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Solvent-Free, Microwave-Assisted Synthesis of Thiophene Oligomers via Suzuki Coupling

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The purpose of this study was to obtain a rapid, efficient, and environmentally friendly methodology for the synthesis of highly pure thiophene oligomers. The solvent-free, microwave-assisted coupling of thienyl boronic acids and esters with thienyl bromides, using aluminum oxide as the solid support, allowed us to rapidly check the reaction trends on changing times, temperature, catalyst, and base and easily optimize the experimental conditions to obtain the targeted product in fair amounts. This procedure offers a novel, general, and very rapid route to the preparation of soluble thiophene oligomers. Thus, for example, quaterthiophene was obtained in 6 min by reaction of 2-bromo-2,2′-bithiophene with bis(pinacolato)diboron (isolated yield 65%), whereas quinquethiophene was obtained in 11 min by reaction of dibromoterthiophene with thienylboronic acid (isolated yield 74%). The synthesis of new chiral 2,2′-bithiophenes is reported. The detailed analysis of the byproducts of some reactions allowed us to elucidate a few aspects of reaction mechanisms. While the use of microwaves proved to be very convenient for the coupling between conventional thienyl moieties, the same was not true for the coupling of thienyl rings to thienyl-*S*,*S*-dioxide moieties. Indeed, in this case, the targeted product was obtained in low yields because of the competitive, accelerated, Diels−Alder reaction that affords a variety of condensation products.

Introduction

Thiophene oligomers have been proven to be important multifunctional materials.[1] Among their most useful properties are good charge mobility[2] and efficient fluorescence.[3] Thiophene oligomers are chemically very stable and easy to functionalize.[4] New dendritic molecular structures have recently been described[5] from which it is reasonable to expect different self-assembly modalities and properties. Thiophene oligomers are currently studied for application in thin film transistors,[6] electroluminescent diodes,[7] lasers,[8] and photovoltaic cells[9] and as fluorescent markers for biological molecules.[10]

Unfortunately, only very few of these compounds are commercial, the synthesis of the most appealing of them is not easy, and the procedures for purification up to the degree useful for applications in electronics or biomedical diagnostics are tedious and time-consuming. Moreover, the two most general procedures used to assemble functionalized thienyl rings for the regiospecific synthesis of thiophene oligomers—namely, the Stille[11] and the Suzuki[12] reactions, based on the coupling of thienyl metalated reagents with thienyl halogenides or triflates in the presence of palladium or nickel catalysts—are critically dependent on functionalization types, steric factors, solvent, temperature, and the catalyst. To the present state of knowledge of reaction mechanisms, the best experimental conditions are not easy to predict and have to be investigated case by case.

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In consequence, there is great need for more expedient and efficient synthetic methodologies for the preparation of thiophene oligomers allowing the best experimental conditions to be rapidly decided for the preparation of the targeted oligomer, minimize the formation of byproducts, and simplify the purification procedures, in particular by reducing the huge amounts of organic solvents needed to purify the oligomers by silica gel chromatography.

In the past few years, great effort has been devoted to the study of the Suzuki reaction for the preparation of a variety of conjugated molecules, including porphyrins and phthalocyanines.[13] While in the Stille reaction aryl stannanes are employed, in the Suzuki reaction the less toxic boronic acids or esters are used. Since boronic acids and esters are not very reactive, the efficiency of the Suzuki reaction has been improved by means of more efficient catalysts,[14] the presence of bases,[15] the accurate choice of solvents,[16] and microwave activation.[17a−c]

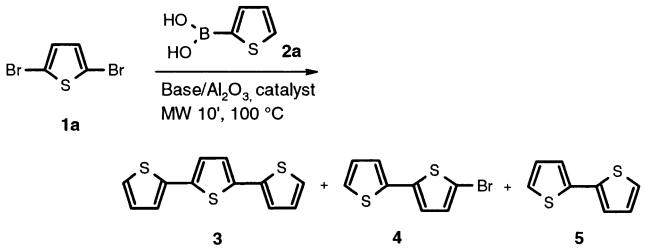
However, while there are many papers in the literature concerning the Suzuki reaction with phenyl boronic derivatives and phenyl halogenides, much less attention has been devoted to the Suzuki reaction with thienyl derivatives, although, as mentioned above, this reaction was found to be useful in the preparation of thiophene oligomers and polymers.[13]

Recently, it has been reported that the use of an alumina/potassium fluoride mixture without solvent but with microwave activation is very effective in palladium-catalyzed reactions, in particular in the Suzuki coupling of phenyl iodides with phenylboronic acids.[18] The interest in this procedure stems from the absence of solvents and the possibility to recover the reaction products by simple filtration, while the catalyst and the salts formed in the course of the reaction remain on the solid support. Thus, when the products are eluted with poorly polar solvents, they result to be free of metals.[18b]

We decided to apply this procedure to the synthesis of thiophene oligomers, some of which are semiconductors often affected by the presence of what has been named "unintentional doping", i.e., the presence of metallic ions introduced by way of chemical synthesis that alter the intrinsic charge transport properties of the material.[19]

We are reporting here initial results, showing that indeed the solvent-free microwave-assisted Suzuki synthesis is a rapid and expedient way for the preparation of highly pure thiophene oligomers.

SCHEME 1. Solvent-Free, Microwave-Assisted Synthesis of 2,5′:2′,5″-Terthiophene 3



Results

The importance of alumina in favoring the reaction of adsorbed organic molecules has been known for a long time.[20] An important factor in obtaining good yields is to have a nice dispersion of reagents and catalyst on the solid support. To this purpose, we added to the mixture of Al_2O_3/reagents/catalyst a few drops of methanol, which were subsequently evaporated under reduced pressure. We carried out all reactions in air at constant temperature using the reactor of our commercial microwave system (see the Experimental Section). A few attempts to use Fluorisil instead of alumina as the solid support were unsuccessful. In some cases the reaction rate was accelerated by addition of a few drops of aqueous KOH.

