Tetrahedron 67 (2011) 6275–6280

Contents lists available at ScienceDirect

Tetrahedron

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

A theoretical approach to the formation mechanism of diphenyldithieno[3,2-b:2′,3′-*d*]thiophene from 1,8-diketone, 4,5-bis(benzoylmethylthio)thiophene: a DFT study

Cihan Ozen[a], Mine Yurtsever[a,*], Turan Ozturk[a,b]

[a] *Istanbul Technical University, Faculty of Science and Letters, Department of Chemistry, Maslak, Istanbul 34469, Turkey*
[b] *TUBITAK UME, Chemistry Group Laboratories, PO Box 54, 41470 Gebze-Kocaeli, Turkey*

ARTICLE INFO

Article history:
Received 30 December 2010
Received in revised form 23 May 2011
Accepted 13 June 2011
Available online 17 June 2011

ABSTRACT

The mechanism of formation of dithieno[3,2-*b*:2′,3′-*d*]thiophene (DTT) through the reaction of 1,8-diketone, 4,5-bis(benzoylmethylthio)thiophene with P_4S_{10} was examined in detail by employing DFT method at B3LYP/6-311+G(d,p) level. Two mechanisms were considered. The first one included two parts (i) transformation of the 1,8-diketone, 4,5-bis(benzoylmethylthio)thiophene to the dithione by the reaction of P_4S_{10} with the carbonyl groups and (ii) cyclization of the dithione to the final product, DTT, through an intramolecular reaction of the thiophene with thiones. The second mechanism consists of an initial attack of the carbonyl oxygen to the phosphorus atom of P_4S_{10} followed by cyclization via an intramolecular attack from the thiophene ring to the highly electrophilic carbons connected to the oxygens to form DTT. According to the calculated Gibbs free energies of the studied paths, the second mechanism is more favorable than the first one and both pathways proceed in a stepwise manner.

1. Introduction

π-Conjugated organic molecules have played a tremendous role in the preparation of materials for electronic and optoelectronic applications as these materials are cheap and easy-to-process when compared to currently widespread applied inorganic materials.[1] Extensive studies have demonstrated that such materials can find a variety of interesting applications in organic thin film transistors (OTFTs),[2] light emitting diodes (OLED),[3] photovoltatic cells,[4] energy storage,[5] electrochromic devices,[6] and sensors.[7] Among the π-conjugated organic molecules, the thiophenes have received much attention as their structure analogous to that of *cis*(CH), polyacetylene, $(CH)_x$, are stabilized by sulfur heteroatom.[8] In addition to their environmental stability, they can easily be manipulated to design and synthesize new organic materials to modulate their electronic and electrochemical properties.[3c,6b,9]

Dithieno[3,2-*b*:2′,3′-*d*]thiophenes (DTT), which possess three fused thiophene rings, are among the most important organic semiconducting materials, as they are building blocks for numerous electronic and optical applications.[10] Although various synthetic methods are available in the literature, theoretical studies for the formation mechanism of DTT are rather scarce. As one of the interesting and versatile method for the synthesis of the DTT analogue **22** is the reaction of 1,8-diketone, 4,5-bis(benzoylmethylthio) thiophene **2** with P_4S_{10}, in this study, its mechanism was investigated thoroughly to obtain a plausible pathway, using density functional theory method in the light of aforementioned experimental findings.[11]

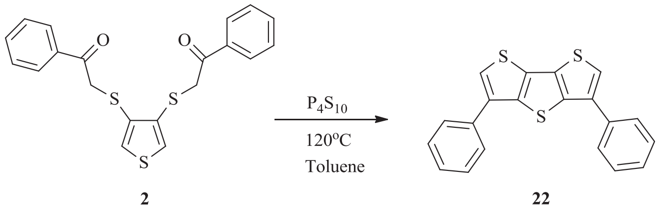


Fig. 1. Reaction of 1,8-diketone, 4,5-bis(benzoylmethylthio)thiophene **2** with P_4S_{10}.

2. Methodology

In the context of this study, all the possible reaction mechanisms, including intermediates and transition states, have been

---

[*] Corresponding author. E-mail address: mine@itu.edu.tr (M. Yurtsever).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.06.037

modeled and discussed in terms of their relative Gibbs free energies calculated at 298 K. The DFT method with the B3LYP functional[12] and the 6-311+G(d,p) basis set implemented in the G03 package,[13] has been employed to perform the full optimization of the compounds of interest in the gas phase. The stationary points were analyzed by vibrational frequency calculations applying the same methodology. All transition states were verified to be saddle points by one imaginary frequency belonging to the reaction coordinate. For all transition state structures, the intrinsic reaction coordinate (IRC) was followed to validate the expected reactants and products.[14] The Natural Bond Orbital (NBO)[15] analysis has been carried out on some structures in order to investigate electronic structure. Three-dimensional structures given throughout the text are the optimized geometries at B3LYP/6-311+G(d,p) level, unless otherwise stated. In some of the geometries, the critical bond lengths (in Å), which are of significance in the reaction coordinate are shown and the hydrogen atoms, which are not involved in the active reaction centers have been omitted for clarity.

