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3,4-Ethylenedioxythiophene and 3,4-Ethylenedioxyselenophene: Synthesis and Reactivity of C_α−Si Bond

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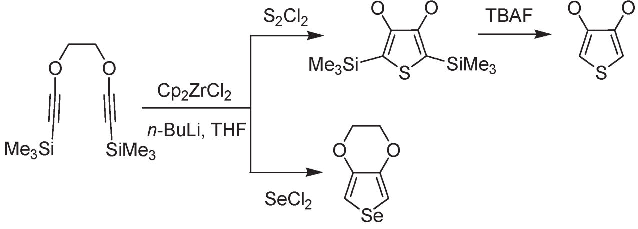

A synthetic approach to synthesize EDOT and EDOS from a common precursor **5** is reported. The method involves zirconocene dichloride mediated reaction of a common diyne **5** followed by treatment with disulfur dichloride (S_2Cl_2) and in situ prepared selenium dichloride ($SeCl_2$). The higher lability of α-trimethylsilyl group in EDOS compared to EDOT is explained using DFT calculations.

Thiophene-containing π-conjugated systems are an attractive class of organic semiconducting materials which have received considerable attention for the development of organic electronic devices, such as light emitting diodes, field-effect transistors, and solar cells.[1] Developing the new synthetic strategies for substituted monomers for the π-conjugated polymers is important and of urgent need. Very few synthetic strategies are available for substituted selenophene.[2] The unavailability of synthetic methodologies for the synthesis of substituted selenophene-based monomeric precursors is another reason why polyselenophenes remained practically unexplored.[3] Replacement of sulfur by the more polarizable selenium offers an interesting route to reduce monomer oxidation potential and, consequently, for fine-tuning of the electrochemical and optical properties of the corresponding polymer.[2a−d] This approach should also lead to increased bandwidths, improved dimensionality, and reduced on-site Coulombic repulsion.[4] There are very few reports in the literature comparing the chemical reactivity of thiophene and selenophene derivatives.[3,5] Theoretical studies[6] indicate that polyselenophenes should have a lower band gap than polythiophenes.

Polyethylenedioxythiophene (PEDOT) is one of the most important examples of polythiophene derivatives. Polymers derived from EDOT and its derivatives provide highly conducting and especially stable doped states, a range of optical properties with electronic band gaps varying across the entire visible spectrum, and enhanced redox properties, making them useful for numerous electronic devices.[7,8] There are only a few reports on polymers of ethylenedioxyselenophene (EDOS) and its derivatives, mostly in the previous couple of years.[2a,c,9]

The most common and industrially applied route is the five-step synthetic methodology of EDOT which contains double-Williamson etherification of 3,4-dihydroxy-2,5-thiophenedicarboxylic acid diethyl ester, which is readily available by Hinsberg reaction of thiodiacetic acid diethyl ester and glyoxal[10] with 1,2-dihaloethanes under basic conditions as the key step.[11−14] Cava et al. reported synthesis of EDOS using a similar synthetic strategy.[2a] Bäuerle et al. reported an efficient synthesis to prepare EDOTs as well as chiral EDOTs substituted at the ethylenedioxy moiety by

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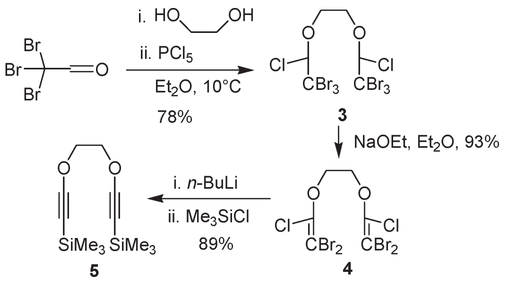
SCHEME 1. Synthetic Route to EDOT (1) and EDOS (2)



Mitsunobu reaction of 3,4-dihydroxythiophene derivatives with diols.[15]

The purity of the EDOT and EDOS is crucial for the polymerization reactions because even traces of quinoline derivatives remaining from the thermal decarboxylation will influence the polymerization significantly as quinolines form rather stable radicals, so that they are commonly used as polymerization inhibitors.[16] As mentioned above, the typical and traditional procedures for the preparation of EDOT and EDOS is the five-step reaction scheme that suffers from several major drawbacks such as high temperatures, pressure build-up, and potential run-away reactions until a simple two-step efficient synthesis of EDOT was achieved by Hellberg et al.[17] in 2004 and the synthesis of EDOS by Bendikov et al.[2c] in 2008.