The experimental conditions were first optimized for the preparation of α-conjugated, unsubstituted terthiophene (section I) and then checked in the preparation of unsubstituted quater- and quinquethiophene (section II), of a dimethylated sexithiophene (section III), of new chiral bithiophenes (section IV), and of oligomers containing the thienyl-*S*,*S*-dioxide moiety (section V). A few experiments to elucidate the reaction mechanisms were also carried out (section VI).

(I) Catalyst and Base Optimization. The optimization of reaction conditions was carried out using as the model reaction the Suzuki coupling of 2,5-dibromothiophene, **1a**, with 2-thiophene boronic acid, **2a**, both of which are commercial products. The target of the reaction is 2,2′:5′,2″-terthiophene, **3**, whose formation is always accompanied by variable amounts of byproducts **4** and **5**, as shown in Scheme 1. All catalysts employed were commercial and used as received.

The relative amounts of **3**, **4**, and **5** formed using different catalysts and bases and estimated by GC/MS analysis are reported in Table 1.

Table 1 shows how crucial the choice of the catalyst is in determining the trend of the reaction. Indeed, there is no formation at all of terthiophene when $Pd_2(dba)_3$ or $PdCl_2$ is used as the catalyst, whereas this compound is formed in 60% isolated yield when commercial $PdCl_2$-(dppf) is employed (entry 5). On the other hand, the attempt to prepare in situ $PdCl_2$(dppf) was unsuccessful, probably due to the scarce formation of the catalyst itself in the experimental conditions used.

Also extremely important is the choice of the base, as shown, for example, by the fact that CsF, one the most used bases in the Suzuki reaction, is less effective than KF for the formation of trimer **3** (compare entries 7 and 5). Apparently, it is the type of base that is important

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TABLE 1. Catalyst and Base Optimization for the Preparation of Terthiophene 3 from 2,5-Dibromothiophene 1a and 2-Thiopheneboronic Acid 2a (Scheme 1)

entry[a]	catalyst	base/Al_2O_3	%[b] (**1a**/**3**/**4**/**5**)
1	$Pd(PPh_3)_4$	KF	(54/−/6.5/3.5)[c]
2	$Pd_2(dba)_3$	KF	(100/−/−/−)
3	$PdCl_2$	KF	(100/−/−/−)
4	$Pd(PPh_3)_2Cl_2$	KF	(81/2/11/2.5)
5	$PdCl_2$(dppf)	KF	(4/73/1/22)
6	$PdCl_2$(dppf) in situ	KF	(61/17/12/10)
7	$PdCl_2$(dppf)	CsF	(16/50/−/34)
8	$PdCl_2$(dppf)	KOtBu	(100/−/−/−)

[a] 1 equiv of **1a**, 2.5 equiv of **2a**, 5 mol % of catalyst, 5 equiv of KF, and 150 mg of Al_2O_3, T = 100 °C. [b]Conversion estimated by GC/MS analysis. [c]Byproducts from phosphine reaction.

TABLE 2. Reaction Conditions[a] and Yields for the Synthesis of Terthiophene (3), Quaterthiophene (7), and Quinquethiophene (12) According to the Patterns of Scheme 2

halide	boronic derivative (equiv)	product	time (min)	T_{max} (°C)	isolated yield (%)
1a	**2a** (2.5)	**3**	10	100	60
1b	**2a** (2.5)	**3**	10	100	10
6[b]	**2a** (5)	**7**	4	80	81
8	**9** (0.5)	**7**	2	80	40
4	**10** (0.5)	**7**	6	80	65
11[c]	**2a** (4.4)	**12**	11	70	74
1a	**13a** (2.0)	**12**	10	90	no reaction
	13b (2.0)	**12**	10	90	28

[a] 5 mol % of catalyst, 5−10 equiv of KF. [b]0.2 mL of KOH added. [c]0.4 mL of KOH added.

rather than its strength, as indicated by the fact that when KOtBu is used, only the starting materials are recovered (entry 8).

Apparently, one never gets rid of byproducts **4** and **5**, whose relative amounts are also dependent on reaction conditions. Since bithiophene **5** is easier to separate by silica gel chromatography than its monobrominated counterpart **4**, the conditions of entry 5 lead also to the mixture from which terthiophene **3** is more easily recovered.

Also very important appears to be the halide chosen for the reaction. Indeed, when the preparation of terthiophene was carried out using 2,5-diiodothiophene (**1b**), instead of the dibromo counterpart (**1a**), the yield dropped to 17% (see below, Table 2).

In the subsequent work we then used mainly mono and dibromo starting materials, $PdCl_2$(dppf) as the catalyst and KF as the base, with the aim of fixing the conditions for a reasonable standardization of the synthetic procedures.

(II) Synthesis of Unsubstituted Quaterthiophene and Quinquethiophene. The different reaction patterns employed for the preparation of α-conjugated quinque- and sexithiophene are summarized in Scheme 2, whereas Table 2 shows the isolated yields for the different patterns and gives, for comparison, also the isolated yields of terthiophene prepared according to the modalities described above.

