

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

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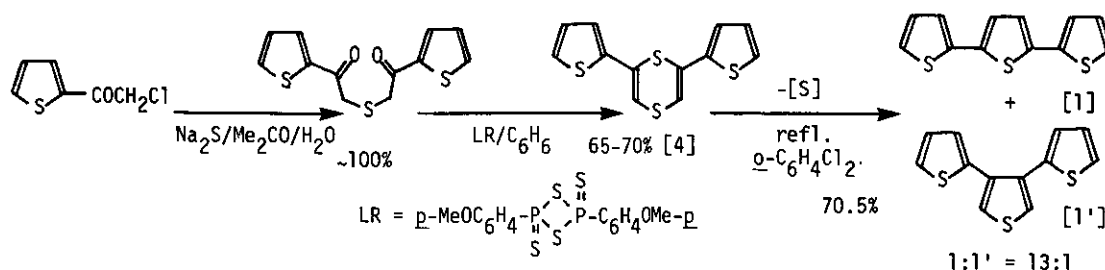
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Abstract — α -Quinque- and α -septithiophenes were synthesized in four steps starting from α -bi- and α -terthiophenes, respectively. One of positional isomers of each oligothiophene described above is also synthesized.

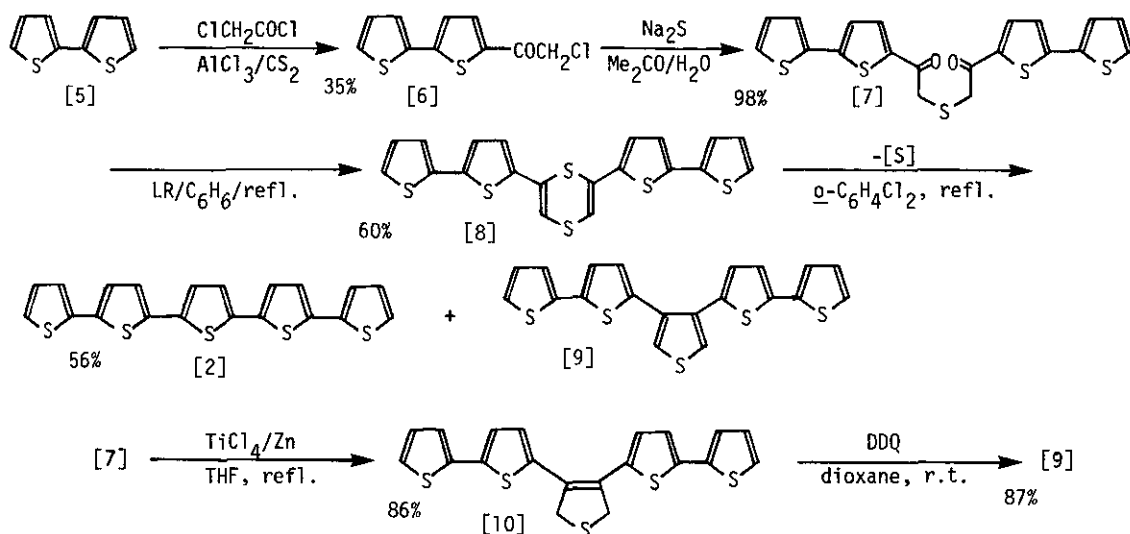
Recently keen interest has been focused on α -terthiophene (**1**).¹ It shows photoenhanced activity against a wide variety of organisms, among which especially notable is activity against nematodes.² Electrochemical polymerization of **1** affords electroconductive crystalline doped polythiophene.³ 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}



