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3,4'-Dibromo-2,2'-bithiophene was converted, in high yield, into the corresponding dibutoxy derivative. The ^1H and ^{13}C nmr data are discussed in comparison with those of 3,3'- and 4,4'-dibutoxy-2,2'-bithiophene in relation to regiochemistry.

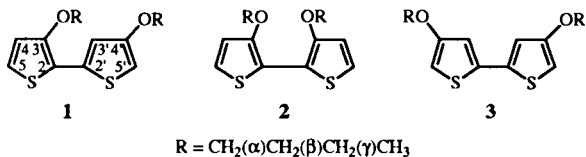
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Introduction.

The wide range of applications of β -substituted oligo- and polythiophenes (electronics, non linear optics, biology) [1-7] makes them very attractive materials. β -Substituted bithiophenes represent the first step for obtaining longer oligomers [7,8]. They can be chemically and electrochemically polymerized and used as model compounds for the understanding of related polymers [9].

Oligo- and polythiophenes bearing electroactive groups have been the subject of increasing interest [10-15]. The alkoxy derivatives, by means of their electrodonating properties, afford materials with reduced oxidation potential and enhanced stability of the conducting state. In particular, it has been reported that the polymers obtained from 3,3'- and 4,4'-dibutoxy-2,2'-bithiophene exhibit a low oxidation potential and a high length of conjugation [11].

3,4'-Dibutoxy-2,2'-bithiophene **1** is obtained from the corresponding dibromo derivative, recently synthesized in our laboratory [16]. This work represents a part of a more general study exploring the versatility of β,β' -dibromo-2,2'-bithiophenes as starting compounds to generate disubstituted bithiophenes. The ^1H and ^{13}C nmr data of **1**, together with those of 3,3'- **2** and 4,4'-dibutoxy-2,2'-bithiophene **3**, are also reported and discussed in relation to the regiochemistry.



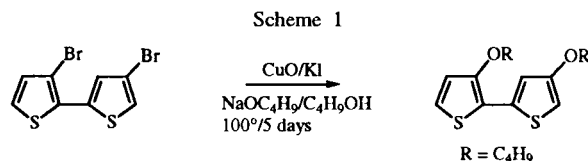
Synthesis.

Two routes are usually followed to synthesize α,α' -disubstituted bithiophenes. The first consists in the oxidative homo-coupling of metallated thiophenes [17], and the second in the cross coupling of α -metallated thiophenes with α -halothiophenes [15,18,19]. Symmetrical dimers can be satisfactorily synthesized by coupling reactions regardless of the type of substituent [11,18,19]. In con-

trast, for *head-to-tail* dimers bearing an electroactive group, this route presents some disadvantages due to difficulties arising during the formation and purification of the suitable substituted starting monomers and to the generation, during the coupling process, of poorly separable isomeric by-products [20].

A third route, reported here, is based on the use of β,β' -dibromo- α,α' -bithiophenes [11,16,18,21], as intermediates for the synthesis of β,β' -disubstituted regioisomers. Whereas 3,3'- and 4,4'-dibromo-2,2'-bithiophenes are already known and can be readily obtained from low-cost starting materials [11,21,22], the synthesis of 3,4'-dibromo-2,2'-bithiophene was only recently reported [16]. It is based on the coupling reaction between 3-bromo-2-(trimethylstannyl)thiophene and 3,5-dibromo-2-(trimethylsilyl)thiophene, followed by desilylation. 3,4'-Dibromo derivative proved to be very useful to obtain the corresponding *head-to-tail* bis(alkylsulfanyl) bithiophenes [16].

The procedure utilized for generation of dimer **1** starting from the corresponding dibromo derivative is depicted in Scheme 1.



Dimer **1** was obtained (90% yield of isolated product) from 3,4'-dibromo-2,2'-bithiophene by reaction with sodium alcoholate in butyl alcohol catalyzed by cuprous oxide/potassium iodide.

By using the same procedure, dimer **2** (85% yield of isolated product) and dimer **3** (98% yield of isolated product) were obtained from 3,3'- and 4,4'-dibromo-2,2'-bithiophene, respectively.

This method allows us to improve the yield in 3,3'-dibutoxy-2,2'-bithiophene **2**, synthesized by oxidative-coupling (33% yield) [11], and in 4,4'-dibutoxy-2,2'-bithiophene **3**, obtained by bromine-substitution (49%) [11]. The increased yield in compound **3** is probably due to the

chromatographic purification performed with silica neutralized with triethylamine, in order to avoid the polymerization of the products.