The results reported in Table 2 show that the careful optimization of the reaction conditions allows obtaining in a few minutes high yields and mixtures that are easy to separate into the different components. Isolated yields of 60−80% can be obtained by choosing the appropriate boron and halogen derivatives. These yields are highly reproducible and competitive with the best yields already reported for quaterthiophene **7** and quinquethiophene **12**.[21]

Our data show that in terms of reaction yields, facility of purification procedures, and solvent saving, it is much better to grow the oligomer size by adding the thiophene rings one at a time rather than reacting longer building blocks. For example, as shown in Table 2, quinquethiophene **12** is obtained in high yield (74% isolated yield) when dibromoterthiophene is reacted with thiopheneboronic acid (**2a**), whereas the yield is drastically reduced (28% isolated yield) when dibromothiophene (**1a**) is reacted with bithiopheneboronic ester (**13b**). In part, this is due to the fact that, in the former case, **12** is more easily purified from the major byproduct of the reaction (bithiophene, generated by homocoupling of thiopheneboronic acid). In the latter case, the major byproduct of the reaction is quaterthiophene, which is less easily separated from the desired quinquethiophene.

Table 2 also shows that no formation of **12** was observed when bithiopheneboronic acid **13a** was used instead of the corresponding ester. We ascribe this result to the greater stability of boronic esters compared to boronic acids.

The synthesis of quaterthiophene, pattern *2*, is of some interest. Indeed, the reaction of 5-bromo-2,2′-bithiophene, **4**, with bis(pinacolato)diboron, **10**, affords quaterthiophene in a few minutes and in good isolated yield (65%).

Bis(pinacolato)diboron is generally used for borylation of aryl halides[22a] and for the one-pot synthesis of biaryls through the in situ formation of aryl boronates.[22b] We found that this reaction works well with thienyl, bithienyl, and terthienyl monobromides, leading to the rapid formation of bi-, quater-, and sexithiophene in fair amounts. Since sexithiophene is insoluble, the methodology described here and the reaction workup had to be modified; then the results concerning this important semiconductor will be reported in a separate paper.

Since it is known that aryl halides in the presence of palladium catalysts may give rise to reductive coupling,[23] the question arose as to whether and to what extent the formation of even number oligothiophenes was the result of the palladium-promoted homocoupling reaction rather than of the two-step borylation-cross-coupling reaction.

Experiments carried out in the absence of bis(pinacolato)diboron in the same experimental conditions showed that the palladium-promoted homocoupling of thienyl halides amounted to a few % at best.

(III) Synthesis of 4″,3‴-Dimethyl-2,2′:5′,2″:5″,2‴:5‴,2⁗:5⁗,2⁗′:5⁗′,2⁗′′-sexithiophene (19). The importance of

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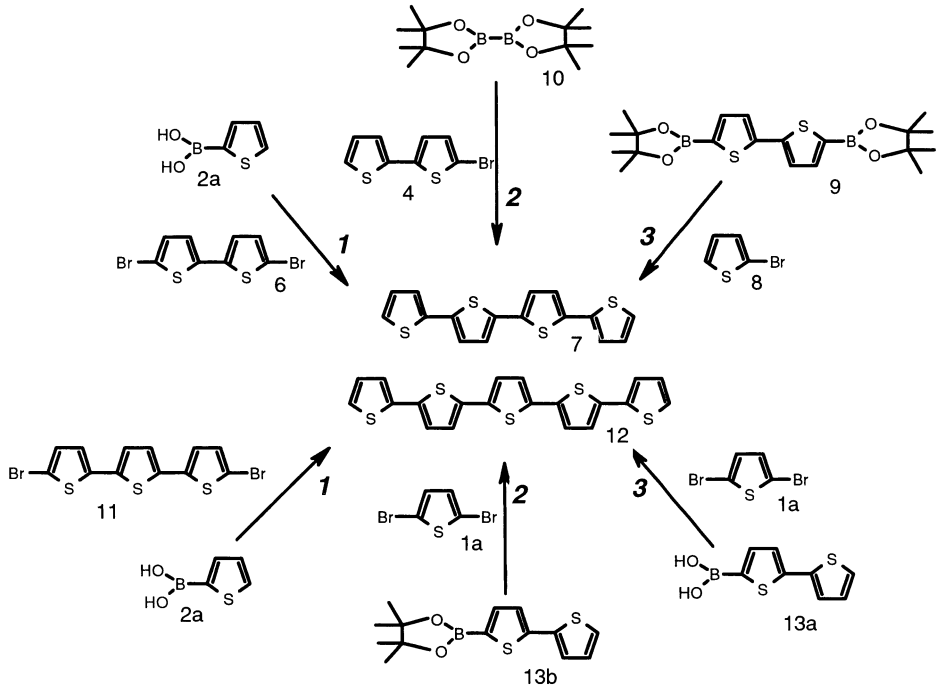
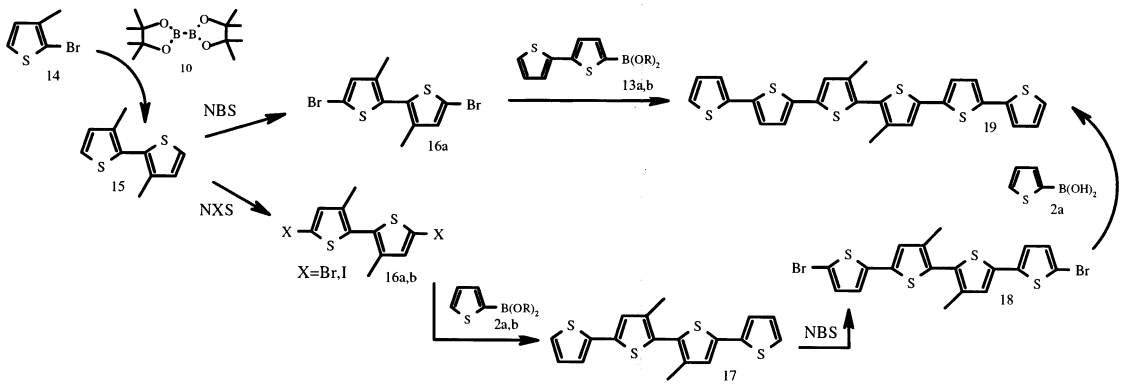
SCHEME 2. Solvent-Free, Microwave-Assisted Synthesis of Quaterthiophene (7) and Quinquethiophene (12)