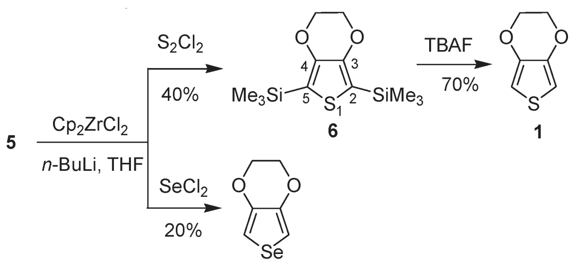
Herein, we report an easy and advantageous synthetic route for the synthesis of EDOT (**1**) and EDOS (**2**) from a common diyne precursor **5** where, most importantly, every intermediate compound is stable enough under ambient conditions. We employed mild conditions in each step for the preparation of EDOT and EDOS. We have observed higher lability of an α-trimethylsilyl group in EDOS compared to EDOT and explained this using the DFT calculations. Recently, by using a similar synthetic approach, we have reported the synthesis of cyclopenta[*c*]selenophene (**7**, Chart 1).[2d]

Compound **4** was prepared following the literature procedure[18] starting from tribromoacetaldehyde and ethylene glycol followed by treatment with PCl_5 and sodium ethoxide (Scheme 1), which was purified by silica gel column chromatography using hexanes as mobile phase. When **4** was treated with 5 equiv of *n*-BuLi followed by trimethylsilyl chloride, the reaction afforded **5** in 89% yield.

Compound **5** was used as the common precursor to prepare EDOT and EDOS. Synthesis of EDOT and EDOS was accomplished by zirconocene dichloride mediated cyclization reaction of the diyne followed by treatment with disulfur dichloride (S_2Cl_2) and in situ prepared selenium dichloride ($SeCl_2$) (Scheme 2).[2d,19]

Treatment of **5** with zirconocene chloride and disulfur dichloride afforded 2,5-bis(trimethylsilyl)-3,4-ethylenedioxythiophene (**6**), which was confirmed by ^{1}H NMR and matched perfectly with the reported data for **6**.[20] EDOT was achieved from **6** following a literature method[21] of protodesilylation. In contrast, the reaction of **5** with zirconocene dichloride and selenium dichloride directly afforded desilylated compound **2** instead of the expected compound **10** under similar experimental conditions and reaction workup. This indicates higher lability of the C_α−Si bond in 2,5-bis(trimethylsilyl)-EDOS compared to the EDOT analogue. This observation indicates considerable difference in the reactivity of 2,5-trimethylsilyl-substituted EDOT and EDOS.

SCHEME 2. Synthesis of Diyne 5



Thus, in each step for the preparation of EDOT and EDOS, mild conditions have been used: first step, mixing two reagents at rt and left overnight under $CaCl_2$ guard tube, no purification required; second step, 10 °C/diethyl ether and PCl_5, no purification required; third step, NaOEt treatment at 0 °C to rt, 4 h, purified on flash column using only hexanes; fourth step, *n*-BuLi treatment at −78 °C and Me_3SiCl addition, rt; fifth step, typical zirconocene coupling to get the **6** and **2**, purified on column; sixth step, for EDOT only, TBAF treatment followed by a filter column.

The synthesis of EDOT can be scaled up without any difficulty; however, yield diminished in the synthesis of EDOS when the reaction was carried out at more than a gram scale. It is probably due to the increased exposure of the thermally less stable $SeCl_2$ to the elevated temperature (rt) during drop by drop transfer using a syringe/septum setup.

To shed more light on the experimentally observed reactivity difference between **6** and **10**, we have carried out DFT calculations[22] at the B3LYP/6-31G(d) level (corrected for unscaled ZPVE). The C_2−Se−C_5 (90.45°) bond angle in the optimized structure of **10** is smaller than the corresponding bond angle C_2−S−C_5 (94.82°) in **6**. In **10**, the angle strain at selenium is relatively higher than at sulfur in **6**. This can be attributed to the larger size of selenium than sulfur. This may contribute to reactivity difference between **6** and **10**.

