PREPARATION OF α-QUINQUE- AND α-SEPTITHIOPHENES AND THEIR POSITIONAL ISOMERS

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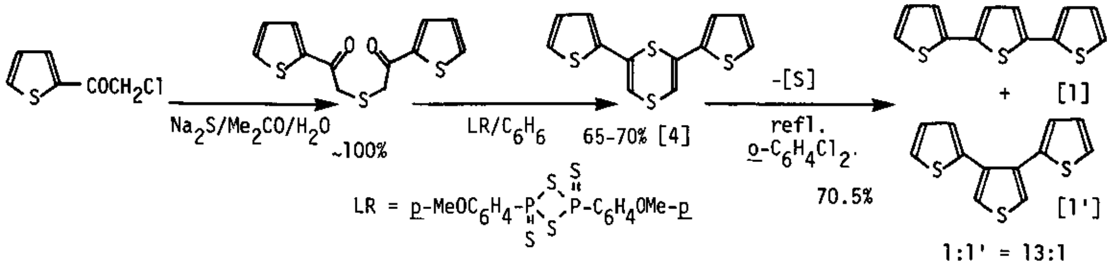
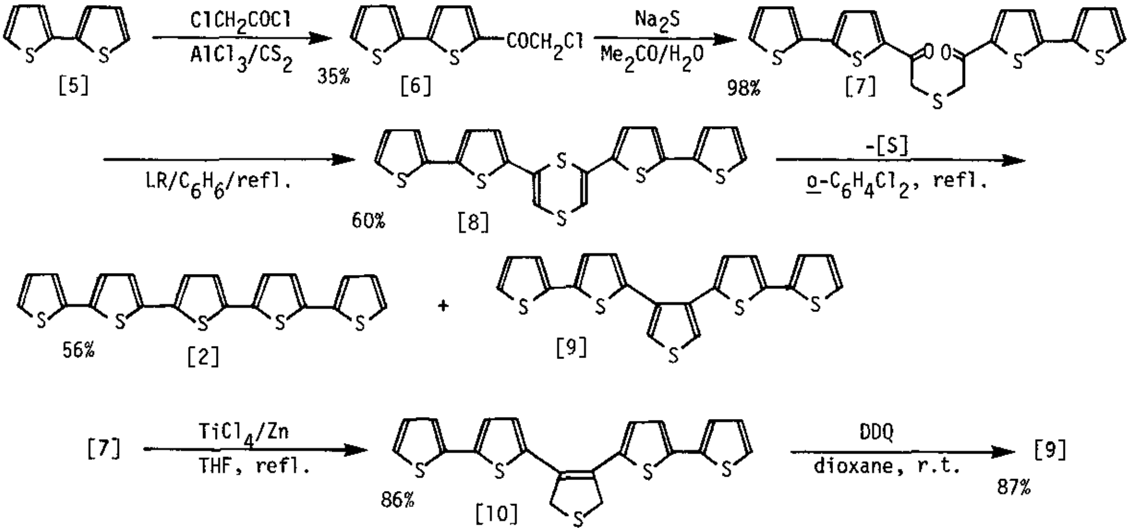
Abstract —— α-Quinque- and α-septithiophenes were synthesized in four steps starting from α-bi- and α-terthiophenes, respectively. One of positional isomers of each oligothiophene described above is also synthesized.

Recently keen interest has been focused on α-terthiophene (**1**).[1] It shows photoenhanced activity against a wide variety of organisms, among which especially notable is activity against nematodes.[2] Electrochemical polymerization of **1** affords electroconductive crystalline doped polythiophene.[3] Many synthetic methods for **1** thus have been devised.[4] In this connection it is important to devise an efficient synthetic method for higher analogs of **1**.[5] Herein we report the preparation of α-quinque- and α-septithiophenes (**2** and **3**).[1]

