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Preparation of Extended Di(4-pyridyl)thiophene Oligomers.

Willem M. Albers*

VTT, Technical Research Centre of Finland, Polymer and Fibre Technology
P.O.Box 14021, FIN-33101 Tampere, Finland

Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University
P.O.Box 9502, 2300 RA Leiden, the Netherlands

Gerard W. Canters and Jan Reedijk

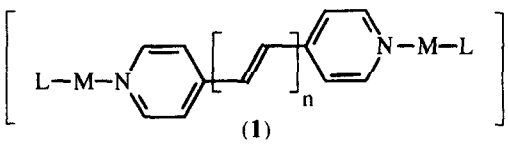
Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University
P.O.Box 9502, 2300 RA Leiden, the Netherlands

Abstract: Different methods for the coupling of 2-(4-pyridyl)thiophene to α-dibrominated thiophene oligomers and their efficiency to produce a homologous series of extended di(4-pyridyl)thiophene oligomers have been studied. The coupling was found to be most efficient with the organozinc derivative of 2-(4-pyridyl)thiophene, using a Pd(dppf) complex as the catalyst in the coupling reaction. The resulting compounds are promising new models for trans-membrane molecular conductors.

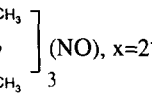
INTRODUCTION

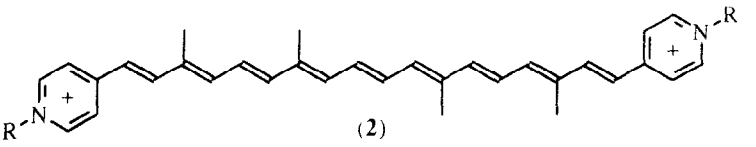
The preparation of functionalized oligo- and polythiophenes is being studied intensively due to the huge potential of these compounds in the construction of molecular electronics, non-linear optics and chemical sensor devices[1,2,3,4]. Our interest lies in the preparation of new organic compounds which function as "molecular wires" in bilayer lipid membranes[5,6], or as amperometric biosensors in conjunction with redox enzymes[7,8]. Molecular wires, as defined in the field of molecular electronics, typically consist of two electroactive functional groups linked together by an extended π-electron network[6,9,10,11]. Electronic conduction should take place over fairly long distances, typically ranging from 20 to 100 Å. For crossing a 50 Å membrane a thiophene oligomer containing 12 or 13 thiophene units would be needed and this is about the maximum length that can be presently attained with a discrete synthesis method, not involving polymerization[12].

Intramolecular electron transfer has been studied of various metal-complexes of the polyene-linked bipyridyls (**1**)[10,11] and trans-membrane electronic conduction has been studied using the carotene-linked bipyridiniums (caroviologens) (**2**)[6,9]. In particular the latter compounds are promising, because their length of about 34 Å approaches the thickness of natural bilayer lipid membranes. As electronic conductors in liposomes they were found to be functional, but not highly effective. For compound (**2**) only a 4-fold increase in transmembrane electronic conductivity has been reported[9]. Also the chemical stability of the carotenes is not very high and they may exhibit photochemical cis-trans-isomerization, which affects the linearity of the molecule[13].



(**1**)

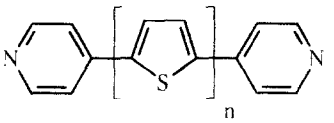
M=Ru, L=$(NH_3)_5$, x=4^+, n=2
or
M=Mo, L=BH[](NO), x=2^+, n=0-4



(2)

Here we present preliminary results of some useful routes to the synthesis of extended di(4-pyridyl)-thiophene oligomers (**3**, n>2). Previously, only a few shorter members of these compounds have been synthesized, 5,5'-di(4-pyridyl)-2,2'-bithiophene (**3**, n=2) by the palladium amalgam-catalyzed dimerization of 2-(4-pyridyl)-5-iodothiophene[14], and 2,5-di(4-pyridyl)thiophene (**3**, n=1) via an organotin intermediate[15]. The compound (**3**, n=2) has been described as a new fluorophore. Longer molecules of this type may prove to be versatile building blocks for molecular wires for a number of reasons. They have a stronger π-donor/π-acceptor character, are chemically more stable and form more stable anion radicals in comparison with their poly-vinylene counterparts[15,16,17]. They also have a good linearity. These are all important prerequisites for effective electronic conduction across bilayer lipid membranes.