The isodesmic reactions as shown in eqs 1 and 2 were considered to study the reactivity difference between **6** and **10**. The disproportionation energy for eq 1 is 3.7 kcal/mol, whereas for eq 2 it is only 0.02 kcal/mol. By summarizing eqs 1 and 2, C_α−$SiMe_3$ bonds in **10** are likely thermodynamically less stable by ~3.7 kcal/mol compared to the C_α−$SiMe_3$ bonds in **6**.

$$\mathbf{6} + \mathbf{8} \rightarrow \mathbf{1} + \mathbf{9} \qquad (1)$$

$$\mathbf{10} + \mathbf{8} \rightarrow \mathbf{2} + \mathbf{9} \qquad (2)$$

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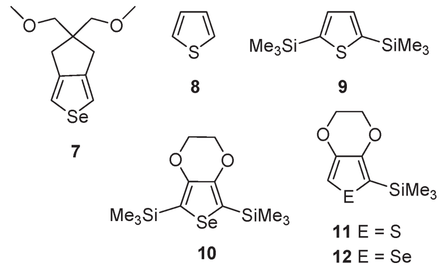
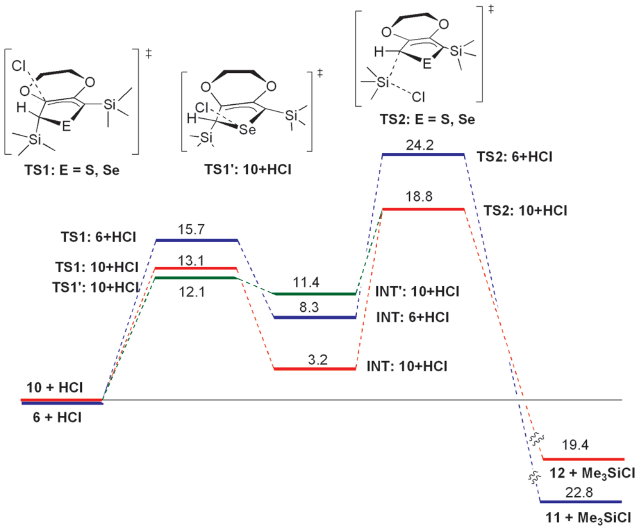
CHART 1



SCHEME 3. Reaction Pathways for Protodesilylation of 6 and 10 at B3LYP/6-31G(d)[a]



[a]The energy levels shown in green correspond to the second pathway for the protodesilylation **10**. The structures of TSs correspond to the first five structures in Figure 1.

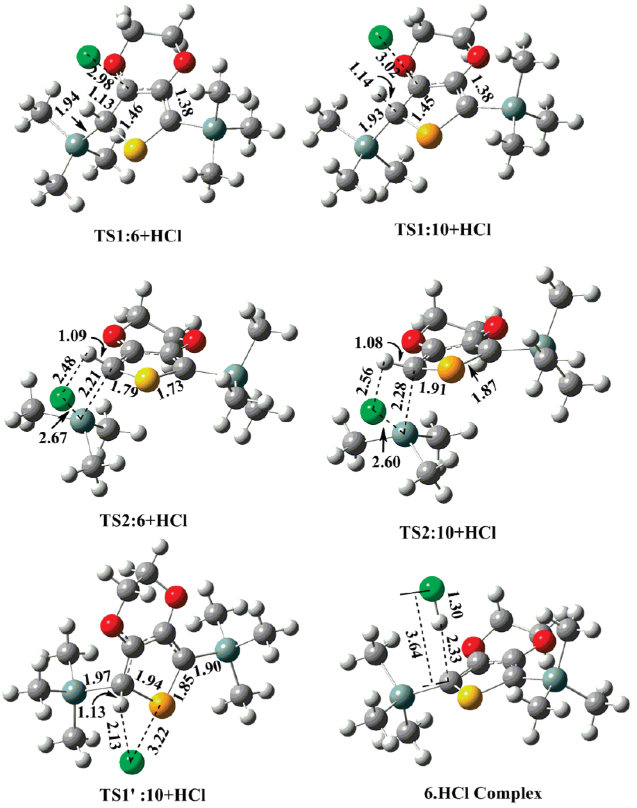


FIGURE 1. Views of TSs and **6**·HCl complex. Significant bond lengths are given in angstroms.

