

On the Nitration of 2-Benzylthiophene and the Spectroscopic Behaviour of Nitro-2-benzylthiophenes

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Received March 20, 1972

Nitration of 2-benzylthiophene with nitric acid (molar ratio 1:1) in acetic anhydride gave only nitro-2-benzylthiophenes, indicating the benzene ring is unreactive to this electrophilic substitution. The main reaction product was 2-benzyl-5-nitrothiophene (about 87%); the amounts of the 3-nitro and 4-nitro isomers were about 10% and 3%, respectively. These percentages, determined by glc and nmr techniques, were found to be constant using various nitration conditions. The syntheses of the nitro-2-benzylthiophenes are described, together with some spectroscopic properties.

The uv spectra confirm that the conjugation of the nitro group in the α position is greater than in the β position. The isomer structures have been assigned by nmr chemical shifts and coupling constant of the thiophene protons. Also infrared spectra are briefly considered.

In this paper the nitration of 2-benzylthiophene is examined in connection with the research on the reactivities and the spectroscopic behaviour (1) of compounds having both thiophene and benzene systems. In 2-benzylthiophene, the insulating effect of the methylene group prevents mesomeric interactions between the two aromatic rings.

The agent used for these nitrations was nitric acid in acetic anhydride. The experimental conditions (e.g. temperature, reaction times, reactive concentrations) were varied and the results reported in Table I.

Under these conditions the nitration of 2-benzylthiophene gave 2-benzyl-5-nitrothiophene as the main product (about 87% of the nitrated product), the 3-nitro isomer (about 10%) and the 4-nitro derivative (about 3%).

SCHEME I

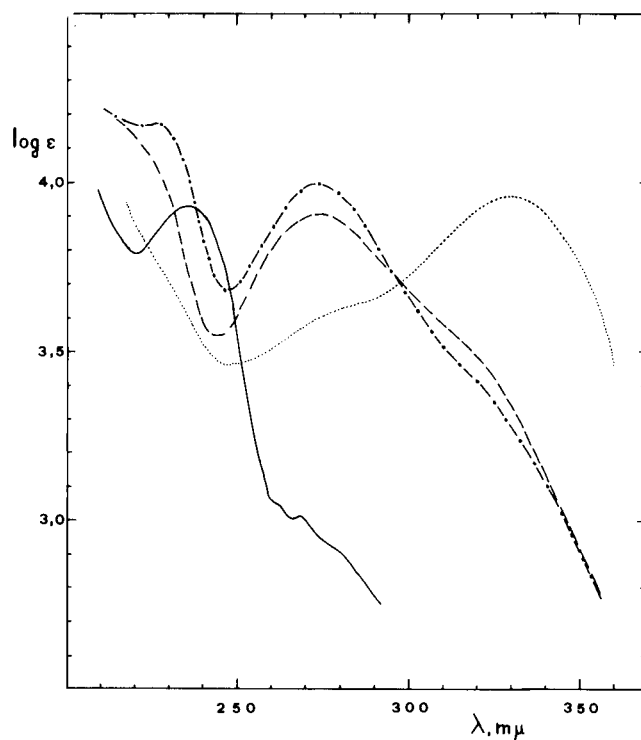
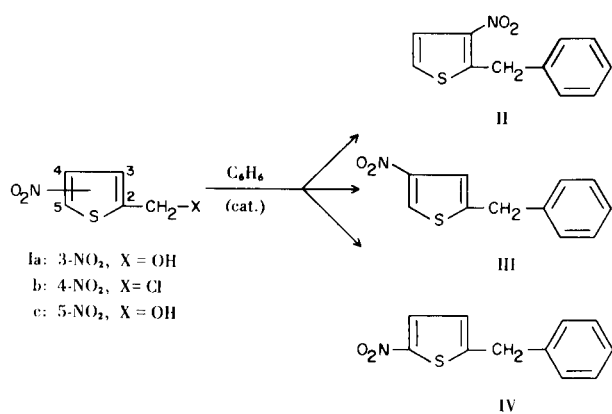


Figure 1. Uv Spectra in Ethanol 95°

2-benzylthiophene —————
 2-benzyl-3-nitrothiophene - - - - -
 2-benzyl-4-nitrothiophene - · - · -
 2-benzyl-5-nitrothiophene · · · · ·