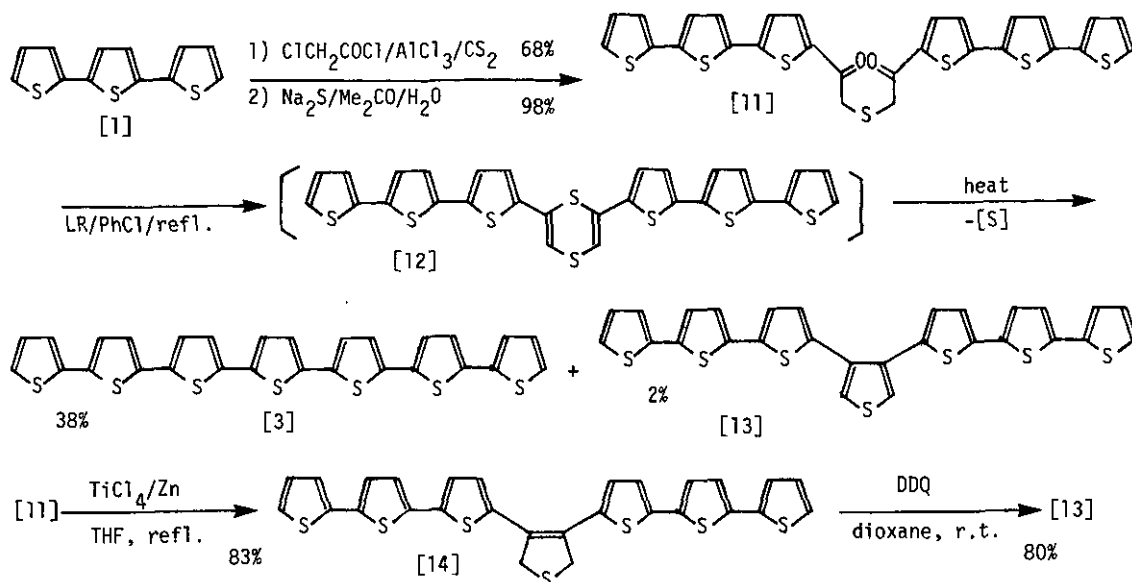
Thus the synthesis of **2** was started from chloroacetylation of α -bithiophene (**5**). The Friedel-Crafts reaction of **5** with chloroacetyl chloride catalyzed by aluminum chloride in carbon disulfide at room temperature afforded the desired chloroacetyl derivative **6** (mp 106-107 °C) in 35% yield

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.

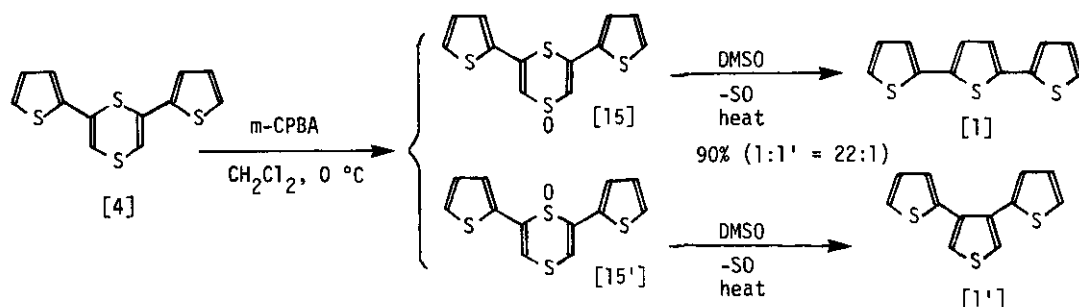


α -Septithiophene **3** was prepared in a similar strategy. The Friedel-Crafts chloroacetylation of **1** afforded the chloroacetyl derivative (mp 164-166 °C) in 68% yield, which reacted with sodium sulfide to give the diketo sulfide **11** (mp 214-216 °C) in 98% yield. The sulfide **11** is slightly 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""-quiquethiophene, 2,2':5',2":5",2""':5""',2""":5""",2""":5""",2""":5"""-septithiophene, 2,2':5',3":4",2""':5""',2"""-quiquethiophene, and 2,2':5',2":5",3""':4""',2""":5""",2""":5""",2""":5"""-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.

Received, 6th January, 1987