INVESTIGATION OF SOME NITROGEN COMPOUNDS OF 2,2'-BITHIOPHENE 7.*

NITRATION OF 5-R-2,2'-BITHIOPHENES CONTAINING ELECTRON-DONATING SUBSTITUENTS

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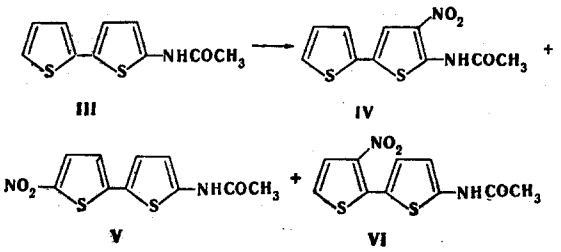
At the present time the nitration of 2,2'-bithiophene and 5-R-2,2'-bithiophenes [2, 3] in which R represents electron-withdrawing substituents has been studied.

In a continuation of previous investigations in the 2,2'-bithiophene series [4] on the effect of structural factors and reaction conditions on the direction of electrophilic substitution, we studied for the first time the nitration of 5-acetamido-2,2'-bithiophene (III) and 5-methyl-2,2'-bithiophene (VII).

The nitration of (III) with nitric acid in an acetic anhydride medium at temperatures between +10 and −20°C with reaction times between 4 and 8 h is accompanied by the formation of a mixture of three mononitro isomers (Table 1):



The nitration of (VII) under analogous conditions is accompanied by the formation of a mixture of only two mononitro isomers (Table 2):

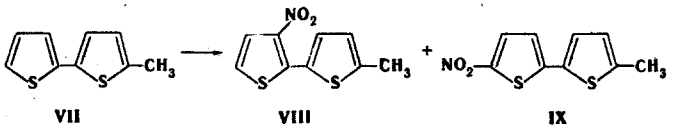


TABLE 1. Quantitative Ratio of the Mononitro Isomers in the Nitration of 5-Acetamido-2,2'-bithiophene (III)

Reaction time, h	Reaction temperature, °C	Overall yield of mononitro isomers, %	Ratio of mononitro isomers			Recovery of unreacted initial compound, %	Overall yield of dinitro isomers, %
			5′-NO_2	4-NO_2	3′-NO_2		
4	0	30	2,0	1,9	1	28	Traces
6	0	49	2,0	1,9	1	4,5	2
8	0	49	2,1	2,0	1	—	4
6	+10	17	0,5	1	1	—	10
6	0	49	2,0	1,9	1	4,5	2
6	−10	31	1,6	1	1	27	Traces
6	−20	18	1	1	1	50	—

*For Communication 6, see [1].

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TABLE 2. Quantitative Ratio of the Mononitro Isomers in the Nitration of 5-Methyl-2,2'-bithiophene (VII)

Reaction time, h	Reaction temperature, °C	Overall yield of mononitro isomers, %	Ratio of mononitro isomers		Recovery of unreacted initial compound, %	Overall yield of dinitro isomers, %
			5'-NO_2	3'-NO_2		
4	0	28	2,2	1	35	—
6	0	35	2,2	1	26	—
8	0	48	2,4	1	10	2
6	+10	48	2,4	1	10	4
6	0	35	2,2	1	26	—
6	−10	29	1,7	1	34	—
6	−20	15	1,4	1	55	—

The structure of the synthesized compounds was demonstrated on the basis of the PMR, IR, UV, and mass spectra. In the PMR spectrum of compound (III) there are three signals, forming a three-spin ABC system [5] and belonging to the protons of the thiophene ring not containing substituents. The signals at 7.44 ($J_{4',5'}$ = 5.0, $J_{3',5'}$ = 1.2 Hz), 7.22 ($J_{3',4'}$ = 3.5, $J_{3',5'}$ = 1.2 Hz), and 7.12 ppm ($J_{4',5'}$ = 5.0, $J_{3',4'}$ = 3.5 Hz) belong to the 5'-H, 3'-H, and 4'-H protons respectively. The protons of the second thiophene ring represent doublets of an AB spin system at 6.64 and 7.07 ppm ($J_{3,4}$ = 4.0 Hz), belonging to 4-H and 3-H respectively. The position of the nitro groups in compounds (IV-VI) was determined from the PMR spectra with due regard to its effect on the chemical shift of the protons [6]. In the spectrum of compound (IV) in the downfield region there is a singlet at 7.69 ppm, indicating the presence of two substituents in one of the thiophene rings. The multiplicity of the signals at 7.71 ($J_{4',5'}$ = 5.0, $J_{3',5'}$ = 1.2 Hz), 7.52 ($J_{3',4'}$ = 3.5, $J_{3',5'}$ = 1.2 Hz), and 7.24 ppm ($J_{4',5'}$ = 5.0, $J_{3',4'}$ = 3.5 Hz) shows that there are no substituents in the second ring. The chemical shift of the singlet at 7.69 ppm indicates the position of the NO_2 group at C_4. In the spectrum of compound (V) there are two pairs of doublets of an AB system. The doublets at 8.03 and 7.26 ppm ($J_{3',4'}$ = 4.5 Hz) are due to the 4'-H and 3'-H protons. The downfield shift of the 4'-H signal (8.03 ppm) showed that the NO_2 group is at $C_{5'}$. In the spectrum of compound (VI), as in the spectrum of (V), there are two pairs of doublets for an AB system, and this shows that the substituents are in different thiophene rings. The spin–spin coupling constant of the doublets at 7.66 and 7.52 ppm (5.0 Hz [7]) shows that these signals belong to 4'-H and 5'-H respectively. The NO_2 group in compound (VI) is therefore at $C_{3'}$.