Furthermore, we have calculated the reaction pathways for protodesilylation of **6** and **10** by the electrophilic ipso-substitution through two transition states (Scheme 3). We have considered a two step reaction: (i) addition of HCl (protonation) and (ii) elimination of Me_3SiCl (desilylation). We have calculated TS for addition of HCl along 2,3-carbons of **6** and **10** (TS1, H and Cl at C_2 and C_3, respectively, Scheme 3, Figure 1). In both cases, only one negative frequency was observed, which indicates the first-order saddle point. In these TS1s, the hydrogen−carbon bonds are rather short and quite close to their final distances, while the carbon−chloride bonds are still pretty long. Thus, the energy of this transition state should be directly related to the protonation energy at the α-position.

For compound **10** the activation energy of 2,3-addition of HCl is 2.6 kcal/mol less than that of **6**. The NPA charges at the same level of theory supports the higher reactivity of the C−Si bond in **10** than in **6**.[23] NPA charges calculation showed that C_2 (or C_5) in **10** is more electronegative compared to that of **6**. This can be seen in terms of more electropositive selenium than sulfur. Trimethylsilyl groups carry the nearly same charge in both the molecules. The TS1s led to form intermediate (INTs, Scheme 3). In case of **10** the intermediate (INT: **10** + HCl) is stabilized more than that of **6** (INT: **6** + HCl). The protonation should be followed by the attack of chloride ion (which is partially bonded to C_3 in TS1) on silicon of the silyl group and desilylation in the form of elimination of Me_3SiCl. The second step is the rate determining step which requires activation energy of 15.9 and 15.6 kcal/mol for **6** and **10**, respectively. The energy difference between two transition states is rather small (only 0.3 kcal/mol) which do not explain the significantly higher reactivity of **10** for the protodesilylation reaction.[24]

Further, we have considered 1,2-addition of HCl to form the transition states and intermediates where H attaches to C_2 and Cl stays in close proximity of Se/S. The activation barrier for 1,2-addition of HCl to **10** is 12.1 kcal/mol, which is 1.0 kcal/mol less than 2,3-addition of HCl to **10** (Scheme 3, Figure 1). All attempts to find the TS for 1,2-addition of HCl to the thiophene analogue **6** were unsuccessful. This may be due to less strength of stabilizing interaction between the S and Cl compared to that of between Se and Cl. The intermediate of the 1,2-addition of HCl to **10** was found to be considerably higher in energy (by 8.2 kcal/mol) than that of 2,3-addition of HCl to **10**. In the case of **6**, the calculation to find the intermediate of 1,2-addition of HCl to **6** resulted in the **6**·HCl complex. Due to higher energy of the intermediate, the activation energy for the TS2 which led to

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[23] In **6** and **10**, the charges on C_2 (or C_5) are −0.75 and −0.80e, respectively. The charges on S and Se are 0.49 and 0.58e, respectively. Trimethylsilyl groups carry same charge (0.50e) in both the compounds.

[24] In TS1, the positions of Cl and $SiMe_3$ are on opposite faces of the thiophene/selenophene ring. Therefore, it is less likely that the intermediate will be followed by TS2. However, it can be possible by considering the dimer and trimer of HCl as the reactive species instead of monomeric HCl.

desilylation of **10** is only 7.4 kcal/mol. Therefore, the rate-determining step for this route is the first step, i.e., protonation by 1,2-addition of HCl to **10**. Thus, the second route for protodesilylation is 3.5 kcal/mol less energetic than the first route. However, this route is not feasible for compound **6**.

Therefore, the calculation again supports our observation that the C−Si bond is more facile for ipso-electrophilic substitution in **10** than in **6**. Therefore, under similar experimental workup conditions, the protodesilylation was observed only for compound **10**, whereas desilylation of **6** required additional one-step reaction, i.e., treatment of **6** with TBAF.

In summary, we have synthesized a new diyne **5** which has been used as a valuable common precursor for the synthesis of EDOT and EDOS, the key monomers in the field of organic electroactive materials. We employed mild condition in each step for the preparation of EDOT and EDOS. The experimentally observed higher lability of the C_α−Si bond in **10** compared to **6** was explained on the basis of DFT calculations.