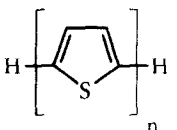
The crosscoupling of Grignard or organozinc reagents with haloarenes, catalyzed by Nickel or Palladium diphosphane complexes[23], has been used extensively for the synthesis of oligothiophenes[3,18,19] and new heteroarene oligomers[20,21]. Apparently very complicated sequences can be achieved with such methods[22] and thus they are promising for the preparation of (**3**, n>2).



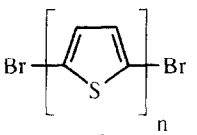
(3)

RESULTS AND DISCUSSION

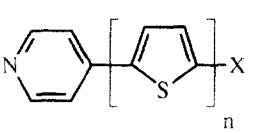
Preparation of intermediates[23,24]



(4)



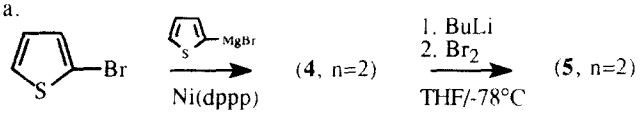
(5)



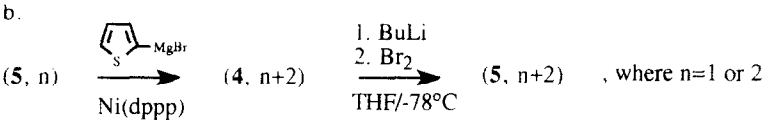
(6)

A sequence of α-dibrominated oligothiophenes (**5**, n=2, 3, 4) was prepared by the butyllithium-mediated α-dibromination of the corresponding thiophene oligomers (**4**, n=2, 3, 4). The latter oligomers were prepared by the Ni(dppp)-catalyzed crosscoupling reaction of 2-thienylmagnesium bromide with 2-bromothiophene (Scheme 1.a.) or with the dibromothiophenes (**5**, n=1, 2) (Scheme 1.b.), as described in the literature[3,18,19,20].

a.

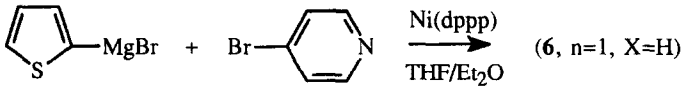


b.



Scheme 1

Although different methods for the preparation of 2-(4-pyridyl)thiophene (**6**, n=1, X=H) have been reported[25,26], the crosscoupling reaction of 2-thienylmagnesium-bromide to 4-bromopyridine, utilizing the Ni(dppp) catalyst, has not been explicitly described[20]. We now have obtained good yields of (**6**, n=1, X=H) by using reaction Scheme 2.



Scheme 2

In a typical procedure, thienylmagnesium bromide (87 mmoles), dissolved in approx. 50 ml diethylether, was added to a solution of 4-bromopyridine[27] (87 mmoles) in 200 ml THF. The mixture was refluxed for 20 hours in the presence of 1 mmole of Ni(dppp), whereafter the reaction was quenched by pouring the mixture in aqueous ammonium chloride/HCl. The product was extracted into dilute hydrochloric acid and, after making the aqueous layer slightly alkaline, extracted back into chloroform. The crude product was dissolved in hexane and recrystallized twice from hexane. The analytical data of the products are summarized in Table 1. and the ^{1}H-NMR data in Table 2.