TABLE I

Nitration of 2-Benzylthiophene with Nitric Acid in Acetic Anhydride

No.	Temp. (°C)	Time (min.)	Molar ratio	Conv. %	3-NO ₂ (a) %	4-NO ₂ (b) %	5-NO ₂ (c) %
1	-20	120	1:1	73.2	9.4	2.8	87.8
2	-10	120	1:1	78.6	10.2	2.5	87.3
3	0	120	1:1	92.3	9.5	2.8	87.7
4	10	120	1:1	92.0	9.8	2.9	87.3
5	20	120	1:1	92.6	10.4	2.5	87.1
6	0	15	1:1	69.6	9.5	2.9	87.6
7	0	30	1:1	74.9	10.9	2.8	86.3
8	0	60	1:1	85.6	10.3	2.6	87.1
(3)	0	120	1:1	92.3	9.5	2.8	87.7
9	0	60	1:0.75	44.1	10.4	2.8	86.8
(8)	0	60	1:1	85.6	10.3	2.6	87.1
10	0	60	1:1.25	95.7	9.9	2.5	87.6

(a) Determined by glc (b) Determined by nmr spectroscopy (c) Determined by glc together with the 4-nitro isomer. The percentage reported has been calculated by subtraction of the 4-nitro percentage known by nmr analysis.

TABLE II

Nuclear Magnetic Resonance Spectra

Compound	Chemical Shifts δ (ppm)					J (cps)	
	H-3	H-4	H-5	-CH ₂ -	C ₆ H ₅ -	J _{CH₂-H₃}	J _{AB}
2-Benzylthiophene	(6.65	----	7.20) (a)	4.10 (b)	7.22	0.75	----
II	----	7.59	7.05	4.57	7.32	----	J _{4,5} = 5.70
III	7.35 (c)	----	8.07	4.10 (b)	7.29	1.00	J _{3,5} = 1.65
IV	6.73	7.71	----	4.10 (b)	7.27	0.9	J _{3,4} = 4.20

(a) Multiplet; (b) Doublet; (c) Partially covered by the peak of the benzene protons.

The isomer distribution has been determined by tlc, glc and nmr spectroscopy (see Experimental).

The nitration products were identified by comparison with the reference compounds, prepared as shown in Scheme I.

Temperature influenced the conversion in the range -20°-0° (Table I. No. 1, 2 and 3), while over 0° (No. 3, 4 and 5), the amount of nitro compounds was approximately constant (92 ± 0.3%). The reactions, carried out for different times (No. 3, 6, 7 and 8), showed that the nitration of 2-benzylthiophene is rather fast; in fact, after 15 minutes, the yield in nitro compounds is about 70%. Isomer distribution did not change under various experimental conditions (temperature, time, molar ratio).

From these results, it is evident that the thiophene ring, as expected, prevails in reactive competition between the two aromatic rings.

Moreover, we considered it interesting to carry out a nitration in acetic anhydride, at 0° for 1 hour, on a mixture of 2-methylthiophene and toluene (1:1), in order to correlate it with the 2-benzylthiophene nitration. It was found by glc that only 2-methylthiophene was nitrated, while toluene did not react. The nitrated mixture, in fact, had the following composition: 2-methyl-5-nitrothiophene (74%), 3-nitro isomer (22%), and 4-nitro isomer (4%). These percentages are similar to those reported for the nitration of 2-methylthiophene (2).

Ultraviolet Spectra.

In Figure 1 are reported the absorption curves of 2-benzylthiophene and nitro-2-benzylthiophenes. The nitro group in the thiophene ring of 2-benzylthiophene, characterized by a max at 235 m μ (log ϵ = 3.93) and a fine structure (269 m μ log ϵ = 3.01), has a remarkable

bathochromic effect.

In particular, for β -nitrothiophenes, (II and III), the max are located at $273 \pm 0.5 \mu\mu$ and show different intensity values, $\log \epsilon = 3.91$ and 4.00 respectively. This hypochromic effect in II can be related to an interference between the two vicinal groups.

In IV, instead, an inflection at about $285 \mu\mu$ ($\log \epsilon = 3.65$) and a wide absorption band toward lower frequencies (λ max at $330 \mu\mu$ and $\log \epsilon = 3.96$), are observed in agreement with the behaviour of α -nitrothiophene and α -nitro- α' -methylthiophene spectra (3).