SCHEME 3. Solvent-Free, Microwave-Assisted Synthesis of Sexithiophene 19



this compound stems from the fact that it is a soluble thienyl hexamer, which in the solid state is nearly planar, self-assembles in parallel layers, and displays good charge transport properties.[24a]

We were first able to synthesize this compound in very low yield by means of the Stille coupling;[24a] then higher yields were obtained by means of the Suzuki coupling and the use of microwaves in solution.[24b] It was after having obtained these results that we become aware of the usefulness of microwaves in the synthesis of thiophene oligomers.

The present methodology allows hexamer **19** to be obtained in much higher yields than before, since all steps afford high yields when one ring is added at a time and the diiodo derivative **16b** is employed instead of the corresponding dibromo derivative **16a** (see Scheme 3 and Table 3).

TABLE 3. Reaction Conditions[a] and Yields for the Synthesis of Sexithiophene 19 (Scheme 3)

halide	boronic derivative (equiv)	product	time (min)	T_{max} (°C)	isolated yield (%)
14	**10** (0.5)	**15**	6	80	70
16a	**2a** (R = H, 3.5)	**17**	32	80	34
	2b (R = pinacol, 2.2)	**17**	3	80	18
16b	**2a** (4.4)	**17**	7	70	85
	2b (2.2)	**17**	3	70	90
18[b]	**2a** (4.4)	**19**	30	80	73
16a	**13a** (R = H, 2.5)	**19**	10	90	no reaction
16a	**13b** (R = pinacol, 2.5)	**19**	3	90	36

[a] 5 mol % of catalyst, 10 equiv of KF. [b] 0.5 mL of KOH added.

As shown in the table, the reaction of 5,5′-diiodo-3,3′-dimethyl-2,2′-bithiophene, **16b**, with thiophene boronic derivatives affords quaterthiophene **17** in much higher yields than the corresponding dibromo derivative **16a**, contrary to what was observed in the preparation of

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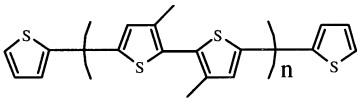


FIGURE 1.

terthiophene, where the dibromo derivative worked much better than the diiodo one.

The reaction of 5,5′-dibromo-3,3′-dimethyl-2,2′-bithiophene, **16a**, with thienylboronic acid or ester leads to the formation of quaterthiophene **17** in low yield. In this case, the main reaction products are a variety of oligomers containing repeated dimethylbithiophene subunits (see Figure 1) and terminating with an unsubstituted thienyl ring, as already observed when thienylstannane was used (Stille coupling).[24a] Tetramethylsexithiophene ($n = 2$) and hexamethyloctathiophene ($n = 3$) were separated in sizable amount. This reaction is highly reproducible and can be viewed as an expedient way to prepare in one pot regioregular head-to-head methyl-substituted sexi- and octathiophenes, which are easily separated by chromatography.

(IV) Synthesis of Chiral 2,2′-Bithiophenes. One of the objectives of our current research work is to investigate the influence of chirality on the self-assembly properties of thiophene oligomers. Thus, we have checked the new methodology presented here for the synthesis of the two enantiomers of bithiophene bearing *R*(−) and *S*(+) chiral groups at the terminal positions (compounds **23**, **24**). The synthetic pattern is shown in Scheme 4.

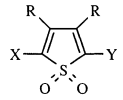
As shown in the scheme, the monobrominated monomers **21** and **22** were obtained by condensation of commercial 5-bromo-2-thiophene aldehyde with *R*(−) and *S*(+) 1-phenylethylamine. Afterward, they were reacted with bis(pinacolato)diboron using the same experimental conditions employed for the preparation of quaterthiophene. After a few minutes of microwave irradiation, bithiophenes **23** and **24** were recovered in high yield (isolated yield in both compounds: >70%). The NMR spectrum of the crude product showed the presence of a second iminic peak at 8.43 ppm, indicating that under microwave irradiadion partial isomerization of the iminic bond (<10%, from ^{1}H NMR) takes place.

To exclude the possibility that microwave irradiation can cause racemization, we first measured the optical rotatory dispersion value, α, of monomer **21**, *R*(−)-(5-bromothiophen-2-ylmethylene)(1-phenylethyl)amine, before and after microwave irradiation (3 min, $T = 80$ °C). Within the limits of experimental error, the two values ($[\alpha]_D$ −133.30° and $[\alpha]_D$ −127.38°, respectively) were found to be the same.

Interestingly, we found that the optical rotatory dispersion of bithiophene **23** increased to $[\alpha]_D$ −536.61° and that of bithiophene **24** to $[\alpha]_D$ +485.52° ($[\alpha]_D$ +183.63° for monomer **22**).

(V) Coupling of Thienyl-*S*,*S*-dioxide Moieties. The solvent-free, microwave-assisted methodology was also tested for the preparation of oligothiophene-*S*,*S*-dioxides, which are compounds characterized by high photoluminescence quantum efficiencies in the solid state, high electron affinities,[24c] and good electroluminescence[7b] and lasing[8] properties.