Preparation of extended di(4-pyridyl)thiophene oligomers

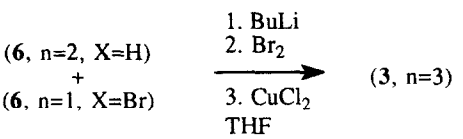
Short oligomers

A small amount of 2,5-di(4-pyridyl)-thiophene (**3**, n=1) was prepared, for NMR reference purposes, by the Ni(dppp) catalyzed crosscoupling of the Grignard reagent of 2,5-dibromothiophene with 4-bromopyridine. The product (**3**, n=1) was isolated by TLC. 2-(4-pyridyl)-5-iodothiophene (**6**, n=1, X=I) and 5,5'-di(4-pyridyl)-2,2'-bithiophene (**3**, n=2) were prepared with the methods reported by Nakajima[14,28]. (**6**, n=1, X=I) and (**3**, n=2) were both recrystallized from chloroform and (**3**, n=2) was additionally purified by sublimation at 250°C.

5,5''-di(4-pyridyl)-2,2':5',2''-terthiophene, (3, n=3)

according to the $CuCl_2$ method

Initially fairly pure, but small (17 mg) amounts of (**3**, n=3) were obtained by the route depicted in Scheme 3. A mixture of (**6**, n=1, X=Br)[29] and (**6**, n=2, X=H)[30], both approx. 1.25 mmol, was lithiated with 1,28 mmol of butyllithium at -60 °C and allowed to react with anhydrous copper chloride[23] in THF for 0.5 hours at -30°C and 4 hours at room temperature. Upon pouring the reaction mixture in dilute hydrochloric acid a red precipitate formed, which was collected on a Büchner filter. The precipitate was converted into the free base with dilute ammonia and washed with methanol, ether and hexane and finally air dried. This yielded (**3**, n=3) as an orange powder. (Analytical data (**3**, n=3)/I, Table 1.)

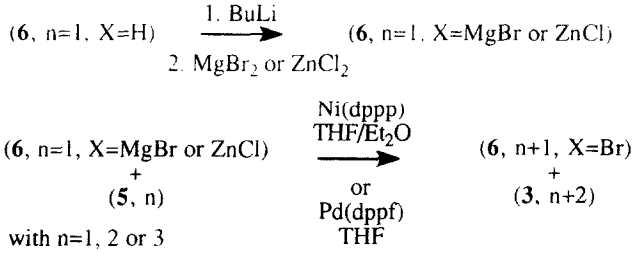


Scheme 3

according to the Ni(dppp) method

The preparation of (**3**, n=3) via the Ni(dppp) route according to Scheme 4. gave very small (approx. 0.5%) yields. 10 mmol of (**6**, n=1, X=H) was lithiated at -78 °C and cross-metalated with 1.85 g of anhydrous magnesium bromide at -60 °C. The Grignard reagent (**6**, n=1, X=MgBr) formed as a black tar deposit. 4 mmol of 2,5-dibromothiophene and 50 mg of Ni(dppp) were dissolved in 100 ml THF and 100 ml

diethylether and this mixture was added to the Grignard reagent. The coupling reaction was conducted under reflux for 20 hrs. Reaction products were extracted first into dilute hydrochloric acid and, after neutralization into chloroform. The fraction soluble in chloroform and insoluble in hexane contained mainly (**3**, n=2) and only a minor amount of the (**3**, n=3). The oligomer (**3**, n=3) could be isolated with column chromatography (silica/chloroform) and gave an identical spectrum as the compound obtained from the $CuCl_2$ method.



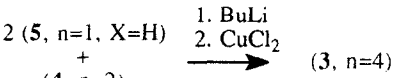
Scheme 4.