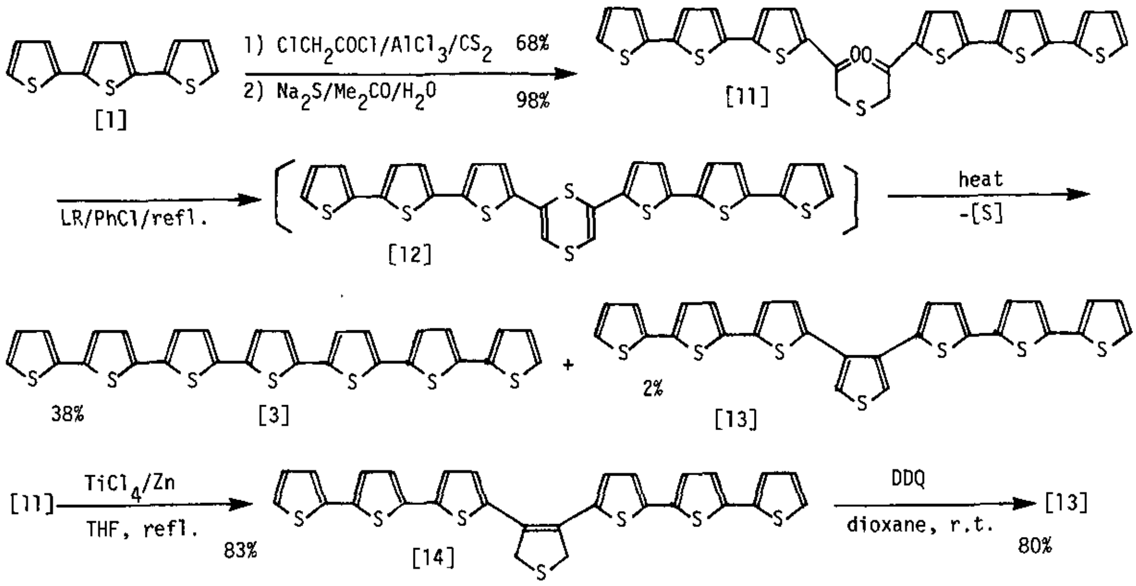
Our synthetic strategy for **2** and **3** stems from our previous finding that treatment of properly substituted diketo sulfides with Lawesson's reagent affords 2,6-diaryl-1,4-dithiins,[6] which, on being heated in boiling o-dichlorobenzene, give 2,5-diarylthiophenes, though not exclusively, with extrusion of the sulfur atom of 4-position.[7] A typical example is found in our α-terthiophene synthesis as depicted below.[4a]



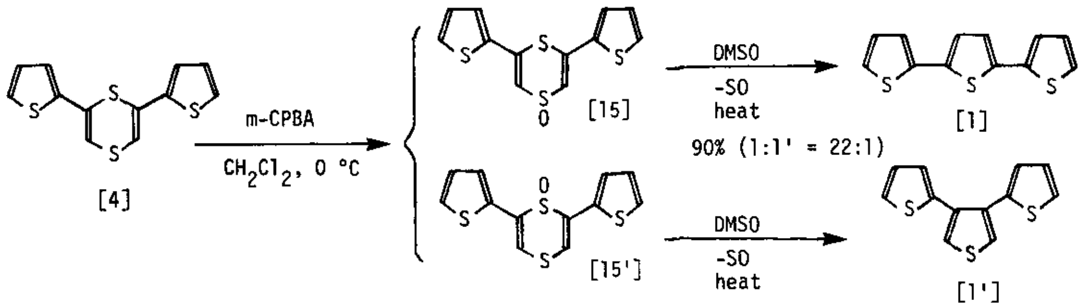
Thus the synthesis of **2** was started from chloroacetylation of α-bithiophene (**5**). The Friedel-Crafts reaction of **5** with chloroacetyl chloride catalyzed by aluminum chloride in carbon disulfide at room temperature afforded the desired chloroacetyl derivative **6** (mp 106-107 °C) in 35% yield along with 5,5'-bis(chloroacetyl)-2,2'-bithiophene (mp 239 °C) in 34% yield. Dropwise addition of an aqueous solution of sodium sulfide nonahydrate (0.5 equiv) to a stirred solution of **6** in acetone furnished the diketo sulfide **7** (mp 167-169 °C) in 98% yield. Treatment of **7** with Lawesson's reagent (2 equiv) in boiling benzene for 1 h gave the 1,4-dithiin **8** (mp>170 °C, dec) in 60% yield. Finally heating **8** in refluxing o-dichlorobenzene for 1 h afforded the expected quinquethiophene **2**, mp 253 °C (lit.,[5a] mp 253 °C), in 56% yield along with a small amount of its positional isomer **9**[1] (mp 88-89 °C). The isomeric thiophene **9** was also synthesized independently. We previously reported that treatment of diketo sulfides with a low-valent titanium reagent, prepared from titanium(IV) chloride and zinc powder in tetrahydrofuran, leads to 2,5-dihydrothiophenes in good yields.[8] Thus, treatment of **7** with the above low-valent titanium reagent in refluxing tetrahydrofuran afforded the dihydrothiophene **10** in 86% yield. Oxidation of **10** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dioxane at room temperature produced **9** in 87% yield.



α-Septithiophene **3** was prepared in a similar strategy. The Friedel-Crafts chloroacetylation of **1** afforded the chloroacetyl derivative (mp 164-166 °C) in 68% yield, which reacted with sodium sulfide to give the diketo sulfide **11** (mp 214-216 °C) in 98% yield. The sulfide **11** is slightly soluble in boiling benzene, while soluble in boiling chlorobenzene. Therefore, the reaction of **11** with Lawesson's reagent was carried out by heating the both compounds in refluxing chlorobenzene for 1 h. This directly resulted in the formation of 38% yield of **3**, mp 328 °C (lit.,[5a] mp 326-328 °C), along with 2% yield of its positional isomer **13**[1] (mp 203 °C) since the dithiin intermediate **12** loses the sulfur atom under the applied conditions. The thiophene **3** is hardly soluble in organic solvents and therefore precipitated from the reaction mixture and was purified by sublimation.[9] The isomeric thiophene 13 was also independently synthesized. Treatment of the sulfide 11 with the foregoing titanium reagent furnished the dihydrothiophene 14 in 83% yield, which was converted to 12 by treatment with DDQ in dioxane in 80% yield.



