

THE SYNTHESIS OF ALPHA-THIOPHENE OLIGOMERS VIA ORGANOBORANES

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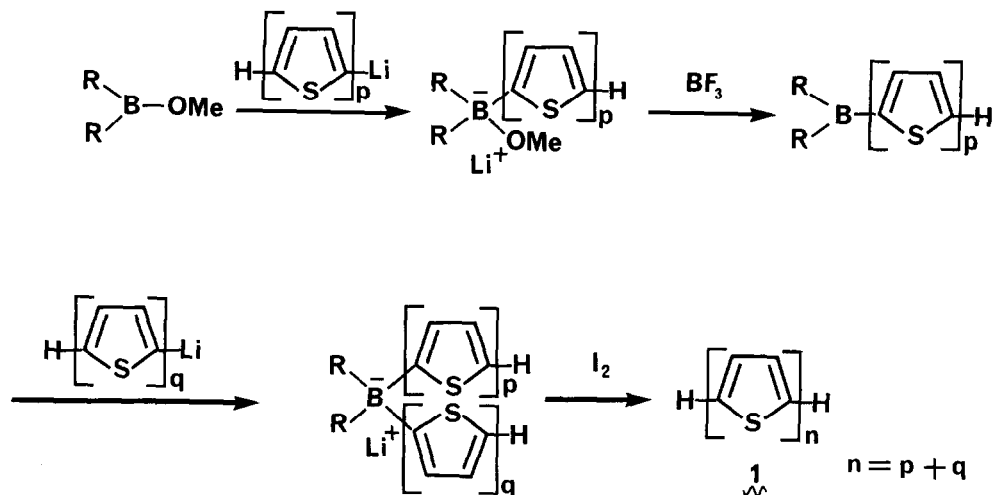
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Summary - Oligomers containing from 2 to 6 thiophene units attached by their 2 and 5 positions were synthesized unambiguously by iodine oxidation of a suitable ate complex obtained by stepwise reactions of 9-BBN with methanol, a 2-lithiothiophene, boron trifluoride etherate, and a second 2-lithiothiophene. This is a one-pot procedure, carried out under nitrogen between -80°C and 0°C .

No general procedures are presently available for the efficient synthesis of all the individual alpha-thiophene oligomers. Minuscule yields of oligomers possessing 2 to 7 thiophene units have been obtained from the reaction of 2-iodothiophene with copper,¹ or from mixed coupling reactions of 2-iodothiophene with either 5-iodo-2,2'-bithienyl or 5,5'-diiodo-2,2'-bithienyl.² These reactions cannot be optimized to give exclusively, or even predominantly, one single product. More recently the biologically active α -terthienyl (1 , $n = 3$) was synthesized in good yield with reactions which did not produce any of the related oligomers, namely the cyclization of 1,4-di-(2'-thienyl)-1,3-butadiyne with sodium sulfide,^{3,4} or that of 1,4-di-(2'-thienyl)-1,4-butanedione with hydrogen sulfide,^{5,6} or a modified Wittig reaction.⁷ The synthesis of the other individual members in this series of polythiophenes has not received the same attention.

We now report that unsubstituted 2,5-thiophene oligomers can be prepared individually in greatly improved yields with organoborane reagents. This strategy extends to the field of heterocyclic chemistry the selective coupling reactions via organoboranes known with aliphatic and aromatic moieties.⁸ The

reaction sequence is outlined in Scheme 1.



The procedure is very flexible, and allows the choice of reagent in each of the steps in which a thiophene is introduced. Therefore, either identical or different 2-lithiothiophenes may be used. As the size of the oligomer to be synthesized increases, the number of different possibilities for its synthesis likewise increases. All the alternatives are equally easy to put into practice, and depend only upon the availability of the smaller oligomers to be used as starting materials.

This stepwise approach is illustrated here with the synthesis of several oligomers. The satisfactory yields with which particularly the larger ones were obtained testify to the value of the procedure.