according to the Pd(dppf) method

When performing Scheme 4. via the organozinc intermediate instead of the Grignard reagent and using Pd(dppf)[23] as the catalyst instead of Ni(dppp) we obtained quite different and improved results. The following procedure was used: To a mixture of 1.61 g (10 mmol) of (**6**, n=1, X=H) in 100 ml THF, cooled to -70 °C, was added 6.25 ml (10 mmol) butyllithium. After 1 hour stirring, 10 ml of $ZnCl_2$ (a 1 M anhydrous solution in THF) was added dropwise. After stirring 2 hrs at -55 °C a dark red-brown tar formed. 1.21 g (5 mmol) of 2,5-dibromothiophene and 25 mg of Pd(dppf) were added and the reaction mixture was allowed to reach room temperature slowly. The mixture was then stirred under reflux for 20 hours. An orange precipitate formed, which was collected on a Büchner filter, rinsed with chloroform and pentane and dried in vacuo. The elemental constitution of the precipitate was: C 41,54%, H 2,76%, N 4,47%, S 14,0%, Cl 9.32%, Br 8.33% and Zn 13.5%, corresponding with a bruto formula of $C_{16.8}H_{13.3}N_{1.6}S_{2.1}Cl_{1.3}Br_{0.5}Zn_{1.0}$. Treatment of this insoluble zinc complex with an aqueous 1% solution of Na_2H_2edta (Titriplex III, Merck) at 80 °C for 1 hour yielded an orange powder, which was washed with ethanol and ether and dried in vacuo. Yield: 66% of pure (**3**, n=3). (Analytical data (**3**, n=3)/II, Table 1.) The ^{1}H-NMR spectrum, at 600 MHz resolution, is given in Figure 1.[31] The intermediate (**6**, n=2, X=Br) was isolated from the remaining supernatant of the reaction (^{1}H-NMR. Table 2.).

5,5‴-di(4-pyridyl)-2,2′:5′,2″:5″,2‴-quaterthiophene, (3, n=4)

Initially scheme 5 was used to produce also small amounts (< 10 mg) of (**3**, n=4). The coupling reaction with copper chloride was conducted at room temperature for 18 hours. The main product was (**3**, n=2) together with many other compounds. The product (**3**, n=4) could be identified with ^{1}H-NMR after column chromatography (silica/chloroform).



Scheme 5

The reaction of Scheme 4. with $MgBr_2$/Ni(dppp) was used in the same fashion to investigate the formation of (**3**, n=4) from (**5**, n=2) and (**6**, n=1, X=MgBr). The reaction, however, failed to produce the desired product: the fraction that dissolved in chloroform and not in hexane contained largely (**3**, n=2) and

the half product 5-(4-pyridyl)-5''-bromo-2,2':5',2''-terthiophene (**6**, n=3, X=Br) (according to mass-spectrometry and ^{1}H-NMR data).

When Scheme 4. was followed with $ZnCl_2$/Pd(dppf) for coupling (**6**, n=1, X=ZnCl) to (**5**, n=2) also the formation of a red zinc complex was observed: Elemental analysis: C 41.23%, H 2.80%, N 3.81%, S 16.5%, Cl 9.44%, Br 9.72%, Zn 11.4% corresponding to $C_{19.7}H_{15.9}N_{1.6}S_{3.0}Cl_{1.5}Br_{0.7}Zn_{1.0}$. The treatment of this complex with 1% edta yielded an orange/brown powder, which appeared to be largely the half-product (**6**, n=3, X=Br) (according to ^{1}H-NMR data).