3. Results and discussion

The synthesis of the DTT analogue **22** from 1,8-diketone, 4,5-bis (benzoylmethylthio) thiophene **2**, using P_4S_{10},[16] is one of the most efficient methodologies. Its mechanism was reported to proceed by an initial attack from the carbonyl oxygen to P_2S_5, which is a dissociation product of P_4S_{10} during the reaction, and then the ring closure takes place by an attack from the thiophene ring to the positively charged carbonyl carbon. As P_4S_{10} is a strong sulfurizing agent, it is not clear if the conversion of the oxo group to thione takes place first and then the reaction proceeds by an attack on the thione from thiophene. Moreover, the experimental results revealed that such a transformation would not be possible in the absence of P_4S_{10}. In the experiment, the reaction of 1,8-diketone, 4,5-bis(benzoylmethylthio)thiophene **2** with P_4S_{10} was carried out in refluxing toluene (Fig. 1), and when the reaction was performed with acid, such as HCl, in the absence of P_4S_{10}, starting material **2** was recovered, which indicates that the presence of P_4S_{10} plays a vital role in this reaction.[11] Hence, in this study, two possible reaction mechanisms were studied, (i) transformation of the diketone to the dithione followed by the cyclization of the dithione to the final product and (ii) the direct cyclization from the diketone to thiophene ring in the presence of P_2S_5.

Before modeling a transition state for the first step, the lowest energy conformers of the reactants were searched. Results indicated that only one conformer for P_2S_5 (**1**) (Fig. 2) and for the diketone **2** had the lowest Gibbs free energy even though a series of ketone conformers exist, which are energetically close to each other due to the free rotations of the terminal benzoyl groups.

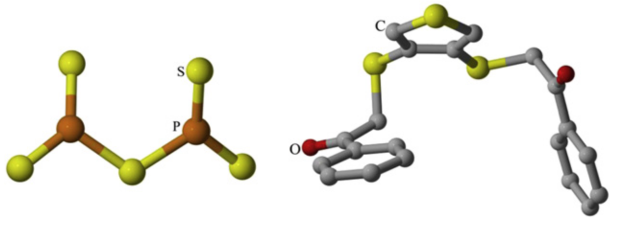


Fig. 2. 3D Representations of the lowest energy conformers of P_2S_5 **1** and 1,8-diketone, 4,5-bis(benzoylmethylthio)thiophene **2**.

The lowest barrier energy for the formation of the transition complex **3** (**2**+P_2S_5) was found to be 19.3 kcal/mol, the geometry of which includes a four-membered ring in the reaction center due to the partially formed P···O and S···C bonds having distances of 1.76 and 2.70 Å, respectively (Fig. 3).

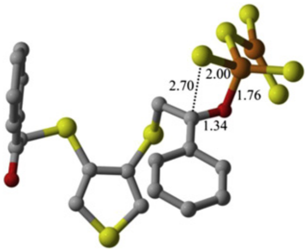


Fig. 3. 3D Representation of the transition complex **3**.

In the thionation mechanism of the carbonyl group, the intermediate **4** was found to be 10.2 kcal/mol less stable compared to the reference point in the reaction coordinate (Scheme 1). The final stage in the transformation of one of the (−C═O) to (−C═S), the four-membered ring starts to break at the P−S and C−O bonds and the reaction proceeds through another transition state where P_2S_5 abstracts the carbonyl oxygen to form OP_2S_4 and then OP_2S_4 excludes itself from the reaction center. In the transition complex **5**, the distances of the weakened bonds C···O and P···S were calculated to be 2.21 and 2.26 Å, respectively. The distances of the partially and fully formed C···S bonds in **5** and **6** were calculated to be 1.78 and 1.65 Å, respectively (Fig. 4).