Thus, compounds **25**−**28**[24d] were reacted with thienylboronic derivatives **2a** and **2b** under microwave irradiation, at $T = 80$ °C, 5 mol % of catalyst, 5 equiv of KF for



25 R = H, X = Y = Br
26 R = Me, X = Y = Br
27 R = H, X = Y = I
28 R = *neo*-Pentyl, X = Y = Br
29 R = *n*-Hexyl, X = H, Y = Br

1−10 min and $PdCl_2$(dppf) as the catalyst. The best results in terms of isolated yields in trimer were obtained using $NiCl_2$dppf as the catalyst. However, the coupling yields never exceeded 30% (15% using palladium catalysts).

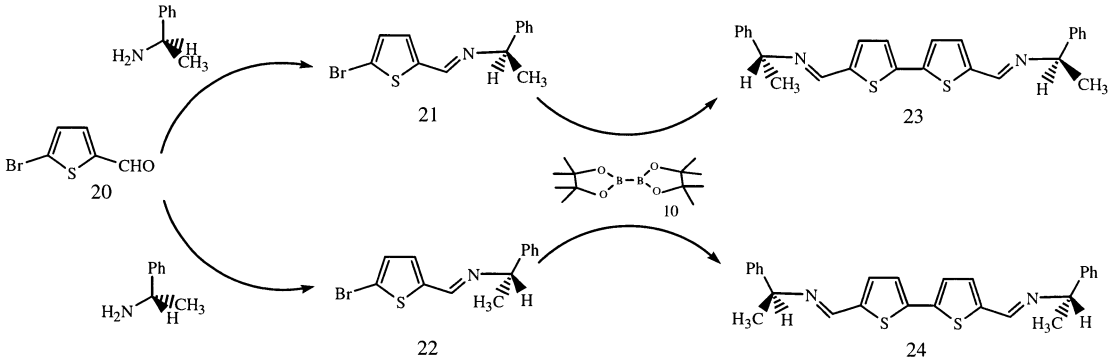
While more detailed studies are currently under way, on the basis of the NMR spectra, cycloaddition adducts seem to be in all cases the major reaction products.[25]

Moreover, attempts to obtain the dimer of monobromo **29** by reaction with bis(pinacolato)diboron were unsuccessful.

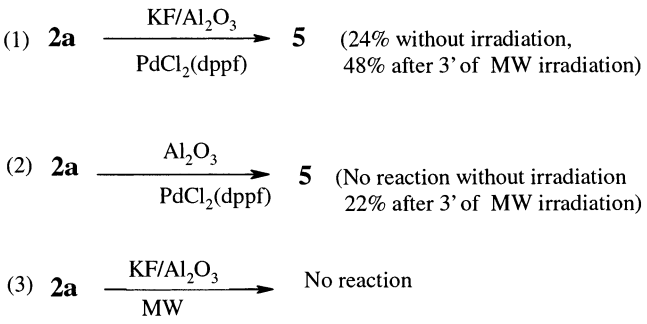
(VI) Experiments to Elucidate the Reaction Mechanism. To get some insight into the reaction mechanisms, the experiments described in Scheme 5 were carried out using thiopheneboronic acid **2a** as the starting material, to check the self-coupling reaction of this compound on changing the reaction conditions.

The yields reported in parentheses are those estimated by GC/MS analysis. The results show that, while no homocoupling is observed in the absence of catalyst even in the presence of microwaves (item 3), the use of microwaves always leads to the formation of dimer **5**, even in the absence of the base (item 2).

SCHEME 4. Solvent-Free, Microwave-Assisted Synthesis of *R*,*R*(−)- and *S*,*S*(+)-5,5′-[Methylene(1-phenylethyl)amine]-2,2′-bithiophenes 23 and 24



SCHEME 5. Self-Coupling Reaction of Thiophene Boronic Acid 2a in Different Experimental Conditions



When the catalyst and the base are both present, as well as microwave irradiation (item 1), the percentage of self-coupling is rather high (item 1).

Discussion

One of the main advantages of the Suzuki reaction is its versatility and the many tunable parameters that can be exploited to accelerate the reaction and improve the yields.

The microwave-assisted methodology described here allows for the rapid exploitation of the many possibilities offered by this reaction. The best set of catalyst, base, and halogen derivative to be used can rapidly be checked and the experimental conditions optimized. Once the best synthetic pattern to follow is established, thiophene oligomers are obtained in high yields and in mixtures that can easily be purified. Generally, the formation of the thienyl−thienyl linkage occurs in a few minutes, and the crude reaction product may be recovered by filtration free of catalyst and boron salts, from which the desired oligomers are separated in high isolated yields and very pure.

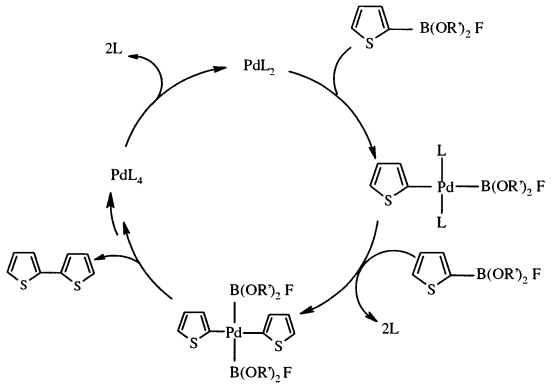
One of the most interesting results of the present work is the fact that in the synthesis of the longer oligomers it is much more convenient, in terms of purification and isolated yields, to increase the size by addition of the thiophene rings one at a time, rather than trying to react longer building blocks.

One of the reasons for this is that, in the presence of microwaves, there is always palladium-promoted self-coupling of the boronic derivatives. When thienylboronic acid or ester is used, bithiophene is the main byproduct to be formed, which is easily removed by chromatography. The self-coupling is more effective with thienylboronic acid than with the corresponding esters; thus the latter are more convenient to use than the former.