Moreover the bathochromic effect in IV, $\Delta \lambda$ max = $57 \pm 0.5 \mu\mu$, in comparison with II and III points out the greater conjugation of the nitro group in the α position (4).

Infrared Spectra.

Nitro-2-benzylthiophenes show in the region 3200 - 2800 cm^{-1} , the CH-stretching bands, typical of aromatic (3110 - 3000 cm^{-1}) and methylene (2955 - 2760 cm^{-1}) groups. The two nitro group bands are located at 1540 - 1545 for $\nu \text{ NO}_2$ (asym.) and 1325 - 1340 cm^{-1} for $\nu \text{ NO}_2$ (sym.) (5). In the range 900 - 775 cm^{-1} the spectral differences among the isomers are more evident. In II, besides the band of weak intensity at $825 \pm 5 \text{ cm}^{-1}$ present in the three isomers, two other bands at 780 (s) and 850 (m) cm^{-1} are observed. In III the absorption bands occur at 790 (s), 850 (m), and 880 (m) cm^{-1} . In IV besides a weak absorption at 775 cm^{-1} , also a band of strong intensity at 818 cm^{-1} , characteristic of the 2-substituted-5-nitrothiophenes (6), is observed.

Nuclear Magnetic Resonance Spectra.

In Table II are provided the nmr spectral data for the nitro compounds investigated, together with those of 2-benzylthiophene (7).

The methylene protons resonance of 2-benzylthiophene (III and IV) occurs at 4.10 ppm, while in II the peak is shifted downfield (4.57 ppm), due to the deshielding effect of the nitro group in the vicinal position.

The structure of the nitro compounds has been confirmed by the coupling constant values of the thiophene protons (8).

Also, the CH_2 -H-3 coupling is useful for the characterization of nitro-2-benzylthiophenes. In fact in IV a doublet at 7.71 ppm due to H-4 and two triplets at 6.73 ppm, ascribed to CH_2 -H-3 coupling ($J = 0.90$ cps), are observed. In III the doublet due to H-5 occurs at 8.07 ppm, while the two triplets ($J = 1.00$ cps), shifted downfield are partially covered by the peak of the benzene protons. In II, obviously, only an AB quartet, whose doublets are at 7.59 (H-4) and 7.05 (H-5) ppm, is observed.

EXPERIMENTAL.

Products.

3-Nitro- and 5-Nitro-2-thenyl Alcohols (Ia and Ic).

2-Thenyl acetate (9) was nitrated with nitric acid ($d = 1.52$) in acetic anhydride at -10° to give 3-nitro and 5-nitro-2-thenyl acetate (10). The mixture was hydrolyzed by refluxing with 10% sulfuric acid for 1 hour (11). The distilled mixture (24 g.) of Ia and Ic was eluted from a silica-gel column ($L = 30 \text{ cm}$, $\phi = 2.5 \text{ cm}$), using carbon tetrachloride as eluent; 3 g. of Ia (m.p. 71 - 72° from ether-petroleum ether) and 18 g. of Ic (b.p. $148^\circ/3.5 \text{ mm}$) were isolated.

4-Nitro-2-thenyl Chloride (Ib).

3-Nitrothiophene (12), was chloromethylated with trioxane and zinc chloride in a stream of hydrogen chloride (b.p. 105 - $107^\circ/2 \text{ mm}$) (11).

2-Benzylthiophene.

2-Benzoylthiophene (13) was reduced by semicarbazide hydrochloride and potassium hydroxide in triethylene glycol (b.p. 73 - $74^\circ/0.2 \text{ mm}$; 84% yield) (14).

2-Benzyl-3-nitrothiophene (II).

To a stirred mixture of Ia (5 g.) and anhydrous benzene (200 ml.), 30 ml. of 96% sulfuric acid were added during 10 minutes. The solution was poured into water, the organic layer was separated and the aqueous layer was extracted with benzene. The collected extracts were washed with dilute sodium carbonate solution, dried and evaporated. The residue was purified from a silica-gel column ($L = 25 \text{ cm}$; $\phi = 2 \text{ cm}$), using a mixture carbon tetrachloride-chloroform (1:1) as eluent. The 1-8 fractions (15 ml. each) yielded 3.0 g. of II (m.p. 62 - 63° , colorless needles from petroleum ether).

Anal. Calcd. for $\text{C}_{11}\text{H}_9\text{NO}_2\text{S}$: C, 60.25; H, 4.14; N, 6.39; S, 14.62. Found: C, 60.34; H, 4.17; N, 6.51; S, 14.64.