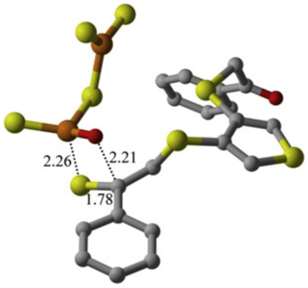
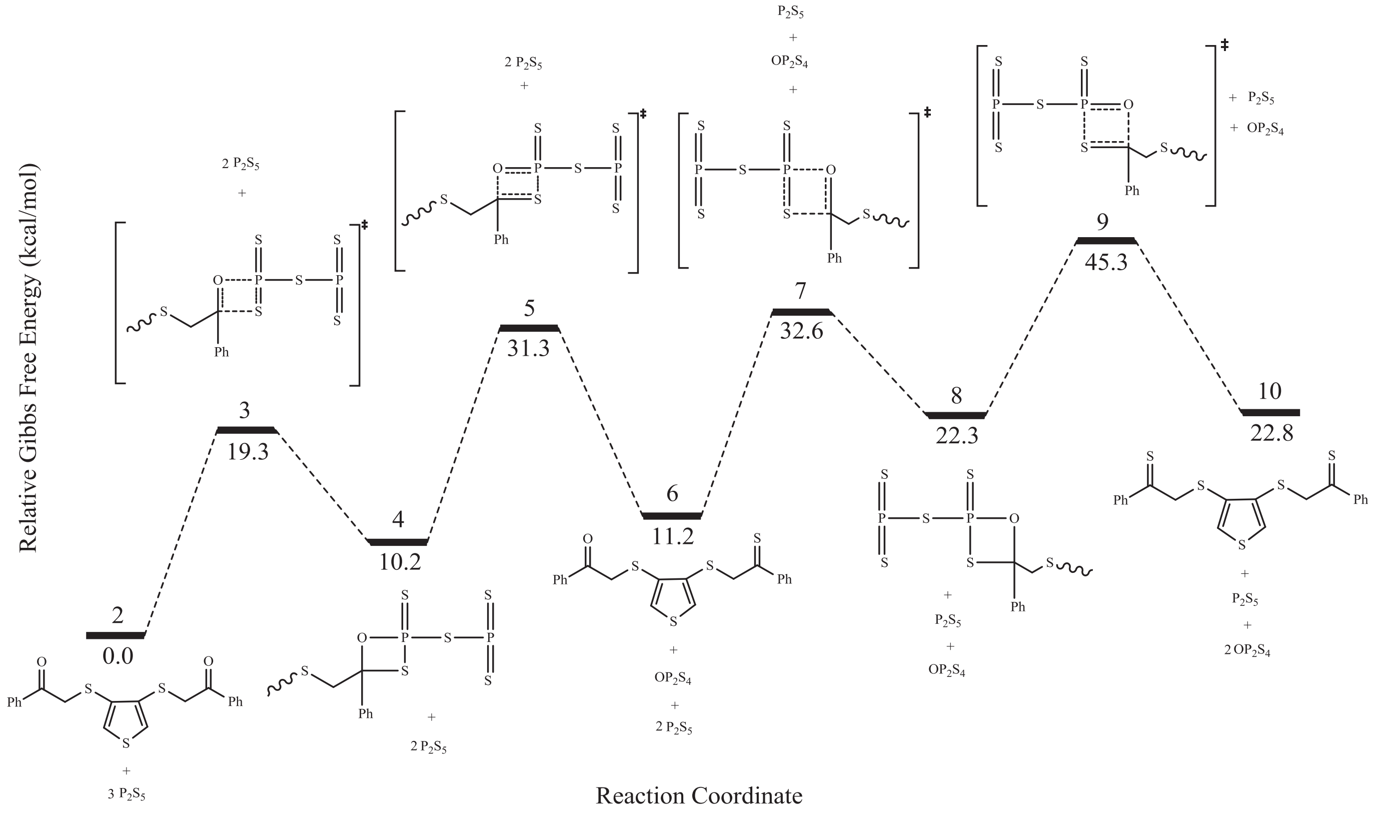


Fig. 4. 3D Representation of the transition state **5**.

After transformation of the first CO moiety to CS was completed, the same mechanism was repeated for the second CO. The complete pathway of dithione transformation is depicted in Scheme 1. The possibility that OP_2S_4, instead of P_2S_5, may react with the other CO moiety was not considered since this would be highly unfavorable due to the kinetic reasons and also OP_2S_4 becomes inactive against thionation reaction.[17]

The second part of the mechanism involves the cyclization of dithione **10** to yield the product **22**. In transition state **11** (Fig. 5), the α-carbon of the thiophene ring interacts with the carbon atom of a thione at a distance of 2.14 Å under the catalytic assistance of P_2S_5. This step has the highest point on the energy profile with a barrier energy of 50.3 kcal/mol. While the ring closure occurs, the proton connected to the α-carbon of the thiophene ring is transferred to a sulfur atom and connected to the phosphorus atom to produce the intermediate **12** without a barrier.



