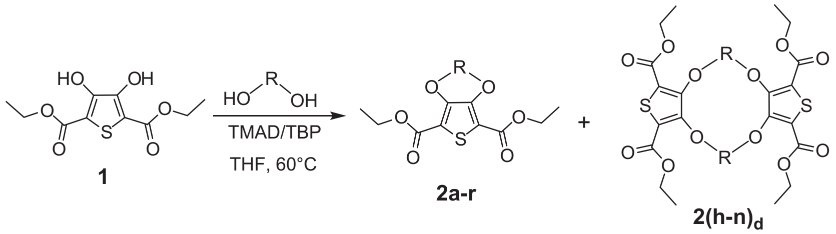
In summary, a new series of large ring 3,4-alkylenedioxythiophene (ADOT) derivatives were synthesized successfully via the Mitsunobu reaction, which provides an easy process and high yield to modify ethylenedioxythiophenes (EDOTs).

Acknowledgments

We gratefully acknowledge the financial support from National Research Foundation of Korea (NRF) (SRC: 2011-0001340, 2011-



Scheme 1. Synthesis of 3,4-alkylenedioxythiophenes (ADOTs).



Scheme 2. Monomer and dimer synthesis of 3,4-alkylenedioxythiophenes (ADOTs).

0001334, NRL: 2010-0018895), WCU program (R31-2008-000-10010-0) and State Key Laboratory of Fine Chemicals of China (KF0809). We also thank Professor Bongjin Moon for his helpful discussion. Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.03.062.

