Functional Derivatives of Thiophene. II. Synthesis and ^{1}H-NMR Spectra of 1-[2'-(5'-Nitrothienyl)]pyrazoles

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The preparation of 5-methyl-3,5-dimethyl- and 3,4,5-trimethyl-1[2'-(5'-nitrothienyl)]pyrazoles from thienylhydrazines are described. The ^{1}H-nmr spectra of these compounds are discussed.

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In addition to arylhydrazines, hydrazines of the heteroaromatic series used for the preparation of condensed pyrrole systems under the conditions of the Fischer reaction (1-3).

Communications regarding the use of thienylhydrazines (4) or its *N*-acylderivatives (5,6) in the synthesis of substituted thienopyrroles have recently appeared.

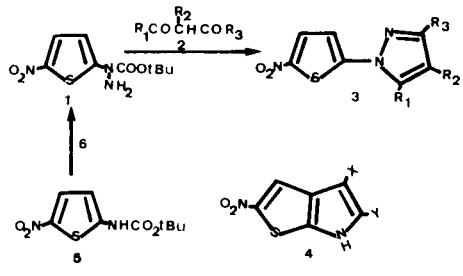
In the present paper we wish to report the results obtained in the reaction of *N*-*t*-butoxycarbonyl-*N*-[2'-(5'-nitrothienyl)]hydrazine (**1**) with several β-carbonyl compounds, **2**, in the presence of an acid catalyst (*cf.* Scheme 1). None of the thieno[2,3-*b*]pyrrole (**4**) was isolated. By contrast 1-[2'-(5'-nitrothienyl)]pyrazoles, **3**, were identified. This class of compounds (1-thienylpyrazoles) have not been very studied. In connection with a study of the chemistry of heterocyclic biaryls Gronowitz (7) has recently synthesized the 1-(2'-thienyl)pyrazole in good yield from 2-bromothiophene by reaction with the sodium salt of pyrazole using copper (II) oxide as catalyst.

In this paper the preparation of compounds **3** is described by an alternative method and the ^{1}H-nmr spectra are discussed.

The thienylhydrazine **1** was prepared by reaction of compound **5** (8) with *O*-(4-nitrobenzoyl) hydroxylamine (**6**) according to the method of Binder, *et al.*, (6).

Under our conditions the reaction between compound **1** and the β-ketobutyracetal (4,4-dimethoxy-2-butanone) (**2a**) gave only the 5-methyl isomer, **3a**, which is one of two possible **3a** isomeric structures.

Scheme I



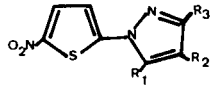
	R_1	R_2	R_3
a	CH_3	H	H
b	CH_3	H	CH_3
c	CH_3	CH_3	CH_3

The assignment of structures to *N*-substituted derivatives of unsymmetrical pyrazoles has been a problem for a number of years. However, today a study of nuclear magnetic resonance spectra of *N*-substituted pyrazoles permits the establishment of equivocal structures of the isomers of these 1-substituted compounds.

The following arguments have been used for the assignment of the structure of compound **3a**: i) The measure of the spacing (△) $\delta_{3\text{-H}}$-$\delta_{4\text{-H}}$ is 1.37 ppm for **3a**. This value in agreement with the value obtained by Habraken and Moore (9) in the 3- or 5-methyl substituted 1-methylpyrazoles for the 5-methyl isomer (△ = 1.20 for the 3-methyl isomer. ii) Ring proton coupling constants of 3-or 5-methyl-1-phenylpyrazoles have been discussed by Tensmeyer and Ainsworth (10). These authors found that $J_{4,5}$ was numerically much larger than $J_{3,4}$ (2.56 Hz for $J_{4,5}$ and 1.5 Hz for $J_{3,4}$). In our own case, the coupling constant measured for **3a** showed a value of 1.2 Hz.