The assignment of the signals in compounds (VII-IX), given in the experimental section, was made similarly. The position of the NO_2 group was also demonstrated by successive conversion of the methyl group into a carboxyl group with subsequent decarboxylation and the production of the corresponding known [8, 9] 5-nitro- and 3-nitro-2,2'-bithiophenes.

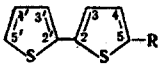
The nitro group is in conjugation with the remaining part of the molecule, as shown by the bathochromic shift of λ_{max} for the long-wave band by 66-117 nm in the electronic spectra, due to an increase in the length of the total chain of conjugation with the introduction of the nitro group.

The nitro group in compound (IV) gives rise to a shift of the amide $\nu_{C=O}$ in the IR spectrum toward the long-wave region by 49 cm^{-1}, indicating the presence of a strong electron acceptor at the o position to the $NHCOCH_3$. A shift of the amide $\nu_{C=O}$ by 59 and 50 cm^{-1} respectively was observed in the 3-nitro-2-acetamidothiophene [10] and o-nitroacetanilide [11] synthesized for IR spectroscopic investigations.

In parallel with the experimental work, the reactivity indices of the molecules (III) and (VII) were calculated. For this purpose the energies of electrophilic localization (L_E) and the overall charges of the rings (ΣQ), calculated by the PPP method [12-14], were used (Table 3).

It was shown that, according to the L_E values, electrophilic substitution at positions 5',3', and 4 is preferred both in (III) and in (VII). In fact, 5'-, 3'-, and 4-nitro isomers were isolated and identified during the nitration of (III), whereas it was not possible to detect the 4-nitro isomer in the mixture during the nitration of (VII) under the given conditions. Evidently, the +M effect of the amide group considerably activates position 4 in comparison with the +I effect of the methyl, and in comparative respects this is confirmed experimentally during nitration of the biphenyl analogs [15, 16] of compounds (III) and (VII).

TABLE 3. Reactivity Indices of the Carbon Atoms of (III) and (VII)



R	Atom No.	5′	4′	3′	3	4
$NHCOCH_3$	L_E	10,319	11,374	10,782	11,432	11,240
	ΣQ		−0,003		−0,088	
CH_3	L_E	9,621	12,862	10,393	11,292	11,085
	ΣQ		−0,038		−0,082	

The larger values of the overall charges ΣQ for the substituted thienyl fragments in (III) and (VII) show that they have an activating effect on the ortho–para orientation in the unsubstituted thiophene rings. The obtained experimental data, given in Tables 1 and 2, show that the introduction of $NHCOCH_3$ and CH_3 groups at position 5 of the 2,2′-bithiophene molecule leads to an increase in the ratio of the 5′-NO_2/3′-NO_2 isomers compared with the nitration of unsubstituted 2,2′-bithiophene [2, 3]. At the same time, there is no significant difference in the effect of the amide and methyl groups on the ratio of the 5′/3′-nitro isomers. The decrease in the 5′-NO_2/3′-NO_2 ratio with decrease in temperature from +10 to −20°C from 2.1:1 to 1:1 in the nitration of (III) and from 2.4:1 to 1.4:1 in the nitration of (VII) is evidently due to a decrease in the steric hindrances for substitution at position 3′, as observed earlier in the mononitration of 2,2′-bithiophene [2, 3]. A reaction temperature of 0°C and a reaction time of 8 h must be considered optimum for the nitration of (III) and (VII) in order to obtain the highest overall yield of the mononitro isomers, the preferential formation of the 5′-NO_2 isomer, and the minimum recovery of the initial compound.

EXPERIMENTAL

The PMR spectra were obtained on a Varian XL-100 instrument with TMS as internal standard in DMSO-d_6. The IR spectra were recorded on a UR-20 spectrophotometer in tablets with potassium bromide. The UV spectra were recorded on a Specord UV-vis spectrophotometer in alcohol ($c = 3 \cdot 10^{-4}$ M). The mass spectra were recorded on an LKB-9000 instrument with direct injection of the sample into the source at an ionization potential of 70 eV. Silufol UV-254 plates were used for TLC, and Chemapol L100/250 μ silica gel was used for column chromatography.