Experimental Section

Tetrahydrofuran (THF) was distilled from sodium/benzophenone under nitrogen. All of the reactions were carried out under nitrogen. Silica gel (230−400 mesh) was used for column chromatography. NMR spectra were recorded on a 400 MHz spectrometer as a solution in $CDCl_3$ with trimethylsilane (TMS) as the internal standard; chemical shifts (δ) are reported in parts per million.

Synthesis of Diyne 5. A solution of **4** (0.74 g) in dry THF was slowly added to *n*-BuLi (4.7 mL, 1.6 M solution in hexanes) at −78 °C. An immediate white precipitation was observed. After the mixture was stirred for an additional 1.5 h at the same temperature, trimethylchlorosilane (0.6 mL) was added at the same temperature, and the resulting mixture was warmed to room temperature and stirred for additional 1 h while the solution became clear. The reaction was quenched by addition of saturated ammonium chloride solution. The organic phase was separated and extracted with diethyl ether and solvent evaporated. Compound **5** (0.33 g) was isolated using column chromatography (1% ethyl acetate in hexanes) as a colorless liquid in 89% yield: IR (KBr, cm^{-1}) 2959, 2897, 2181, 1448, 1249, 1023, 841, 759, 640; ^1H NMR (400 MHz, $CDCl_3$) δ 4.3 (4H, s), 0.13 (18H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.4, 75.1, 38.1, 0.7; HRMS calcd for $C_{12}H_{23}O_2Si_2$ [M + H] 255.1237, found 255.1251.

General Synthetic Procedure for EDOT 1 and EDOS 2. To Cp_2ZrCl_2 (380 mg) in 40 mL of dry THF was added *n*-BuLi (1.9 mL, 1.6 M solution in hexanes) at −78 °C. After the solution was stirred for about 30 min, **5** (0.3 g) in 5 mL of dry THF was added dropwise. The resulting solution was allowed to warm to room temperature and stirred for an additional 2 h. The color of the solution changed from pale yellow to orange. (i) S_2Cl_2 (95 μL) was added at rt, and the solution was stirred for 2 h at room temperature to afford EDOT−TMS_2 (40% yield) followed by desilylation in the next step using tetrabutylammonium fluoride to afford EDOT (70% yield). (ii) $SeCl_2$ (Se = 103 mg, SO_2Cl_2 = 105 μL) in 3 mL of dry THF was added slowly, drop by drop, at 0 °C, and the solution was stirred for 2 h at room temperature to afford EDOS (20% yield). The reaction was quenched by pouring the resulting solution into ice-cold water, and the reaction mixture was extracted with diethyl ether. The organic layer was washed with brine and then dried over Na_2SO_4. The volatile material was then removed to get the desired product, which was purified on a silica gel column using 2% ethyl acetate/hexanes. All of these reported compounds were confirmed by ^1H NMR, and the spectral data matched with the literature data.

EDOT−TMS_2[20] 6: ^1H NMR (400 MHz, $CDCl_3$) δ 4.16 (4H, s), 0.28 (18H, s).

EDOT[25] 1: ^1H NMR (400 MHz, $CDCl_3$) δ 4.19 (4H, s), 6.32 (2H, s).

EDOS[2c] 2: ^1H NMR (500 MHz, $CDCl_3$) δ 4.16 (4H, s), 6.78 (2H, s).

Computational Details. The Gaussian 03[22] series of programs were used for all calculations. All molecules were fully optimized by using the hybrid density functional[26] B3LYP level[27] of theory with the 6-31G(d) basis set. The relative energies included unscaled zero-point vibrational energies (ZPVE). Transition structures were located by using the TS routine as implemented in Guassian 03. Frequency calculations were performed at the same level for all stationary points to differentiate them as minima or saddle points. Transition states were characterized by one imaginary frequency and checked by intrinsic reaction coordinate (IRC)[28] calculations. Charges were calculated by using natural population analysis (NPA charges)[29] at B3LYP/6-31G(d).

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Supporting Information Available: ^1H and ^{13}C NMR of diyne **5**; ^1H NMR of compounds **6**, **1**, **2**; calculated absolute energies and coordinates of all the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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