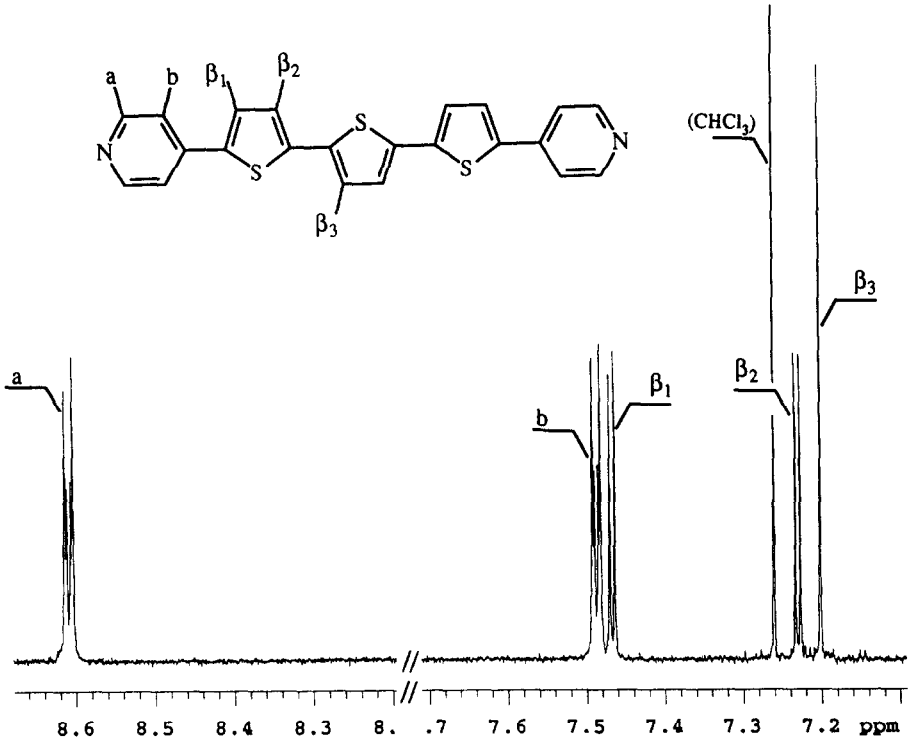


Figure 1. The 600 MHz ^{1}H-NMR spectrum of 5,5''-di(4-pyridyl)-2,2':5',2''-terthiophene.

5,5''''-di(4-pyridyl)-2,2':5',2'':5'',2''':5''',2'''':quinquethiophene, (3, n=5)

The coupling product of (**6**, n=1, X=H) with (**5**, n=3) under the same conditions yielded 3.60 g of dark red powder. Elemental analysis: C 42.32%, H 2.95%, N 3.09%, S 19.7%, Cl 7.46%, Br 8.47%, Zn 9.27%, bruto formula $C_{24.9}H_{20.6}N_{1.6}S_{4.3}Cl_{1.5}Br_{0.8}Zn_{1.0}$. After edta-workup, ^{1}H-NMR analysis indicated the presence of the desired product (**3**, n=5) and the half product (**6**, n=4, X=Br) in approximately 1:1 molar ratio. The solubility of these compounds in $CHCl_3$ and DMSO, however, appeared to be very poor.

Longer oligomers

It was found that the reaction of (**6**, n=1, X=ZnCl) with (**5**, n=4) did not proceed under the same reaction conditions. This is most likely due to the fact that the reactant (**5**, n=4) has a very low solubility and hardly dissolves in the reaction medium, THF.

Table 1. Analytical data.

Compound	Yield / %	m.p. /°C (litt.)	Elemental analysis						MW	Mass spectrometry M/z of main peak (peaks of minor impurities)
				C%	H%	N%	S%	Br%		
(**4**, n=2)	66	31	found	57.54	3.61		38.0		166.26	166 (248)
$C_8H_6S_2$		(33)	calc.	57.79	3.64		38.6			
(**4**, n=3)	21	81	found	57.44	3.22		38.0		248.38	248 (330)
$C_{12}H_8S_3$		(94)	calc.	58.03	3.25		38.7			
(**4**, n=4)	57	203	found	56.49	3.05		37.0		330.5	330
$C_{16}H_{10}S_4$		(212)	calc.	58.15	3.05		38.8			
(**5**, n=2)	60	141	found	28.77	1.18		18.5	52.0	324.05	324
$C_8H_4S_2Br_2$		(143)	calc.	29.65	1.24		19.8	49.3		
(**5**, n=3)	50	151	found	35.60	1.65		23.2	38.0	406.17	406
$C_{12}H_6S_3Br_2$		(160)	calc.	35.49	1.49		23.7	39.3		
(**5**, n=4)	66	245	found	38.12	1.88		25.1	32.2	488.29	488 (408, 330,
$C_{16}H_8S_4Br_2$			calc.	39.36	1.65		26.3	32.8		324, 248)
(**6**, n=1, X=H)	70	90.5	found	66.87	4.38	8.90	18.7		161.22	161
C_9H_7NS		(93.0)	calc.	67.05	4.38	8.69	19.9			
(**6**, n=1, X=H)			found	38.84	3.30	4.82	10.3	40.3	303.16	
N-methylated			calc.	39.62	3.32	4.62	10.6	41.9		
$C_{10}H_{10}NSI$										
(**3**, n=2)	49	240	found	66.89	3.80	8.75	19.6		320.43	320
$C_{18}H_{12}N_2S_2$		(241-2)	calc.	67.47	3.77	8.74	20.0			
(**3**, n=3)/I	≈1.7		found	61.13	3.38	6.10	23.1		402.55	402 (320, 243)
$C_{22}H_{14}N_2S_3$			calc.	65.64	3.51	6.96	23.9			
(**3**, n=3)/II	66		found	64.28	3.42	6.77	22.4		402.55	
$C_{22}H_{14}N_2S_3$			calc.	65.64	3.51	6.96	23.9			