In a representative example, 9-BBN (6.100 g, 50 mmol) was converted into the B-methoxy derivative by treatment with methanol (1.600 g, 50 mmol) in 50 ml of THF. A solution of 2-lithiothiophene in 50 ml of dry THF was prepared by reacting thiophene (8.400 g, 100 mmol) with lithium diisopropylamide (from 50 mmol of n-butyllithium and 5.050 g, 50 mmol, of diisopropylamine), and was added at -78°C . After 1 hr, the ate complex was neutralized with boron trifluoride etherate (9.400 g, 66 mmol) at -78°C , warmed to room temperature, and cooled again to -78°C . The mixture was kept for 1 hr at this temperature, and a

second equivalent of 2-lithiothiophene was added as above. After 30 min, the complex was treated with iodine (12.800 g, 50 mmol) in 25 ml of THF for 1 hour at -78°C . The mixture was allowed to warm up to room temperature before being extracted with 15 ml of 3 M NaOH, and worked up with 20 ml each of 30% H_2O_2 and 3 M NaOH. The whole procedure took place under dry nitrogen atmosphere in a single flask. After extraction with ether, the organic layer was washed with water, dried over K_2CO_3 , concentrated, and distilled under reduced pressure to give unreacted thiophene (8.000 g, 95 mmol) and 2,2'-bithienyl (6.700 g, 40.36 mmol, 80.7% yield based on LDA); mass spec: m/e 166 (M^+ , 100%); nmr (CDCl_3): 6.67 (t, $J = 4$ Hz, 2 H) and 7.30 ppm (d, $J = 4$ Hz, 4 H). No higher thiophene oligomers were detected by tlc analysis of the crude reaction mixture.

2,2'-Bithienyl could be lithiated and coupled with 2-lithiothiophene to produce, in 37% yield after recrystallization from ethanol, α -terthienyl (1 , $n = 3$); mp $95\text{--}95.5^{\circ}\text{C}$ (lit mp $94\text{--}95^{\circ}\text{C}^1$); nmr (CDCl_3) 7.0–7.25 (m); mass spec m/e 248 (M^+ , 100%).

α -Quaterthienyl (1 , $n = 4$) was formed by coupling either bithienyl with bithienyl (48% yield), or thiophene with α -terthienyl (50% yield). After recrystallization from 95% EtOH, it had mp $211\text{--}212^{\circ}\text{C}$, (lit mp $210\text{--}212^{\circ}\text{C}^1$); mass spec m/e 330 (M^+ , 100%); nmr ($\text{DMSO-}d_6$) 6.85–7.60 ppm (m).

Two of the three possible alternatives were tested for the synthesis of α -quinquethienyl (1 , $n = 5$), utilizing the coupling of 2,2'-bithienyl with α -terthienyl (55% yield), and that of thiophene with α -quaterthienyl (53% yield). The product had been recrystallized from dioxane-water, and had mp $257\text{--}258^{\circ}\text{C}$ (lit mp $256\text{--}257^{\circ}\text{C}^1$); mass spec m/e 412 (M^+ , 100%).

The attractive α -sexithienyl (1 , $n = 6$) was obtained by coupling α -terthienyl with α -terthienyl (45% yield), or 2,2'-bithienyl with α -quaterthienyl (59% yield). It had been purified by sublimation, and had mp $303\text{--}305^{\circ}\text{C}$ (lit mp 304°C^1); mass spec m/e 494 (M^+ , 100%).

The syntheses illustrated here are particularly simple to execute. In addition to producing individual polythiophenes cleanly and with satisfactory

yields, they have one important advantage over procedures which utilize 2-iodothiophenes, in that the initial functionalization avoids the use of the expensive mercuric oxide traditionally required for the iodination step.⁹

Because individual alpha-thiophene oligomers are now readily available,¹⁰ further biochemical and chemical investigations will become possible.

We intend to study the scope of the present method with α -substituted thiophenes, and to explore its potential for coupling thiophenes through the beta positions, for coupling other heterocycles, and for obtaining molecules having different types of heterocycles attached to each other.

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