References and notes

1. (a) Burroughes, J. H.; Bradley, D. D. C.; Brown, A. R.; Marks, R. N.; Mackay, K.; Friend, R. H.; Burns, P. L.; Holmes, A. B. *Nature* **1990**, *347*, 539; (b) Halim, M.; Pillow, J. N. G.; Samuel, I. D. W.; Burn, P. L. *Adv. Mater.* **1999**, *11*, 371.
2. (a) Gunes, S.; Neugebauer, H.; Sariciftci, N. S. *Chem. Rev.* **2007**, *107*, 1324; (b) Cheng, Y.-J.; Yang, S.-H.; Hsu, C.-S. *Chem. Rev.* **2009**, *109*, 5868; (c) Segura, J. L.; Martin, N.; Guldi, D. M. *Chem. Soc. Rev.* **2005**, *34*, 31.
3. (a) Sonmez, G. *Chem. Commun.* **2005**, 5251; (b) Beaujuge, P. M.; Reynolds, J. R. *Chem. Rev.* **2010**, *110*, 268.
4. (a) Sirringhaus, H.; Tessler, N.; Friend, R. H. *Science* **1998**, *280*, 1741; (b) Perepichka, I. F.; Perepichka, D. F.; Meng, H.; Wudl, F. *Adv. Mater.* **2005**, *17*, 2281.
5. (a) Thomas, S. W., III; Joly, G. D.; Swager, T. M. *Chem. Rev.* **2007**, *107*, 1339; (b) Kim, H. N.; Guo, Z.; Zhu, W.; Yoon, J.; Tian, H. *Chem. Soc. Rev.* **2011**, *40*, 79; (c) Jiang, H.; Taranekar, P.; Reynolds, J. R.; Schanze, K. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 4300; (d) Fan, L.-J.; Zhang, Y.; Murphy, C. B. S.; Angell, E.; Parker, M. F. L.; Flynn, B. R.; Jones, W. E. J., Jr. *Coord. Chem. Rev.* **2009**, *253*, 410; (e) Ho, H.-A.; Najari, A.; Leclerc, M. *Acc. Chem. Res.* **2008**, *41*, 168; (f) Ahn, D. J.; Kim, J.-M. *Acc. Chem. Res.* **2008**, *41*, 805; (g) Duan, X.; Liu, L.; Feng, F.; Wang, S. *Acc. Chem. Res.* **2010**, *43*, 260; (h) Kim, S.; Lim, C.-K.; Na, J.; Lee, Y.-D.; Kim, K.; Choi, K.; Leary, J. F.; Kwon, I. C. *Chem. Commun.* **2010**, *46*, 1617; (i) Chen, X.; Lee, J.; Jou, M. J.; Kim, J.-M.; Yoon, J. *Chem. Commun.* **2009**, *45*, 3434; (j) Chen, X.; Kang, S.; Kim, M. J.; Kim, J.; Kim, Y. S.; Kim, H.; Chi, B.; Kim, S.-J.; Lee, J. Y.; Yoon, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 1422; (k) Chen, X.; Yoon, J. *Dyes and Pigments* **2011**, *89*, 194; (l) Lee, K. M.; Chen, X.; Fang, W.; Kim, J.-M.; Yoon, J. *Macro. Rapid. Commun.* **2011**, *32*, 497–500.
6. (a) Groenendaal, L.; Jonas, F.; Freitag, D.; Pielartzik, H.; Reynolds, J. R. *Adv. Mater.* **2000**, *12*, 481; (b) Groenendaal, L.; Zotti, G.; Aubert, P.-H.; Waybright, S. M.; Reynolds, J. R. *Adv. Mater.* **2003**, *15*, 855.
7. (a) Sirringhaus, H.; Kawase, T.; Friend, R. H.; Shimoda, T.; Inbasekaran, M.; Wu, W.; Woo, E. P. *Science* **2000**, *290*, 2123; (b) Kros, A.; van Hövell, S. W. F. M.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. *Adv. Mater.* **2001**, *13*, 1555; (c) Shin, S.; Jang, J. *Chem. Commun.* **2007**, 4230; (d) Luo, S.-C.; Jiang, J.; Liour, S. S.; Gao, S.; Ying, J. Y.; Yu, H. *Commun.* **2009**, 2664; (e) Mishra, A.; Ma, C.-Q.; Bauerle, P. *Chem. Rev.* **2009**, *109*, 1141; (f) Isaksson, J.; Kjäll, P.; Nilsson, D.; Robinson, N. D.; Berggren, M.; Richter-Dahlfors, A. *Nat. Mater.* **2007**, *6*, 673.
8. (a) Lin, T. H.; Ho, K. C. *Sol. Energy Mater. Sol.* **2006**, *90*, 506; (b) Ko, H. C.; Kim, S.; Lee, H.; Moon, B. *Adv. Funct. Mater.* **2005**, *15*, 905; (c) Argun, A. A.; Cirpan, A.; Reynold, J. R. *Adv. Mater.* **2003**, *15*, 1338.
9. Roncali, J.; Blanchard, P.; Frère, P. *J. Mater. Chem.* **2005**, *15*, 1589.
10. (a) Heywang, G.; Jonas, F. *Adv. Mater.* **1992**, *4*, 116; (b) Dietrich, M.; Heinze, J.; Heywang, G.; Jonas, F. J. *Electroanal. Chem.* **1994**, *369*, 87; (c) Kumar, A.; Welsh, D. M.; Morvant, M. C.; Pirous, F.; Abboud, K. A.; Reynolds, J. R. *Chem. Mater.* **1998**, *10*, 896; (d) Welsh, D. M.; Kumar, A.; Morvant, M. C.; Reynolds, J. R. *Synth. Met.* **1999**, *102*, 967; (e) Leriche, P.; Blanchard, P.; Frere, P.; Levillain, E.; Mabon, G.; Roncali, J. *Chem. Commun.* **2006**, 275.
11. (a) Kieseritzky, F.; Allared, F.; Dahlstedt, E.; Hellberg, J. *Tetrahedron Lett.* **2004**, *45*, 6049; (b) Frontana-Uribe, B. A.; Heinze, J. *Tetrahedron Lett.* **2006**, *47*, 4635; (c) Welsh, D. M.; Kumar, A.; Meijer, E. W.; Reynolds, J. R. *Adv. Mater.* **1999**, *11*, 1379.
12. (a) Zong, K.; Madrigal, L.; Groenendaal, L.; Reynolds, J. R. *Chem. Commun.* **2002**, 2498; (b) Dyer, A. L.; Grenier, C. R. G.; Reynolds, J. R. *Adv. Funct. Mater.* **2007**, *17*, 1480.
13. (a) Caras-Quintero, D.; Bäuerle, P. *Chem. Commun.* **2002**, 2690; (b) Caras-Quintero, D.; Bäuerle, P. *Chem. Commun.* **2004**, 926.
14. Swamy, K. C. K.; Kumar, N. N. B.; Balaraman, E.; Kumar, K. V. P. P. *Chem. Rev.* **2009**, *109*, 2551.
15. Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380.
16. (a) Tsunoda, T.; Yamamiya, Y.; Itô, S. *Tetrahedron Lett.* **1993**, *34*, 1639; (b) Tsunoda, T.; Yamamiya, Y.; Kawamura, Y.; Itô, S. *Tetrahedron Lett.* **1995**, *36*, 2529.
17. Kim, J.; Yoon, D.; Lee, S. H.; Ko, S.; Lee, Y.-S.; Zong, K. *Bull. Korean Chem. Soc.* **2006**, *27*, 1910.
18. See postulated mechanism for Mitsunobu reaction explained in Ref. 14.