The data reported in Scheme 5 (items 1−3) unambiguously show that in the presence of microwaves there is always a sizable amount of self-coupling—even in the absence of base—if the palladium catalyst is present.

It is known that palladium-promoted self-coupling of phenylboronic acids occurs when the cross-coupling reaction is slow. Moreno-Manas et al. have carried out a detailed mechanistic study of the self-coupling reaction of phenylboronic acids.[26] We suggest that the self-coupling of thienylboronic derivatives occurs according to a similar mechanism, consisting of two steps of oxidative addition of palladium to the "ate" complex of the thienylboronic derivative, followed by the reductive elimination of bithiophene, as shown in Scheme 6.

SCHEME 6. Palladium-Promoted Homocoupling of Thienyl Boronic Acid or Esters



When the boronic acid or ester of 2,2′-bithiophene is employed, the self-coupling product is quaterthiophene, which is more difficult to separate from the targeted oligomer. In this case, the self-coupling reaction may even become the predominant one, probably because the cross-coupling becomes very slow. For example, when the boronic acid of 2,2′-bithiophene was reacted with 2,5-dibromothiophene, no formation of quinquethiophene was observed, whereas when the boronic ester was employed, the yield in isolated quinquethiophene was only 28% (see Scheme 2 and Table 2). In both cases, quaterthiophene was the major product recovered. Once again, the use of the boronic ester was more convenient for the synthesis of the targeted product, probably because the self-coupling of boronic esters is slower than that of boronic acids and the cross-coupling reaction becomes competitive. Anyway, our results show that by adding one ring at a time, repeated and easily standardized cycles of bromination/microwave-assisted Suzuki coupling lead to **7**, **12**, and **19** in fair amounts (isolated yields up to 80%) and very rapidly.

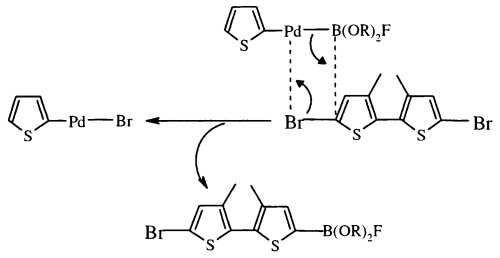
The best halogen derivative to employ as the starting material depends very much on the substrate, and at the present stage of knowledge, it is rather difficult to make a choice a priori. For example, terthiophene can be prepared in good yield (73%) by reaction of 2,5-dibromothiophene, **1a**, with thiophene boronic acid, but when **1a** is replaced by the corresponding diiodo derivative **1b**, the yield drops drastically (Table 2).

On the contrary, in the synthesis of sexithiophene **19** (Scheme 3 and Table 3), the use of the diiodo derivative of the electron-rich 3,3′-dimethyl-2,2′-bithiophene (**15**) leads to much better yields in the intermediate quaterthiophene (**17**) than the corresponding dibromo derivative (**16a**). Indeed, when the dibromo derivative is used, there is formation of oligomers up to the octamer and more, characterized by repeating 3,3′-dimethyl-2,2′-bithiophene subunits (see Figure 1), which are not formed when the diiodo derivative is employed.

(25) (a) Jursic, B. S. *J. Heterocyclic Chem.* **1995**, *32*, 1445. (b) Gronowitz, S. *Phosphorus, Sulfur Silicon* **1993**, *74*, 113.

(26) Moreno-Manas, M.; Perez, M.; Pleixats, R. *J. Org. Chem.* **1996**, *61*, 2346.

SCHEME 7. Possible Mechanism for the Palladium-Promoted Boron−Bromine Exchange of 5,5′-Dibromo-3,3′-dimethyl-2,2′-bithiophene



The compounds with repeating dimethylated bithiophene subunits can be formed only if boron−halogen exchange takes place. On the basis of the mechanism proposed by Masuda et al. for the palladium-catalyzed borylation of aryl halides,[27] we suggest that one possible mechanism for boron−bromine exchange would be that shown in Scheme 7, consisting in the oxidative addition of palladium on the C−B bond followed by metathesis of the borate-palladium complex with the halide.

Our data show that when the dibromo derivative is employed, the boron−bromine exchange is more rapid than the cross-coupling and compound **17** is formed in very low yield. On the contrary, when the diiodo derivative is used, **17** is formed in much greater yield since iodine is a better leaving group than bromine, and the Suzuki coupling is favored because of kinetic factors that are still to be explored in detail.

As shown in Schemes 2 and 4, even number oligothiophenes are formed in good yields in the one-pot borylation−Suzuki coupling of monobromo derivatives with bis(pinacolato)diboron, a compound that is used for the one-pot synthesis of biphenyls through the in situ formation of phenyl boronates.[22b] Currently, we are experimenting with some modifications of the procedure described here to apply this reaction also to the preparation of unsubstituted sexithiophene, which is one of the best organic semiconductors but is insoluble and difficult to prepare in very pure form.[2,28]

The one-pot borylation−Suzuki coupling was also effective in the preparation of chiral 2,2′-bithiophenes (Scheme 4). Since, according to our data, microwave irradiation does not alter the chirality, the condensation reaction of commercial thienyl aldehyde with a variety of chiral amines and the subsequent doubling of the number of thienylene rings through reaction with bis(pinacolato)diboron appears to be a viable way to obtain chiral thiophene oligomers, whose self-assembly properties are a matter of great current interest.[29]

Unfortunately, the methodology presented here cannot be applied to the preparation of building blocks containing the thienyl-*S*,*S*-dioxide moiety. The aromatic character of thienyl-*S*,*S*-dioxide is much less pronounced than that of thiophene.[25a] In consequence, thienyl-*S*,*S*-dioxides are more reactive and capable of behaving as dienes in Diels−Alder reactions.[25b] Our data show that microwave irradiation accelerates the formation of Diels−Alder adducts from compounds **25**−**29**, which becomes largely prevalent over the Suzuki coupling.