Scheme 1. Energetics and mechanism of transformation from diketone to dithione (some parts of structures is not shown because of clarity).

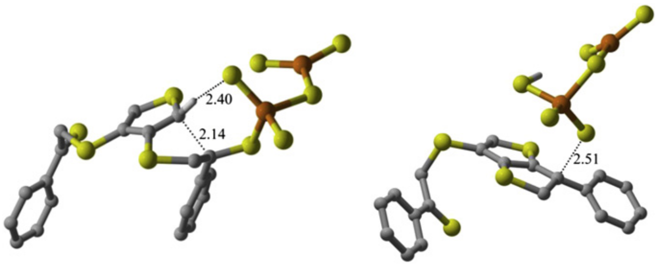


Fig. 5. 3D Representations of the transition states **11** (left) and **13** (right).

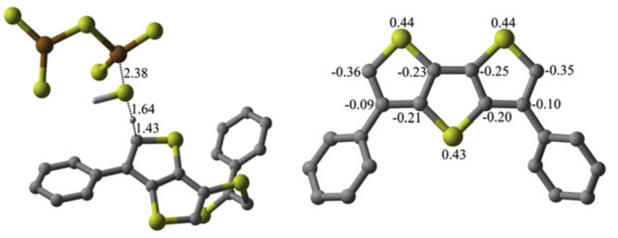


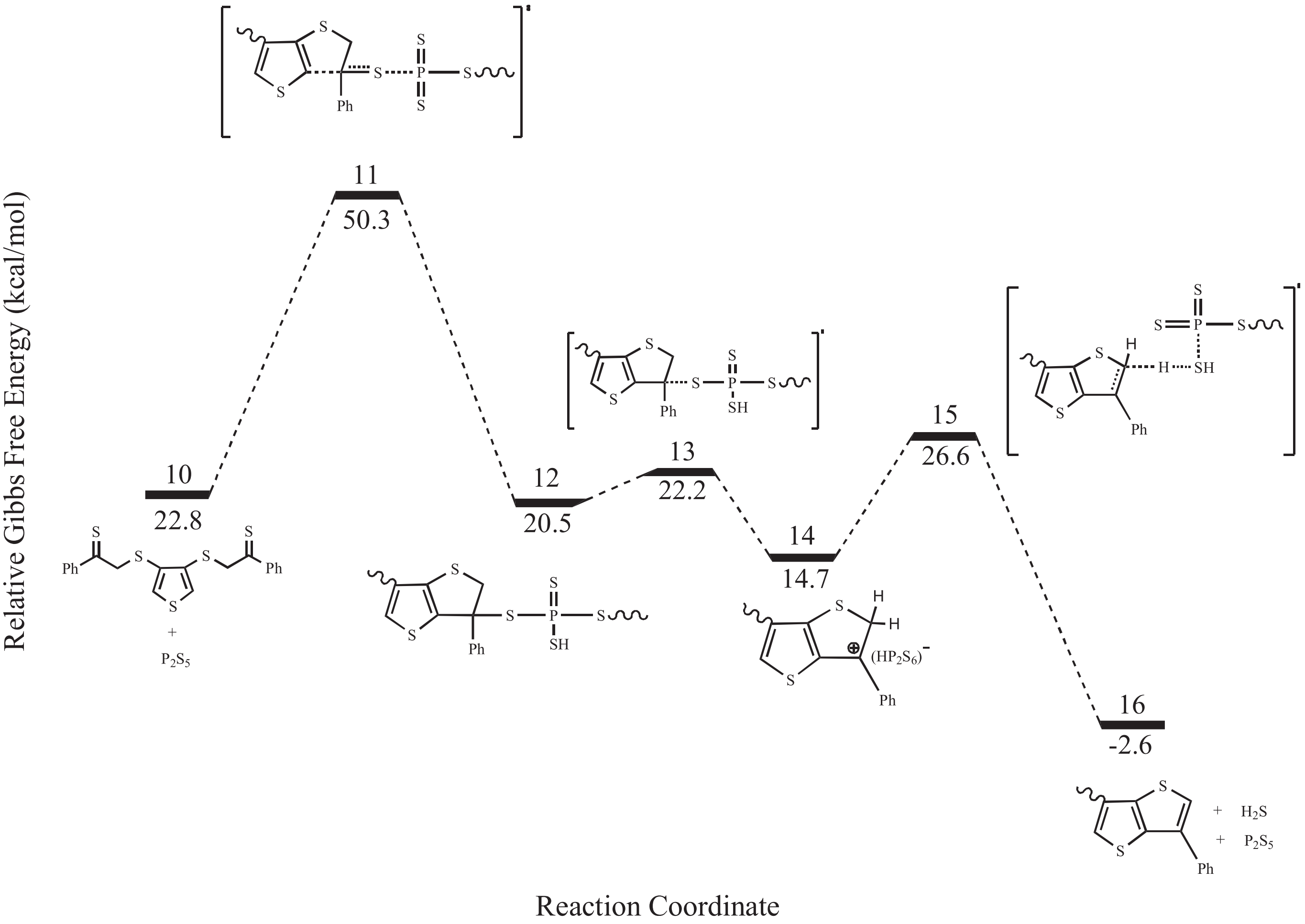
Fig. 6. 3D Representations of the transition state **15** (left) and the product **22** (right) (with NBO charges).