Finally effort was made to improve the yield and selectivity in the conversion of 2,6-di-(2-thienyl)-1,4-dithiin (4) to 1. It is known that monosulfoxides of 1,4-dithiins thermally lose sulfur monoxide to produce the corresponding thiophenes.[10] Thus, to an ice-cooled solution of 4 in methylene chloride was added m-chloroperoxybenzoic acid (m-CPBA) until 4 is completely consumed (ca. 1.5 equiv of m-CPBA was used). When this mixture was warmed and then heated under reflux, a mixture of 1 and its isomeric thiophene 1' was formed in a yield of less than 50% along with a considerable amount of the starting dithiin 4. This suggests that the sulfur monoxide produced from sulfoxide 15 (15') reduces 15 (15') to give 4 and sulfur dioxide.[10,11] Therefore, in order to eliminate this reaction by scavenging sulfur monoxide, a large excess of dimethyl sulfoxide was



added to the mixture after the completion of the oxidation by m-CPBA, and then the resulting mixture was heated to reflux. This resulted in the formation of a mixture of **1** and **1'** in a ratio of 22:1 in 90% yield. The predominant formation of **1** shows that the *sulfur atom of 4-position is* preferentially oxidized to give **15** by steric and/or electronic reasons. The procedure described above provides a revised method for conversion of **4** to **1**.

REFERENCES AND NOTES

1. IUPAC names of oligothiophenes **1**, **2**, **3**, **9**, and **13** are 2,2':5',2"-terthiophene, 2,2':5',2":5",2"':5"',2""-quinquethiophene, 2,2':5',2":5",2"':5"',2"":5"",2""':5""',2"""-septithiophene, 2,2':5',3":4",2"':5"',2""-quinquethiophene, and 2,2':5',2":5",3"':4"',2"":5"",2""':5""',2"""-septithiophene, respectively.
2. For example, see J. Kagan and S. K. Arora, *J. Org. Chem.*, 1983, **48**, 4317.
3. Y. Yumoto and S. Yoshimura, *Synthetic Metals*, 1986, **13**, 185.
4. (a) J. Nakayama, Y. Nakamura, T. Tajiri, and M. Hoshino, *Heterocycles*, 1986, **24**, 637.
   (b) J. Kagan and S. K. Arora, *Tetrahedron Lett.*, 1983, **24**, 4043 and references cited therein.
5. (a) α-Ter-, α-quater-, α-quinque-, α-sexi-, and α-septithiophenes were first obtained as by-products in the preparation of α-bithiophene; W. Steinkopf, R. Leitsmann, and K. H. Hoffmann, *Justus Liebigs Ann. Chem.*, 1941, **546**, 180. See also W. Steinkopf, H. -J. v. Petersdorff, and R. Gording, *Justus Liebigs Ann. Chem.*, 1937, **527**, 272.
   (b) For other syntheses of higher analogs of **1**, see T. Kauffmann, *Angew. Chem.*, 1974, **86**, 321, J. Kagan and S. K. Arora, *Heterocycles*, 1983, **20**, 1937, and refs 2 and 4b.
6. J. Nakayama, H. Motoyama, H. Machida, M. Shimomura, and M. Hoshino, *Heterocycles*, 1984, **22**, 1527.
7. J. Nakayama, M. Shimomura, M. Iwamoto, and M. Hoshino, *Heterocycles*, 1985, **23**, 1907.
8. J. Nakayama, H. Machida, and M. Hoshino, *Tetrahedron Lett.*, 1985, **26**, 1981. See also J. Nakayama, H. Machida, R. Saito, and M. Hoshino, *Tetrahedron Lett.*, 1985, **26**, 1983.
9. Prior to purification by sublimation, the precipitate obtainable from the reaction mixture was washed with 2N-NaOH in order to remove materials formed from Lawesson's reagent.
10. H. H. Szmant and L. M. Alfonso, *J. Am. Chem. Soc.*, 1957, **79**, 205.
11. Recently Kobayashi proposed a mechanism involving bimolecular disproportionation for the decomposition of 2,5-diphenyl-1,4-dithiin-1-oxide leading to 2,4-diphenylthiophene, 2,5-diphenyl-1,4-dithiin, and sulfur dioxide; K. Kobayashi and K. Mutai, *Phosphorus and Sulfur*, 1985, **25**, 43.

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