Conclusion

The solvent-free microwave-assisted synthesis of thiophene oligomers through the Suzuki reaction presented in this paper is an environmentally friendly methodology allowing the rapid optimization of reaction conditions and the facile preparation of these important multifunctional materials in very pure form.

There are many intriguing mechanistic and kinetic aspects of the Suzuki reaction when thiophene-based building blocks are employed that it is not possible at the moment to place within a well-defined framework. We believe that the elucidation of these different aspects would be of great interest, both from a fundamental point of view and for further improvements in the synthetic accessibility of functionalized thiophene oligomers.

Experimental Section

General Procedures. $PdCl_2(dppf)$, $Pd_2(dba)_3$, $PdCl_2$, $Pd(PPh_3)_2Cl_2$, $Pd(PPh_3)_4$, 2-bromothiophene, 2,2′-bithiophene, 2,5-dibromothiophene, 2,5-diiodothiophene, bis(pinacolato)diboron, 5-bromo-2-thiophene aldehyde, 1-phenylethylamine, KO^{t}Bu, CsF, KF, 2-thiopheneboronic acid, and *n*-butyllithium were commercially available. All reagents were used without further purification. Flash chromatographies were carried out using silica gel (200−300 mesh ASTM) and analytical thin-layer plates. The visualization in TLC was accomplished by UV lights (356 and 254 nm).

Microwave-assisted reactions were carried out in air in a 20 mL reactor and were performed using a commercial system Synthewave 402 manufactured by Prolabo. The typical experimental procedure was the following: the microwave oven reactor was charged with 1 equiv of thienyl halide mixed with 2−5 equiv of boronic derivative, 5 mol % catalyst, and 10 equiv of KF and Al_2O_3 (KF/Al_2O_3, 1:3 w:w). To make the mixture more homogeneous, 0.1−0.5 mL of methanol was added and evaporated under reduced pressure. Afterward the mixture was allowed to undergo the action of microwaves and the reaction was followed by TLC. In some cases (synthesis of compounds **7**, **12**, and **19**), 10^{-1} M KOH was added to accelerate the reaction. The detailed procedure is illustrated below by the synthesis of quaterthiophene **7**.

Materials. The characteristics of compounds **3**−**7**,[21] **12**,[21] **15**,[21a] **16a**,[24a,b] **16b**,[24a,b] and **17**−**19**[24a,b] have already been described.

4,4,5,5-Tetramethyl-2-thiophene-2-yl[1,3,2]dioxaborolane, 2b. A 1.0 g sample of commercial 2-thiopheneboronic acid (7.81 mmol), 1.2 g of anhydrous pinacol (10 mmol), and 300 mg of anhydrous Na_2SO_4 were added to 25 mL of distilled Et_2O, and the mixture was stirred for 24 h. Afterward the mixture was filtered through Celite. After evaporation and crystallization from pentane 1.4 g of a white powder (90% yield) was obtained. The characteristics of **2b** have already been described.[27]

2,2′:5′,2″:5″,2‴-Quaterthiophene, 7. The microwave oven reactor was charged with 0.1 g (0.31 mmol) of 5,5′-dibromo-2,2′-bithiophene **6**, 0.011 g (0.0155 mmol) of $PdCl_2(dppf)$, 0.18 g (3.1 mmol) of KF, and 0.54 g of Al_2O_3. Afterward 0.2 g (1.55 mmol) of 2-thiopheneboronic acid **2a** was added (in two portions). The mixture was homogeneized with methanol and the solvent evaporated under reduced pressure. The reaction was followed by TLC, and after 1 min irradiation 200 μL of 10^{-1} M KOH was added. After 3 min irradiation at $T = 80$ °C the solid mixture was chromatographed on silica gel using

(27) Murata, M.; Oyama, T; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **2000**, *65*, 164.
(28) Dodalabapur, A.; Torsi, L.; Katz, H. E. *Nature* **1995**, *268*, 270.
(29) Schenning, A. P. H. J.; Kilbinger, A. F. M.; Biscarini, F.; Cavallini, M.; Cooper, H. J.; Derrick, P. J.; Feast, W. J.; Lazzaroni, R.; Leclère, Ph.; McDonell, L. A.; Meijer, E. W.; Meskers, S. C. J. *J. Am. Chem. Soc.* **2002**, *124*, 1269.

petroleum ether → petroleum ether/CH_2Cl_2/AcOEt, 80:10:10. A total of 0.083 g (81% yield) of a yellow solid with the characteristics of α-conjugated quaterthiophene **7**[21] was separated.

2,2′-Bithiophene-5-boronic Acid, 13a. To a solution of 2,2′-bithiophene (2.5 g, 15 mmol) in anhydrous THF (20 mL) cooled to −78 °C was added dropwise ^{n}BuLi (2.5 M, 6.6 mL, 16.5 mmol). The resulting orange mixture was allowed to react at this temperature for 1 h, then for an additional 2 h at room temperature. The mixture was cooled to −78 °C, and $B(OMe)_3$ (2.66 mL, 23 mmol) was added (solution turned blue). The mixture was stirred for 12 h, then quenched with 2 M HCl (80 mL). After separation of the layers, the aqueous phase was extracted with Et_2O. The resulting organic layers were dried over Na_2SO_4. Evaporation of Et_2O gave 2.1 g (66% yield) of **13a** (dark green oil). The product was utilized without further purification: MS (*m*/*z*) 210 [M$^{\bullet+}$]; ^{1}H NMR (acetone-d_6) δ 7.60 (m, 1H), 7.41 (m, 1H), 7.31 (m, 2H), 7.06 (m, 1H), 5.75 (s, 2H).