Once the five-membered ring in the transition state **13** was formed, the thione sulfur started to leave the compound (Fig. 5). According to NBO analysis, the intermediate **14** has an interaction of H with the sulfur lone pairs having the stabilization energy of 16 kcal/mol. The **14** is a stable molecule and it has been identified with all positive frequencies. At the final stage of the first mechanism, the cyclization of the first half of the symmetrical molecule **2** was completed when the transition complex **15** was converted to **16**. In **15** (Fig. 6), the SH moiety interacted with one of the two H atoms of the α-carbon of the newly formed S containing five-membered ring at a distance of 1.64 Å, which led to the weakening of the S⋯P bond with a distance of 2.38 Å. As shown in the product of the first cyclization reaction **16**, the H atom was abstracted by the SH group leading to the formation of H_2S, which leaves the molecule as soon as it forms. The cyclization of the second half of the molecule follows exactly the same pathway to yield the final product **22** (Fig. 6), dithieno[3,2-*b*:2′,3′-*d*]thiophene as explained in Scheme 2. The Gibbs free energy barrier values for the second cyclization steps are similar to the first cyclization (Table 1).

The second mechanism involves the direct cyclization of diketone. As a first step, the P is coordinated to O atom of the carbonyl in the transition state **23**. At the same time, the carbonyl carbon attacks the other carbon in the ring at a distance of 2.07 Å to form a new thiophene ring (Fig. 7). Energetically, this transition requires 32.4 kcal/mol Gibbs free energy to occur. The formation of the thiophene ring favors the migration of a proton to the sulfur atom.

Subsequently, in the transition state **25** (Fig. 8), HOP_2S_5 detachment requires a barrier energy of 2.0 kcal/mol. The C⋯O bond distance increases from 1.50 Å in the intermediate **24** to 1.83 Å in **25**.

The final step is the H_2S extrusion step. In the transition state **27** (Fig. 9), to obtain aromaticity in the formed fused ring, the proton is transferred to the SH moiety of HOP_2S_5 to produce H_2S. This requires 12.9 kcal/mol energy. The C⋯H, S⋯H,



Scheme 2. Energetics and mechanism of cyclization reaction of dithione (some parts of structures and second stage of cyclization are not shown because of clarity).

Table 1
Relative Gibbs free energies of the molecules in the first and second cyclization processes of the first mechanism

First cyclization		Second cyclization	
Structure	Relative Gibbs free energy (kcal/mol)	Structure	Relative Gibbs free energy (kcal/mol)
10 (Reactant)	22.8	**16** (Reactant)	−2.6
11 (TS)	50.3	**17** (TS)	22.9
12 (I)	20.5	**18** (I)	−2.0
13 (TS)	22.2	**19** (TS)	−0.8
14 (I)	14.7	**20** (I)	−6.6
15 (TS)	26.6	**21** (TS)	3.4
16 (Product)	−2.6	**22** (Product)	−27.9

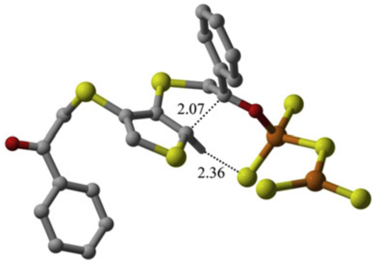


Fig. 7. 3D Representation of the transition state **23**.

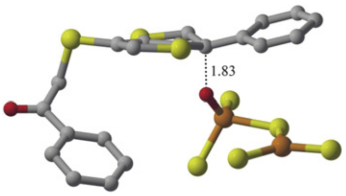


Fig. 8. 3D Representation of the transition state **25**.