The reaction reported in Scheme 1 generalizes the known route of bromine substitution that has been applied to symmetrical bithiophenes [11,18,21].

NMR Spectroscopy Structural Assignment.

The aromatic region of the ^1H nmr spectrum of derivative 1 shows the characteristic pattern for asymmetric β,β' -disubstituted bithiophenes. Two different chains are also detected in the aliphatic region.

The assignment of the direct and long-range connected protons and carbons was performed through a single inverse detected heteronuclear multiple-quantum coherence experiment (HMQC) [23]. The inverse detected $^1\text{H},^{13}\text{C}$ uncoupled chemical-shift correlation spectrum is depicted in Figure 1. In the experimental conditions utilized (evolution delay corresponding to a $^n\text{J}(\text{C},\text{H}) = 7$ Hz), the spectrum contains information about direct and long-

range connected protons and carbons and about the ^1J and ^nJ coupling constants.

The directly bonded C-H pairs were assigned by observing the difference between $^1\text{J}[\text{C}(\alpha),\text{H}(\alpha)]$ and $^1\text{J}[\text{C}(\beta),\text{H}(\beta)]$ [24]. The assignment of the quaternary carbons was achieved through the relayed protons and the relative values of the $^n\text{J}(\text{C},\text{H})$ coupling constants [23].

The existence of a long-range coupling constant between $\text{CH}_2(\alpha)$ protons and the quaternary carbon bearing the alkoxy chain of the thiophene ring allowed the assignment of each chain to the proper ring to be accomplished. As a result, $\text{CH}_2(\alpha)$ at 4.10 ppm belongs to the 3-chain whereas $\text{CH}_2(\alpha)$ at 3.90 ppm to the 4'-chain. The ^1H spectra of derivatives 2 and 3 show the pattern of 2,3- and 2,4-disubstituted thiophene rings, respectively. The proton and carbon assignments were performed following the above procedure. The ^1H and ^{13}C nmr chemical shifts for derivatives 1-3 are reported in Tables 1 and 2.

Inspection of Table 1 indicates some regiochemical features of the chemical shifts which can be used for future analysis of related higher oligomers and polymers. In this view, particular attention must be paid to β -aromatic and aliphatic protons. The more deshielded β -proton is found in the *tail* unit of the *head-to-tail* dimer 1. In the same derivative, the chemical shifts of the 3-butoxy chain are nearly equal to those of the *head-to-head* dimer 2, whereas the chemical shifts of the 4'-butoxy chain are similar to those of the *tail to tail* dimer 3, the former being deshielded with respect to the latter. This behavior is markedly different to that found for the corresponding dihexyl [25] and bis(butylsulfanyl)-2,2'-bithiophenes [16,18] and is probably related to a difference in conformation of the corresponding dimers. The deshielding of the butoxy chain in derivative 2 and in the *head* unit of derivative 1, is attributable to the anisotropy effect of the adjacent aromatic ring as a consequence of a conformation in solution similar to that found in the solid state for 3,3'-dipentoxy-2,2'-bithiophene [12]. For this last derivative an *anti-planar* conformation (probably due to an attractive interaction between the O atom of the 3-substituent and the S ring atom of the adjacent thiophene) has been found, whereas for analogue alkyl and *S*-alkyl derivatives containing the *head-to-head* subunit a distorted *cisoid* or *transoid* conformation is generally reported [26]. Hence, the deshielding of the butoxy chains of *head* units of derivatives 1 and 2 is strong indication of an *anti-planar* conformation of the two thiophene rings in contrast with the results of MM2 calculations on the three isomeric β,β' -dimethoxy-2,2'-bithiophenes, recently reported [15].

Chemical shifts of the junction carbons and those of the carbons bearing the alkoxy substituents (Table 2) are