Methylation of the imine nitrogens

All pyridylthiophene compounds could be methylated with an excess of methyliodide in chloroform at room temperature, standing in a closed erlenmeyer flask. Most of the compounds neatly crystallized in the course of a week reaction time. The products were collected on a Büchner filter and washed with chloroform and hexane and dried in vacuo. For the short di(4-pyridyl) thiophene oligomer (**3**, n=2) predominantly monomethylation occurred, while for the longer oligomers (**3**, n=3, 4) both pyridines were methylated[32].

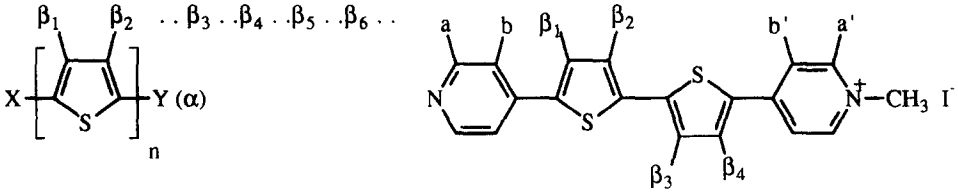
Structural characterization with ^{1}H-NMR

Proton NMR-data for different series of compounds are presented in Table 2. The table lists also data of shorter compounds for comparison purposes. Using NMR data from shorter compounds, we could tentatively assign most of the thiophene β-protons of the new oligomers, by employing addition of substituent effects. At least for the compounds encountered in this study, good predictions of the chemical shifts were obtained in this fashion. In those cases where resonances of the thiophene β-pairs come very close together the assignments were, however, still inconclusive. For monomethylated (**3**, n=2), assignments were based on the long-range ^{13}C-^{1}H correlated 2D-NMR spectrum[33].

Table 2. ^{1}H-NMR Chemical Shift Values of Thiophene- and Pyridylthiophene oligomers, δ/ppm.