5-Nitro-2,2′-bithiophene (I) was obtained by the method in [2]; mp 108-109°C (from methanol). Published data [8]: mp 109°C (from ethanol).

Complex Tin Salt of 5-Amino-2,2′-bithiophene Hydrochloride (II). To a suspension of 4.22 g (0.22 mole) of (I) in 42 ml of hydrochloric acid (d = 1.19) over 30 min in small portions we added 5.3 g of tin, while keeping the temperature at 20-25°C. The mixture was stirred until the tin had completely dissolved. The precipitate was filtered off, washed with ether, and dried. The yield was 6.6 g (95%). The product formed light-yellow prisms. Found, %: Sn 16.96. $C_{16}H_{16}Cl_6N_2S_4Sn$. Calculated, %: Sn 16.98.

5-Acetamido-2,2′-bithiophene (III). To a suspension of 6.6 g of (II) in 13 ml of water at 0°C we added 7 g of acetic anhydride in 22 ml of ether. While not allowing the temperature to rise above 10°C and slowly stirring, we added a 10% solution of sodium hydroxide to a weakly alkaline reaction. The stirring was continued for 30 min, and the ether was removed by bubbling with air. The precipitate was filtered off, washed with water, dried, and purified by chromatography on a column. The yield was 2.97 g (70%); mp 152-153°C (from chloroform). R_f 0.085. IR spectrum: 1652 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 334.2 nm (4.23). PMR spectrum, δ: 2.17 (3H, s, $NHCOCH_3$); 6.64 (d, 4-H); 7.07 (d, 3-H); 7.22 (d, 3′-H); 7.12 (d, 4′-H); 7.44 ppm (d, 5′-H). Found, %: C 53.59; H 3.91; N 6.35; S 28.56. Mol.wt. 223. $C_{10}H_9NOS_2$. Calculated, %: C 53.78; H 3.06; N 6.27; S 28.72. Mol.wt. 223.

Nitration of (III) with Nitric Acid in Acetic Anhydride. A 0.223-g sample (0.001 mole) of (III) was dissolved in 50 ml of acetic anhydride. While keeping the temperature at 0°C, we added 0.069 g (0.001 mole) of nitric acid (d 1.5) in 15 ml of acetic anhydride. The mixture was stirred at 0°C for 6 h. It was then added to water. The nitro product was

extracted with ether, and the ether extracts were washed to a neutral reaction with water and dried. The ether was distilled to dryness, the residue was dissolved in chloroform, and the solution was separated on a column with chloroform as eluent.

The first fraction was 4-nitro-5-acetamido-2,2'-bithiophene (IV); mp 198-199°C (from chloroform). The yield was 0.05 g (19%). R_f 0.48. IR spectrum: 1701 (C=O), 1512 and 1348 cm^{-1} (NO_2). UV spectrum, λ_{max} (log ε): 400 nm (4.04). PMR spectrum, δ: 2.49 (3H, s, $NHCOCH_3$); 7.69 (s, 3-H); 7.52 (d, 3'-H); 7.24 (d, 4'-H); 7.71 ppm (d, 5'-H). Found, %: C 44.75; H 2.98; N 10.15; S 23.82. Mol.wt. 268. $C_{10}H_8N_2O_3S_2$. Calculated, %: C 44.76; H 3.00; N 10.44; S 23.90. Mol.wt. 268.

The second fraction contained 0.005 g (1.9%) of a mixture of the 5',4- and 3',4-dinitro derivatives of (III).

The third fraction contained 0.012 g (4.5%) of the initial (III).

The fourth fraction contained 5'-nitro-5-acetamido-2,2'-bithiophene (V); mp 247-248°C (from chloroform). The yield was 0.053 g (20%). R_f 0.07. IR spectrum: 1661 (C=O), 1515 and 1314 cm^{-1} (NO_2). UV spectrum, λ_{max} (log ε): 451.2 nm (4.29). PMR spectrum, δ: 2.14 (3H, s, $NHCOCH_3$); 6.68 (d, 4-H); 7.45 (3-H); 7.26 (d, 3'-H); 8.03 ppm (d, 4'-H). Found, %: C 44.80; H 3.11; N 10.32; S 23.82. Mol.wt. 268. $C_{10}H_8N_2O_3S_2$. Calculated, %: C 44.76; H 3.00; N 10.44; S 23.90. Mol.wt. 268.