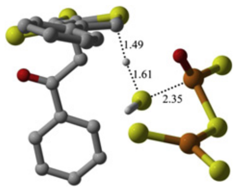
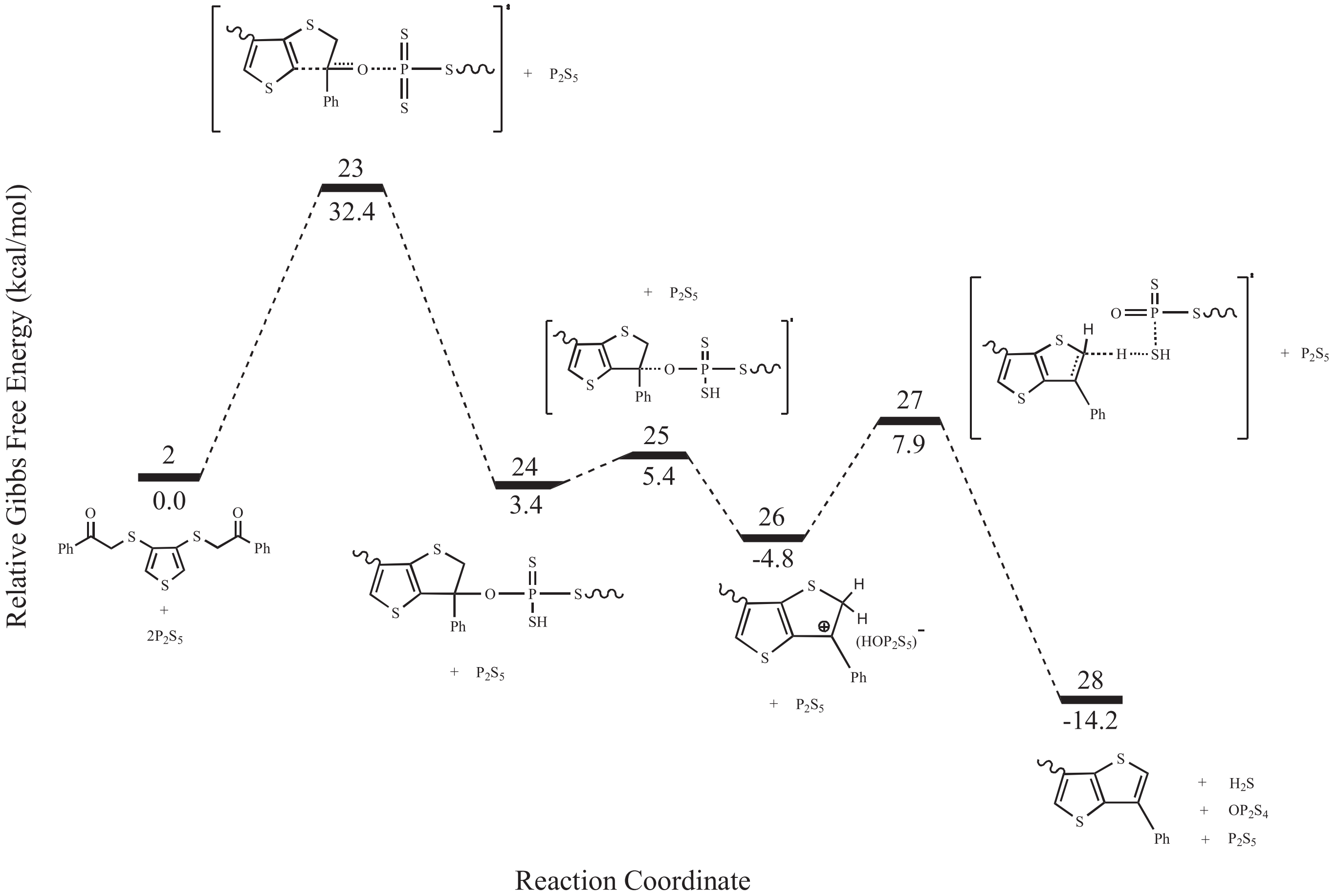


Fig. 9. 3D Representation of the transition state **27**.