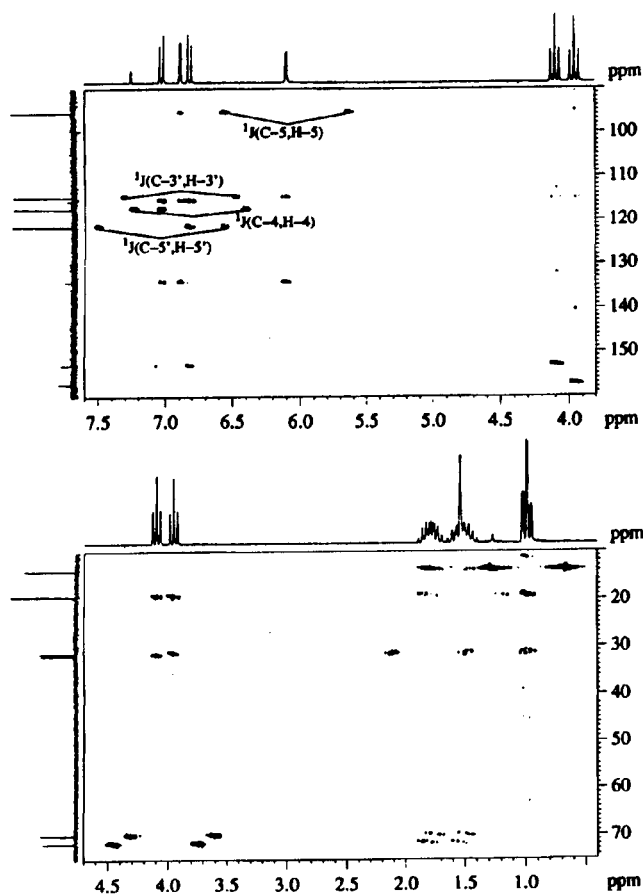


Figure 1. ^1H , ^{13}C HMQC nmr spectrum of 1. Proton and carbon 1D nmr spectra are shown as traces in F2 and F1 dimensions, respectively. Top: Expanded region corresponding to aromatic carbons. The ^1H and ^{13}C direct correlations are labelled. Bottom: Expanded region corresponding to aliphatic carbons.

Table 1
¹H Chemical Shifts[a] (ppm) of Derivatives 1-3

Derivative	3-H/3'-H	4-H/4'-H	5-H/5'-H		CH ₂ (α)	CH ₂ (β)	CH ₂ (γ)	CH ₃
1	-	6.82	7.03	3-chain	4.10	1.82	1.55	0.98
	6.89	-	6.10	4'-chain	3.90	1.76	1.48	0.97
2	-	6.83	7.07		4.10	1.83	1.55	0.99
3	6.80	-	6.10		3.95	1.76	1.50	0.98

[a] δ Values are referred to internal tetramethylsilane.

Table 2
¹³C Chemical Shifts[a] (ppm) of Derivatives 1-3

Derivative	C-2/C-2'	C-3/C-3'	C-4/C-4'	C-5/C-5'		CH ₂ (α)	CH ₂ (β)	CH ₂ (γ)	CH ₃
1	115.5	153.0	117.4	121.4	3-chain	71.6	31.7	19.3	13.8
	133.9	114.7	157.2	95.5	4'-chain	69.8	31.3	19.3	13.8
2	114.2	152.0	116.1	121.6		71.7	31.8	19.3	13.9
3	136.0	115.9	157.6	96.4		69.8	31.3	19.2	13.8

[a] δ Values are referred to internal tetramethylsilane.

regiochemically dependent; the more shielded and the more deshielded C2-C2' are present in the *head-to-head* and the *tail-to-tail* dimer, respectively. An intermediate situation is present for the *head-to-tail* derivative. The carbons bearing the substituents are more deshielded in the *tail* units than in the *head* ones. A similar behavior is found for the carbons of the aliphatic chains. The two chains in the *head-to-tail* dimer are difficult to distinguish from those of the *head-to-head* and the *tail-to-tail* dimers, when both carbon and proton chemical shifts are taken into account. This implies that a fine analysis of the aliphatic region of poly(3-butoxythiophene), in terms of all four configurational triads, as was done for poly(3-hexylthiophene) [24], will be hardly achieved. In particular, the regiochemical assignment should be better obtained from the analysis of the proton and carbon aromatic patterns.

EXPERIMENTAL

All of the reactions were performed in argon or nitrogen atmospheres in a flame-dried apparatus. Copper(II) oxide and potassium iodide were dried under vacuum (10 mmHg) over phosphorus pentoxide at 70-120°. *n*-Butanol was refluxed with magnesium activated with iodine and distilled.

Melting points (uncorrected) were recorded with a Büchi apparatus. All uv-vis spectra were taken on 1 • 10⁻⁴ M solutions in chloroform (spectroscopic grade) using a Varian-Cary 3 spectrophotometer. Purity of all compounds was monitored by thin layer chromatography (Merck thin layer chromatography plates 10-20 cm silica gel 60 F₂₅₄). Preparative column chromatography was performed using glass columns of different size, packed with silica gel RS, grain size 0.05-0.20 mm (Carlo Erba) neutralized with a 2% triethylamine solution.

The ¹H and ¹³C nmr spectra were recorded on a Bruker DPX-200 spectrometer operating at 200.13 and 50.61 MHz, respectively. All nmr spectra were recorded in deuteriochloroform and the chemical shifts are reported in ppm as δ relative to internal tetramethylsilane at 0.0 ppm. Coupling constants are given in Hz.