2-[2,2′]Bithiophenyl-5-yl-4,4,5,5-tetramethyl[1,3,2]dioxaborolane, 13b. To a solution of 2,2′-bithiophene (1.4 g, 8.57 mmol) in anhydrous THF (20 mL) cooled to −78 °C was added dropwise ^{n}BuLi (2.5 M, 3.77 mL, 9.43 mmol). The resulting orange mixture was allowed to react at this temperature for 2 h, then for an additional 2 h at room temperature. The mixture was cooled to −78 °C, and $B(OMe)_3$ (1.3 mL, 11.1 mmol) was added (solution turned blue). The mixture was stirred for 2 h, then 1.2 g (10.28 mmol) of anhydrous pinacol was added. After 12 h the mixture was filtered through Celite and the solvent was evaporated under reduced pressure. The crude product was chromatographed on silica gel, using CH_2Cl_2/*c*-Hex, 80:20, 1.1 g (44% yield) of **13b** (dark green oil), and 0.35 g of **9** (light green solid). **13b**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, ^3J = 3.60 Hz 1H), 7.23 (m, 3H), 7.01 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.99, 144.26, 138.07, 137.44, 128.08, 125.15, 125.12, 124.55,0.84.46, 25.20.

2,2′-[2,2′]-Bithiophenyl-5,5′-ylbis(4,4,5,5-tetramethyl)-[1,3,2]dioxaborolane, 9: light green solid; mp 155 °C; MS (*m*/*z*) 418 [M$^{\bullet+}$]; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 (d, ^3J = 3.60 Hz 2H), 7.28 (d, ^3J = 3.6 Hz, 2H), 1.35 (s, 24 H); ^{13} C NMR ($CDCl_3$, 100 MHz) δ 143.71, 137.82, 125.50, 84.19, 24.88.

***R*(−)-(5-Bromothiophen-2-ylmethylene)(1-phenylethyl)amine, 21**. This compound was quantitatively obtained by condensation of 5-bromo-2-thiophene aldehyde with *R*(−)-phenylethylamine by mixing an equimolar amount of reagents and stirring for 6 h at room temperature: MS (*m*/*z*) 293 [M$^{\bullet+}$]; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.29 (s, 1H), 7.31 (m, 5H), 6.98 (d, 2H), 2.46 (m, 1 H), 1.54 (d, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.8, 144.8, 144.5, 130.2, 128.5, 126.9, 126.6, 116.9, 69.0, 24.7; $[\alpha]_D$ −133.30° (*c* 0.336, $CHCl_3$).

***S*(+)-(5-Bromothiophen-2-ylmethylene)(1-phenylethyl)amine, 22** was obtained with the same modalities as compound **21**. Mass and NMR spectra were the same as **21**: $[\alpha]_D$ +183.63° (*c* 0.336, $CHCl_3$).

***R,R*(−)-(1-Phenylethyl)(5′-[1phenylethylimino)methyl]-[2,2′]bithiophenyl-5-ylmethylene)amine, 23.** A 0.3 g (1.02 mmol) sample of **21**, 0.129 g (0.51 mmol) of bis(pinacolato)-diboron, 0.026 g (0.036 mmol) of $PdCl_2$(dppf), 0.296 g (5.1 mmol) of KF, and 0.9 g of Al_2O_3 were introduced in the microwave oven reactor. A 0.5 mL portion of methanol was added, then the solvent removed under reduced pressure and the mixture irradiated for 2 min at T = 70 °C. A 10 mL portion of Et_2O was added to the crude product, and the mixture was filtered through Celite. After solvent evaporation, a yellow-orange oil was obtained. Crystallization from *n*-Hex afforded 140 mg (65% yield) of a yellow powder, mp 115 °C; MS (*m*/*z*) 428 [M$^{\bullet+}$]; λ_{max} (CH_2Cl_2) 377 nm; IR 3435, 2974, 2853, 1633 (cm^{-1}); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.36 (s, 2H), 7.21 (m, 14H), 4.55 (m, 2H), 1.61 (d, ^3J = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.32, 144.92, 142.29, 140.10, 130.95, 128.42, 126.85, 126.62, 124.44, 69.02, 24,67; $[\alpha]_D$ −536.61° (*c* 0.336, $CHCl_3$). Anal. Calcd for $C_{26}H_{24}N_2S_2$: C 72.86; H 5.64. Found: C 72.62; H 5.62.

***S,S*(+)-(1-Phenylethyl)(5′-[1phenylethylimino)methyl]-[2,2′]bithiophenyl-5-lmethylene)amine, 24**. The procedure was the same as for compound **23**, and 0.157 g of a yellow crystalline powder (72% yield) was recovered, mp 120 °C; MS (*m*/*z*) 428, λ_{max}, IR); ^{1}H and ^{13}C NMR were the same as compound **23**; $[\alpha]_D$ +485.52° (*c* 0.336, $CHCl_3$). Anal. Calcd for $C_{26}H_{24}N_2S_2$: C 72.86; H 5.64. Found: C 72.68; H 5.63.

Acknowledgment. Thanks are due to Dr. Olga Pudova (Latvian Institute of Organic Synthesis) for the preparation of *R*(−)- and *S*(+)-5-bromothiophen-2-ylmethylene)(1-phenylethyl)amine. This work was partially supported by the project "Nuovi emettitori di luce a semiconduttore organico" (CNR-5% Nanotecnologie).

Supporting Information Available: NMR spectra of boronic esters **9** and **13b** and boronic acid **13a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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