Table 2
Relative Gibbs free energies of the molecules in the first and second cyclization processes of the second mechanism

First cyclization		Second cyclization	
Structure	Relative Gibbs free energy (kcal/mol)	Structure	Relative Gibbs free energy (kcal/mol)
2 (Reactant)	0.0	**28** (Reactant)	−14.2
23 (TS)	32.4	**29** (TS)	16.4
24 (I)	3.4	**30** (I)	−9.6
25 (TS)	5.4	**31** (TS)	−7.6
26 (I)	−4.8	**32** (I)	−20.4
27 (TS)	7.9	**33** (TS)	−1.9
28 (Product)	−14.2	**22** (Product)	−27.9



Scheme 3. Energetic and mechanism of cyclization reaction of diketone (some parts of structures and second stage of cyclization are not shown because of clarity).

and S···P distances are found to be 1.49, 1.61, and 2.35 Å, respectively. At the end, the formation of the first thiophene ring is completed upon release of H_2S and OP_2S_5 and the product **28** is obtained.

In the rest of the second mechanism, the ring closure of the other ketone moiety takes place. The energetics of the second ring closure are depicted in Table 2. Although the first and second barrier energies of the first and second cyclizations are quite consistent with each other, the third barrier energy of the second cyclization is 5.8 kcal/mol higher due to geometrical hindrance.

4. Conclusion

In this study, two possible mechanisms for the formation of dithieno[3,2-*b*:2′,3′-*d*]thiophene from 1,8-diketone, 4,5-

bis(benzoylmethythio)thiophene were examined thoroughly. The first mechanism consisted of transformation of the oxo groups to the thiones through the reaction with P_4S_{10}, followed by attack from the thiophene to the thiones to form DTT. The second mechanism involved an attack of the carbonyl oxygens to P_4S_{10} to form a highly electrophilic carbon atom, which then binds to the thiophene ring to form DTT. According to the calculated Gibbs free energy profiles, the highest points of the first and second pathways belong to the transition states **11** and **23**, respectively. While **11** is located at 50.3 kcal/mol, **23** is located at 32.4 kcal/mol. The energy difference of 17.9 kcal/mol favors the second mechanism as a plausible pathway for the formation of dithieno[3,2-*b*:2′,3′-*d*]thiophene. As a common point, both pathways advance in a stepwise manner. Moreover, structure **23** has been found to be the rate-determining step in the plausible pathway.

As the reaction takes place at 120 °C, the temperature effect on critical barriers, namely **11** and **23** was also investigated. Although there is an increase of about 5 kcal/mol in both barriers at 393 K, the reaction takes place at this temperature. The reason is that the reaction rate increases significantly. The ratio of the rate constants at 393 K and 298 K, k_{393}/k_{298} was found to 7.2×10^5 for the Scheme 2 and 5.5×10^2 for the Scheme 3. We believe that the 5 kcal/mol changes in the barrier energies are not significant for the reaction under consideration and the temperature effect does not change path selectivity.

Acknowledgements

We gratefully acknowledge National Center for High Performance Computing (UYBHM) (Grant no. 20422008) for the computer time provided, the TUBITAK for Grant number 105T395.

Supplementary data

Cartesian coordinates, energetic of the structures. Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.06.037.