HMQC [23] parameters for aromatic and aliphatic region are: spectral width (f2) = 8 ppm, 2048 complex points; spectral width (f1) = 170 ppm, 512 tl increments with 32 scans per tl value; relaxation and evolution delays = 0.5 s and 71 ms, respectively. Zero filling in f1 and f2, sine function in f1 were applied before Fourier transformation.

3,4'-Di(*n*-butoxy)-2,2'-bithiophene (1).

To a solution of sodium (0.40 g, 17.40 mmoles) in *n*-butanol (25 ml), copper(II) oxide (0.25 g, 3.14 mmoles) and potassium iodide (0.04 g, 0.24 mmole) were added, followed by the addition of 3,4'-dibromo-2,2'-bithiophene (1.00 g, 3.09 mmoles). The reaction mixture was stirred at 100° for 3 days and more potassium iodide (0.04 g, 0.24 mmole) was added. Stirring was continued for 2 days at the same temperature and the mixture filtered. The butanol solution was poured into water and extracted with ether. The combined organic layers were washed with water, dried magnesium sulfate, and evaporated.

The crude product was purified by chromatography (petroleum ether bp 30-50°/chloroform = 4:1), to give 0.86 g (90%) of 1, *n*_D²⁷ = 1.5811; λ_{max} (chloroform): 327 nm (ε 1.4 x 10⁴ dm³ mol⁻¹ cm⁻¹); ¹H nmr (deuteriochloroform): δ 1.01 (t, 3H, CH₃'), 1.02 (t, 3H, CH₃), 1.56 (m, 2H, CH₂(γ)'), 1.58 (m, 2H, CH₂(γ)), 1.80 (m, 2H, CH₂(β)'), 1.82 (m, 2H, CH₂(β)), 3.99 (t, 2H, CH₂(α)'), 4.14 (t, 2H, CH₂(α)), 6.14 (d, J_{3,5} 1.7, 1H, 5'-H), 6.85 (d, J_{4,5} 5.3, 1H, 5-H), 6.92 (d, J_{3,5} 1.7, 1H, 3'-H), 7.07 ppm (d, J_{4,5} 5.3, 1H, 4-H).

Anal. Calcd. for C₁₆H₂₂O₂S₂: C, 61.90; H, 7.14; S, 20.65. Found: C, 61.73; H, 7.03; S, 20.78.

3,3'-Di(*n*-butoxy)-2,2'-bithiophene (2).

Following the above procedure, compound 2 [21] was obtained from 3,3'-dibromo-2,2'-bithiophene. The residue was

column chromatographed (petroleum ether) to afford a solid product (85%) from 3,3'-dibromo-2,2'-bithiophene, mp 101-102°C; λ_{max} (chloroform): 325 nm (ϵ 1.5×10^4 dm³ mol⁻¹ cm⁻¹); ¹H nmr (deuteriochloroform): δ 0.99 (t, 6H, CH₃), 1.57 (m, 4H, CH₂(γ)), 1.84 (m, 4H, CH₂(β)), 4.11 (t, 4H, CH₂(α)), 6.84 (d, J_{4,5} 5.5, 2H, 5-H), 7.08 ppm (d, J_{4,5} 5.5, 2H, 4-H).

Anal. Calcd. for C₁₆H₂₂O₂S₂: C, 61.90; H, 7.14; S, 20.65. Found: C, 62.02; H, 7.00; S, 20.51.

4,4'-Di(*n*-butoxy)-2,2'-bithiophene (3).

According to the above procedure, compound 3 [11] was prepared from 4,4'-dibromo-2,2'-bithiophene. Chromatography on silica gel (petroleum ether) gave a solid product (98%), mp 59-62°C; λ_{max} (chloroform): 324 nm (ϵ 7.4×10^3 dm³ mol⁻¹ cm⁻¹); ¹H nmr (deuteriochloroform): δ 0.98 (t, 6H, CH₃), 1.49 (m, 4H, CH₂(γ)), 1.76 (m, 4H, CH₂(β)), 3.94 (t, 4H, CH₂(α)), 6.12 (d, J_{3,5} 1.6, 2H, 5-H), 6.83 ppm (d, J_{3,5} 1.6, 2H, 3-H).

Anal. Calcd. for C₁₆H₂₂O₂S₂: C, 61.90; H, 7.14; S, 20.65. Found: C, 61.77; H, 7.31; S, 20.84.

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