Struct. Nr.	X	Y	n	Solvent	Thiophene resonances									Pyridine resonances	
					α	β1	β2	β3	β4	β5	β6	β7	β8	a	b
4	H	H	1	$CDCl_3$	7.30	7.09									
4	H	H	2	$CDCl_3$	7.21	7.01	7.18								
4	H	H	3	$CDCl_3$	7.22	7.02	7.17	7.08							
4	H	H	4	$CDCl_3$	7.23	7.03	7.19	7.08	7.08						
5	Br	Br	1	$CDCl_3$		6.84									
5	Br	Br	2	$CDCl_3$		6.95	6.83								
5	Br	Br	3	$CDCl_3$		6.98	6.91	7.00							
5	Br	Br	4	$CDCl_3$		6.98	6.91	7.01	7.06						
6	4-P	H	1	$CDCl_3$	7.43	7.52	7.14							8.59	7.49
6	4-P	H	1	DMSO-d_6	7.73	7.80	7.21							8.56	7.64
6	4-MP	H	1	DMSO-d_6	8.10	8.23	7.38							8.86	8.34
6	4-P	Br	1	$CDCl_3$		7.26	7.10							8.60	7.38
				calculated		7.30	7.10								
6	4-P	Br	1	DMSO-d_6		7.66	7.35							8.57	7.59
6	4-MP	Br	1	DMSO-d_6		8.08	7.56							8.89	8.31
6	4-P	I	1	$CDCl_3$		7.17	7.29							8.60	7.39
				calculated		7.23	7.29								
				litt.(ref.14)		7.16	7.28							8.59	7.38
6	4-P	I	1	DMSO-d_6		7.44	7.52							8.56	7.58
6	4-MP	I	1	DMSO-d_6		7.92	7.64							8.86	8.28
6	4-P	H	2	$CDCl_3$	7.28	7.43	7.19	7.25	7.05					8.59	7.46
				calculated		7.44	7.23								
6	4-P	H	2	DMSO-d_6	7.58	7.79	7.40	7.42	7.13					8.56	7.64
6	4-P	Br	2	$CDCl_3$		7.41	7.12	*7.01*	*6.98*					8.60	7.44
				calculated				7.03	7.01						
6	4-P	Br	3	$CDCl_3$		7.44	7.19	7.14	7.05	*6.99*	*6.94*			8.60	7.46
6	4-P	Br	4	$CDCl_3$		7.44	7.20	7.16	7.11	7.09	7.05	*6.99*	*6.94*	8.60	7.47
3	4-P	4-P	1	$CDCl_3$		7.54								8.64	7.51
				calculated		7.57									
				litt. (ref.15)		7.52								8.64	7.50
3	4-P	4-P	2	$CDCl_3$		7.46	7.26							8.61	7.47
				calculated		7.48	7.30								
3	4-P	4-P	2	DMSO-d_6		7.85	7.54							8.59	7.67
3	4-P	4-P	3	$CDCl_3$		7.46	7.22	7.19						8.60	7.47
				calculated				7.21							
3	4-P	4-P	3	DMSO-d_6		7.80	7.41	7.26						8.57	7.64
3	4-P	4-P	4	$CDCl_3$		7.43	7.19	7.15	7.11					8.60	7.47
3	4-P	4-P	5	$CDCl_3$		7.44	7.20	7.16	7.11	7.11				8.60	7.47
3	4-MP	4-P	2	DMSO-d_6		8.26	7.72	7.68	7.90				a'-b':	8.86	8.32
													a-b :	8.61	7.68
3	4-MP	4-MP	3	DMSO-d_6		8.27	7.73	7.66						8.87	8.33
3	4-MP	4-MP	4	DMSO-d_6		8.26	7.69	7.61	7.52					8.85	8.31

4-P = 4-pyridyl, 4-MP = 4-(N-methyl)pyridinium. Resonances which are equivalent by symmetry are not indicated. Values of which the assignments are still inconclusive are printed in italics. The numbering scheme of the compounds is as follows:



CONCLUSIONS

In conclusion, it has been shown that the preparation of *5,5''-di(4-pyridyl)-2,2':5',2''-terthiophene*, (**3**, n=3) and related compounds can be effectively achieved by the crosscoupling of the organozinc intermediate (**6**, n=1, X=ZnCl) to 2,5-dibromothiophene (**5**, n=1) using the Pd(dppf) catalyst. The route via the Grignard intermediate and the Ni(dppp) catalyst only yields *5,5'-di(4-pyridyl)-2,2'-bithiophene*, (**3**, n=2) as the main product, besides very minor amounts of the desired product. The difference in efficiency between these crosscoupling methods is regarded as an interesting observation. One of the reasons that the organozinc intermediate is more suitable, may originate from the formation of a zinc complex with the reaction product, which propagates the reaction. The crosscoupling with longer α-dibrominated thiophene oligomers under the same conditions, (**5**, n=2 or 3), yielded large amounts of half-product (**6**, n=3 or 4, X=Br). This may be explained by the significantly lower solubility of these compounds. The longest oligomer obtained, although not yet in pure form, is *5,5''''-di(4-pyridyl)-2,2':5',2'':5'',2''':5''',2''''-quinquethiophene*, (**3**, n=5). This molecule has an estimated length of 27 Å, which is comparable to the length of a lipid molecule, i.e. half the thickness of a typical biomembrane.