References and notes

1. *Chem. Rev.* **2007**, Issue 4 on Organic electronics and Optoelectronics.
2. (a) Wu, W.; Liu, Y.; Zhu, D. *Chem. Soc. Rev.* **2010**, *39*, 1489; (b) Sekitani, T.; Someya, T. *Adv. Mater.* **2010**, *22*, 2228; (c) Ma, H.; Yip, H.-L.; Huang, F.; Jen, A. K.-Y. *Adv. Funct. Mater.* **2010**, *20*, 1371; (d) Horowitz, G. *Adv. Mater.* **1998**, *10*, 365; (e) Bao, Z.; Rogers, J. A.; Katz, H. E. *J. Mater. Chem.* **1999**, *9*, 1895; (f) Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99.
3. (a) Hoven, C.; Yang, R.; Garcia, A.; Heeger, A. J.; Nguyen, T. Q.; Bazan, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 10976; (b) Hou, L. T.; Huang, F.; Peng, J. B.; Wu, H. B.; Wen, S. S.; Mo, Y. Q.; Cao, Y. *Thin Solid Films* **2006**, *515*, 2632; (c) Perepichka, I. F.; Prepichka, D. F.; Meng, H.; Wudl, F. *Adv. Mater.* **2005**, *17*, 2281; (d) 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; (e) Kovac, J.; Peternai, L.; Lengyel, O. *Thin Solid Films* **2003**, *433*, 22.
4. (a) Gaudiana, R. *J. Phys. Chem. Lett.* **2010**, *1*, 1288; (b) Giridharagopal, R.; Ginger, D. S. *J. Phys.Chem. Lett.* **2010**, *1*, 1160; (c) Steim, R.; Kogler, F. R.; Brabec, C. J. *J. Mater. Chem.* **2010**, *20*, 2499; (d) Bredas, J.-L.; Durrant, J. R. *Acc. Chem. Res.* **2009**, *42*, 1689; (e) Gunes, S.; Neugebauer, H.; Sariciftci, N. S. *Chem. Rev.* **2007**, *107*, 1324; (f) Brabec, C. J.; Sariciftci, N. S.; Hummelen, J. C. *Adv. Funct. Mater* **2001**, *11*, 15; (g) Coakley, K. M.; McGehee, M. D. *Chem. Mater.* **2004**, *16*, 4533.
5. (a) Liu, D. Y.; Reynolds, J. R. *ACS Appl. Mater. Interfaces* **2010**, *2*, 3586; (b) Skotheim, T. A.; Reynolds, J. R.; *Handbook for Conducting Polymers: Processing and Applications*, 3rd ed.; CRC: Boca Raton, FL, 2007; Vol. 1, pp 9/1.
6. (a) Beaujuge, P. M.; Reynolds, J. R. *Chem. Rev.* **2010**, *110*, 268; (b) Sonmez, G.; Wudl, F. *J. Mater. Chem.* **2005**, *15*, 20.
7. (a) Barbarella, G. *Chem.—Eur. J.* **2002**, *8*, 5072; (b) Crone, B.; Dodabalapur, A.; Gelperin, A.; Torsi, L.; Katz, H. E.; Lovinger, A. J.; Bao, Z. *Appl. Phys. Lett.* **2001**, *78*, 2229; (c) Someya, T.; Katz, H. E.; Gelperin, A.; Lovinger, A. J.; Dodabalapur, A. *Appl. Phys. Lett.* **2002**, *81*, 3079.
8. Roncali, J. *Chem. Rev.* **1992**, *92*, 711.
9. (a) Cuesta, L.; Maluenda, I.; Soler, T.; Navarro, R.; Urriolabeitia, E. P. **2010**. doi:10.1021/ic101946n (b) Balaji, G.; Kale, T. S. Keerthi, A.; Della Pelle, A. M.; Thayumanavan, S.; Valiyaveettil, S. **2010**. doi:10.1021/ol1023486 (c) Rance, W. L.; Rupert, B. L.; Mitchell, W. J.; Kose, M. E.; Ginley, D. S.; Shaheen, S. E.; Rumbles, G.; Kopidakis, N. *J. Phys. Chem. C* **2010**, *114*, 22269; (d) Roncali, J.; Blanchard, P.; Frere, P. *J. Mater. Chem.* **2005**, *15*, 1589; (e) Barbarella, G.; Melucci, M.; Sotgiu, G. *Adv. Mater.* **2005**, *17*, 1581.
10. (a) Kim, O.-K.; Woo, H. Y.; Lee, K.-S.; Kim, K.-S.; Shim, K.-S.; Kim, C. Y. *Synth. Met.* **2001**, *121*, 1607; (b) Osterod, F.; Peters, L.; Kraft, A.; Sano, T.; Marrison, J. J.; Feeder, N.; Holmes, A. B. *J. Mater. Chem.* **2001**, *11*, 1625; (c) Ventelon, L.; Moreaux, L.; Mertz, J.; Blanchard-Desce, M. *Chem. Commun.* **1999**, 2055; (d) Kim, O.-K.; Lee, K.-S.; Woo, H. Y.; Kim, K.-S.; He, G. S.; Swiatkiewicz, J.; Prassad, P. N. *Chem. Mater.* **2000**, *12*, 284; (e) Tsivgoulis, G. M.; Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1119; (f) Kim, O.-K.; Fort, A.; Barzoukas, M.; Blanchard-Desce, M.; Lehn, J.-M. *J. Mater. Chem.* **1999**, *9*, 2227; (g) Ozturk, T.; Ertas, E.; Mert, O. *Tetrahedron* **2005**, *61*, 11055.
11. Ertas, E.; Ozturk, T. *Tetrahedron Lett.* **2004**, *45*, 3405.
12. (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648; (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785.
13. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T., Jr.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision D.01*; Gaussian,: Wallingford, CT, 2004.
14. (a) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154; (b) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.
15. (a) Foster, P.; Weinhold, F. *J. Am. Chem. Soc.* **1980**, *102*, 7211; (b) Reed, A.; Weinhold, E. F. *J. Chem. Phys.* **1983**, *78*, 4066; (c) Reed, A. E.; Weihstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735; (d) Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 1736; (e) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.
16. Ozturk, T.; Ertas, E.; Mert, O. *Chem. Rev.* **2010**, *110*, 3419.
17. Curphey, T. J. *J. Org. Chem.* **2002**, *67*, 6461.