The fifth fraction contained 3'-nitro-5-acetamido-2,2'-bithiophene (VI); mp 215-216°C (from chloroform). The yield was 0.027 g (10%). R_f 0.05. IR spectrum: 1650 (C=O), 1508, and 1311 cm^{-1} (NO_2). UV spectrum, λ_{max} (log ε): 424.8 nm (3.85). PMR spectrum, δ: 2.16 (3H, s, $NHCOCH_3$); 6.74 (d, 4-H); 7.48 (d, 3-H); 7.66 (d, 4'-H); 7.52 ppm (d, 5'-H). Found, %: C 44.71; H 3.05; N 10.35, S 23.84. Mol.wt. 268. $C_{10}H_8N_2O_3S_2$. Calculated, %: C 44.76; H 3.00; N 10.44; S 23.90. Mol.wt. 268.

The nitration of (III) was realized similarly at +10, −10, and −20°C for 6 h and at 0°C for 4 and 8 h. The average results from the experiments after threefold repetition are given in Table 1.

5-Methyl-2,2'-bithiophene (VII) was obtained by the method in [4]; bp 142°C (14 mm Hg). Published data [4]: bp 147°C (15 mm Hg).

Nitration of (VII) with Nitric Acid in Acetic Anhydride. A 0.178-g sample (0.001 mole) of (VII) was dissolved in 50 ml of acetic anhydride. While keeping the temperature at 0°C, we added 0.069 g (0.001 mole) of nitric acid (d = 1.5) in 15 ml of acetic anhydride. The mixture was stirred at 0°C for 8 h. It was then added to water. The nitro product was extracted with ether, and the ether extracts were washed to a neutral reaction with water and dried. The ether was distilled to dryness, and the residue was dissolved in heptane and separated on a column with heptane as eluent.

The first fraction contained 0.018 g (10%) of the initial compound (VII).

The second fraction contained 3'-nitro-5-methyl-2,2'-bithiophene (VIII); bp 214-216°C (10 mm Hg). The yield was 0.032 g (14%). R_f 0.094. IR spectrum: 1360 (CH_3), 1510 and 1315 cm^{-1} (NO_2). UV spectrum, λ_{max} (log ε): 382 nm (4.04). PMR spectrum, δ: 2.40 (3H, s, CH_3); 6.97 (d, 4-H); 7.55 (d, 3-H); 7.71 (d, 4'-H); 7.54 ppm (d, 5'-H). Found %: C 48.01; H 3.06; N 6.27; S 28.34. Mol.wt. 223. $C_9H_7NO_2S_2$. Calculated %: C 47.98; H 3.13; N 6.21; S 28.47. Mol.wt. 223.

The third fraction contained 5'-nitro-5-methyl-2,2'-bithiophene (IX); mp 137-138°C (from heptane). The yield was 0.077 g (34%). R_f 0.055. IR spectrum: 1369 (CH_3), 1525 and 1338 cm^{-1} (NO_2). UV spectrum, λ_{max} (log ε): 411.3 nm (4.25). PMR spectrum, δ: 2.51 (3H, s, CH_3); 6.91 (d, 4-H); 7.51 (d, 3-H); 7.32 (d, 3'-H); 8.08 (d, 4'-H). Found %: C 48.07; H 3.01; N 6.32; S 28.32. Mol.wt. 223. $C_9H_7NO_2S_2$. Calculated, %: C 47.98; H 3.13; N 6.21; S 28.47. Mol.wt. 223.

The fourth fraction contained 0.005 g (2%) of a mixture of the 5',4- and 3',4-dinitro derivatives of (VII).

The nitration of (VII) was carried out similarly at +10, −10, and −20°C for 6 h and at 0°C for 4 and 6 h. The average results from the experiments after threefold repetition are given in Table 2.

5-Carboxy-5'-nitro-2,2'-bithiophene (X). Compound (X) was obtained by oxidation of (IX) by the method in [16]; mp 286-288°C (from glacial acetic acid). Published data [16]: mp 286-288°C (from glacial acetic acid).

5-Carboxy-3'-nitro-2,2'-bithiophene (XI). Compound (XI) was obtained by oxidation of (VIII) by the method in [16]; mp 278-280°C (from glacial acetic acid). Published data [16]: mp 278-280°C (from glacial acetic acid).

5-Nitro-2,2'-bithiophene (I). Compound (I) was obtained by decarboxylation of (X) by the method in [16]; mp 109°C (from methanol). Published data [8] : mp 109°C (from ethanol).

3-Nitro-2,2'-bithiophene (XII). Compound (XII) was obtained by decarboxylation of (XI) by the method in [16]; mp 38-39°C (from heptane). Published data [9]: mp 39°C (from petroleum ether).

3-Nitro-2-acetamidothiophene (XIII). Compound (XIII) was obtained by the method in [10]; mp 165-166°C (from ethanol). Published data [10]: mp 166°C (from ethanol).

o-Nitroacetanilide (XIV). Compound (XIV) was obtained by the method in [11]; mp 92-93°C (from water). Published data [11]: mp 93°C (from water).

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