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23. Reagents used: All used solvents were of analytical reagent grade. THF was dried on sodium and stored under dry argon. Diethylether was dried on anhydrous magnesium sulphate or 3 Å molecular sieves. 4-bromopyridine hydrochloride (Aldrich, 99%), methyliodide (Aldrich), 2-bromothiophene (Janssen Chimica, 98%), 2,5-dibromothiophene (Aldrich, 95%), hydrazine hydrate (Aldrich, 98%), sodium periodate (Merck, p.a.), iodine (Merck, doubly sublimated), bromine (J.T. Baker), magnesium shavings (Merck) and n-butyllithium (Aldrich, 1.6 M solution in hexanes) were all used as provided. The commercially available catalysts [1,3-bis(diphenylphosphino)propane]nickel(II) chloride, "Ni(dppp)" (Aldrich, prod. nr. 33,536-3) and [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) chloride, "Pd(dppf)" in a 1:1 complex with dichloromethane (Aldrich prod. nr. 37,967-0) were used in this study. The Ni(dppp) was stored under argon at 4 °C and the Pd(dppf) was used as received. Anhydrous solutions of copper(II) chloride and Zinc(II) chloride were prepared by heating the metal salt in a roundbottom flask under vacuum and, after cooling, adding a dry THF solution. The concentration was 1 M. All reactions with magnesium, butyllithium, Ni(dppp), Pd(dppf) and palladium amalgam were conducted under a dry argon atmosphere delivered by a Schlenk aparatus.
24. Equipment used: Elemental analysis was carried out by Mikroanalytisches Labor Pascher (Remagen, Germany). NMR spectra were acquired on a Bruker WM 300 FT-NMR spectrometer at 300 MHz, or on a Jeol JNM-FX200 FT-NMR spectrometer at 200 MHz, both at Leiden University. Some 600 MHz spectra were also recorded on the Varian Unity 600 spectrometer at VTT Chemical Technology in Otaniemi. Mass spectra were recorded on a Finnigan MAT TSQ-70 quadrupole mass spectrometer, equiped with a Hewlett Packard 59980A particle beam interface. The spectra were recorded in EI impact mode, using an electron energy of 70 eV. The samples, dissolved in methanol, were introduced by means of an LC/MS system in column bypass mode (FIA), using a flow rate of 0.5 ml/min.
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27. Since the free base of 4-bromopyridine is unstable, the compound was freshly prepared from the hydrochloride prior to each coupling reaction. The compound can be obtained from strong ammonia as a clear liquid, followed by drying and neutralization over a 1:1 mixture of anhydrous magnesium sulphate and sodium bicarbonate in a pasteur pipette. The free base thus obtained could be stored stably under Argon at -15 °C. The yield was, however, low with this procedure (approx. 50%). A better yield

of free base was obtained by reaction of the hydrochloride with an equimolar amount of aqueous sodium hydroxide and extraction of the free base into hexane. The solvent was then slowly removed on a rotation film evaporator. The latter preparation was, however, less stable and was always immediately used.

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29. 2-(4-pyridyl)-5-bromothiophene (**6**, n=1, X=Br) was prepared by the butyllithium mediated bromination of (**6**, n=1, X=H). After double extraction, the product was treated with boiling hexane to remove most of the unreacted (**6**, n=1, X=H). The product was 88% pure.
30. 5-(4-pyridyl)-2,2'-bithiophene (**6**, n=2, X=H) was prepared by the crosscoupling of 2-thienylmagnesium bromide to (**6**, n=1, X=Br) using Ni(dppp) as the catalyst, similarly as the oligothiophenes (Scheme 1.).
31. The overlapping resonances can be separated by dissolving the compound in a mixture of $CDCl_3$ and DMSO-d_6.
32. The monomethylation of the shorter compounds may be due to the delocalization of the positive charge within the molecule, which reduces the electrophilic character of the second pyridine. Also the effect on solubility of the methylation is larger for the short compounds. An other short bi(4-pyridyl) derivative, 1,2-bi(4-pyridyl)ethylene, gave a pure monomethylated crystaline product under the same conditions. The product of methylation of (**3**, n=2) gave a pure NMR spectrum, but the elemental analysis was less fitting. Possibly a small amount of unmethylated compound was still present. (**3**, n=3) gave a bis-methylated product, containing some monomethylated compound as an impurity (NMR, elemental analysis).
33. Eventually definitive assignments will still require additional ^{13}C-^{1}H COSY measurements at higher magnetic fields. More elaborate work on the NMR of these compounds is currently in progress and will be published elsewhere.

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