2-Benzyl-4-nitrothiophene (III).

To a stirred solution of Ib (5 g.) in anhydrous benzene (100 ml.) were added 3 g. of anhydrous aluminum trichloride. The mixture was allowed to reflux for 3 hours, poured into water and extracted with benzene. The extract was washed with water, dried and evaporated. The residue was distilled to give 3.15 g. of III, pale yellow oil, b.p. $173^\circ/1.5 \text{ mm}$, $n_D^{20} = 1.6135$.

Anal. Calcd. for $\text{C}_{11}\text{H}_9\text{NO}_2\text{S}$: C, 60.25; H, 4.14; N, 6.39; S, 14.62. Found: C, 60.18; H, 4.05; N, 6.49; S, 14.68.

2-Benzyl-5-nitrothiophene (IV).

Compound IV was prepared from Ic, with the same procedure used for II. The residue was distilled under reduced pressure to give a pale yellow oil b.p. 150 - $151^\circ/0.6 \text{ mm}$; $n_D^{20} = 1.6340$.

Anal. Calcd. for $\text{C}_{11}\text{H}_9\text{NO}_2\text{S}$: C, 60.25; H, 4.14; N, 6.39; S, 14.62; Found: C, 60.33; H, 4.19; N, 6.26; S, 14.77.

Nitration.

Nitration of 2-Benzylthiophene.

To 1.74 g. (0.01 mole) of 2-benzylthiophene in 5 ml. of acetic anhydride at the established temperature, was added dropwise with stirring 10 ml. of nitrating mixture (0.41 ml. of distilled nitric acid (15) and 10 ml. of acetic anhydride) at the same temperature. The solution was stirred for the established time, and then poured into 100 g. of water and crushed ice, neutralized

with sodium carbonate and extracted several times with ether. The extract, dried and filtered, was evaporated and then analyzed by tlc, glc and nmr spectroscopy.

Nitration of a 2-Methylthiophene and Toluene Mixture.

To 0.98 g. (0.01 mole) of 2-methylthiophene and 0.92 g. (0.01 mole) of toluene in 5 ml. of acetic anhydride, 10 ml. of nitrating mixture containing 0.41 ml. (0.01 mole) of anhydrous nitric acid was added at 0° and the solution was stirred for 1 hour. The reaction mixture was poured into ice, neutralized, and extracted with ether. The extract was analyzed by tlc and glc.

Determination of Isomer Distribution.

Tlc, the thin layer chromatogram of the nitration mixture (Silica gel, carbon tetrachloride + 1% ethanol as eluent) showed four spots, identified by the comparison with the reference compounds as 2-benzylthiophene, II, III and IV.

Glc, the quantitative analysis of the isomer percentages was carried out by the internal normalization method, after the determination of the correction factors on known standard mixtures.

As III and IV have similar retention times and give one unresolved peak, it was possible to determine their sum. The quantitative determination of III was carried out by nmr analysis.

Glc of the 2-methylthiophene and toluene nitration, in comparison with that of the reference products indicated nitro-2-methylthiophenes, while nitrotoluenes were absent.

All the products were analyzed at 220° on a 80 cm column packed with methyl silicone polymer SE30 (25%) on chromosorb p (30-60 mesh) using helium as carrier (7.5 l/h).

Nmr, the spectra of the nitration mixtures were useful for the identification and determination of the three isomers. Their relative percentages were confirmed by the relative ratios of the integrated areas of H-4 proton for II (7.59 ppm, $J_{4,5} = 5.70$ cps), of H-5 proton for III (8.07 ppm, $J_{3,5} = 1.65$ cps) and of H-4 proton for IV (7.71 ppm, $J_{3,4} = 4.20$ cps).

Uv spectra were obtained with a Hitachi-Perkin-Elmer mod. EPS-3T spectrometer, in ethanol solutions (1×10^{-5} mole/l).

Ir spectra were recorded on a Perkin Elmer mod. 237 spectrometer, using potassium bromide discs for II, and as liquid film on NaCl plates for III and IV.

Nmr spectra were determined on a Varian A-60 spectrometer in deuteriochloroform with T.M.S. as internal standard.

Acknowledgment.

The authors are grateful to the Italian Research Council (C.N.R.) for the financial support which made this work possible.

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