Table I

^{1}H-NMR Spectra of Thienopyrazoles (**3**) in Deuteriochloroform (a)



				Chemical Shift				
				Pyrazole ring			Thiophene ring	
Compound	R_1	R_2	R_3	R_1	R_2	R_3	$C_{3'}$-H	$C_{4'}$-H
3a	CH_3	H	H	2.5 s	6.25 d (b)	7.6 d (b)	6.9 d (c)	7.85 d (c)
3b	CH_3	H	CH_3	2.25 s	6.1 s	2.5 s	6.85 d (d)	7.85 d (c)
3c	CH_3	CH_3	CH_3	2.3 s	2.0 s	2.45 s	6.7 d (e)	7.65 d (e)

(a) Shifts are reported in δ values (parts per million) downfield from internal tetramethylsilane; (b) $J_{3,4}$ = 1.2 Hz; (c) $J_{3,4'}$ = 4.2 Hz; (d) $J_{3',4}$ = 4.2 Hz; (e) $J_{3',4'}$ = 3.2 Hz.

Finally, in the reaction of **1** with acetylacetone (**2a**) and methylacetylacetone (**2c**) **3b** and **3c** were obtained, respectively. The assignment of the absorption at higher field to the 5-methyl protons instead of the 3-methyl protons (see Table I) was made as recommended by Habraken (9).

EXPERIMENTAL

Melting points were determined on a Büchi apparatus and are uncorrected. Nuclear magnetic resonances spectra were recorded on a 60 MHz Perkin-Elmer R-12B spectrometer using TMS as an internal standard. Chemical shifts are reported as δ values in parts per million (ppm). Infrared spectra were measured on a Pye-Unicam SP 1100 spectrophotometer. Elemental analyses were performed by Instituto de Quimica Organica, Barcelona.

2-*t*-Butoxycarbonylamino-5-nitrothiophene (**5**)

Compound **5** was obtained as reported in a previous paper (8).

N-*t*-Butoxycarbonyl-*N*-[2-(5-nitrothienyl)]hydrazine (**1**).

To a suspension of 0.26 g (0.01 mole) of sodium hydride in 50 ml of dry dioxane under an atmosphere of nitrogen, 0.01 mole of compound **5** in 50 ml of *N,N*-dimethylformamide was added dropwise. The resulting mixture was heated for 2 hours at reflux after which time the solution was allowed to cool to room temperature. *O*-(4-Nitrobenzoyl)hydroxylamine (**6**) (0.01 mole) in 20 ml of dry dioxane was then added. The mixture was stirred overnight at room temperature and the solvent was removed under reduced pressure. The crude product was shaken with sodium carbonate and extracted with methylene chloride. The organic layer was washed and dried with magnesium sulphate. The addition of hexane to the cooled solution gave 72% of compound **1**, as a yellow solid mp 129°; nmr (dueteriochloroform): 7.8 (d, 1, C_4-H, $J_{3,4}$ = 5Hz); 7.0 (d, 1, C_3-H); 4.65 (br. sig., 2, NH_2); 1.65 (s, 9, *t*-butyl); ir (potassium bromide): 3.360, 3.300 cm^{-1} (NH_2); 1720 cm^{-1} (-COO-).

Anal. Calcd. for $C_9H_{13}N_3O_4S$: C, 41.70; H, 5.06; N, 16.21; S, 12.34. Found: C, 41.55; H, 5.05; N, 16.11; S, 12.27.

Thienylpyrazoles **3**. General Procedure.

A solution of 0.02 mole of β-carbonyl compound **2** in acetic acid was heated at reflux for 30 minutes under an atmosphere of nitrogen. Thienylhydrazine **1** (0.002 mole) was then added. The mixture was maintained at reflux for 15 minutes. After this period of time, the acetic acid was removed under reduced pressure. The remaining residue was shaken with a solution of sodium carbonate and extracted with ether. The organic layer was washed with water, dried over anhydrous magnesium sulphate and the ether was removed by distillation. The residue was purified by chromatography on a silica gel column. Recrystallization from benzene gave the thienyl pyrazoles **3**.

5-Methyl-1-[2'-(5'-nitrothienyl)]pyrazoles (**3a**).

On elution of the reaction mixture with benzene 0.21 g (57%) of a yellow solid, mp 152° was obtained and characterized as compound **3a**.

Anal. Calcd. for $C_8H_7N_3O_2S$: C, 45.94; H, 3.37; N, 20.09; S, 15.30. Found: C, 45.77, H, 3.35; N, 20.11, S, 15.28.

3,5-Dimethyl-1-[2'-(5'-nitrothienyl)]pyrazole (**3b**).

On elution of the reaction mixture with benzene 0.22 g (54% of a yellow solid, mp 149-150° was obtained and characterized as compound **3b**.

Anal. Calcd. for $C_9H_9N_3O_2S$: C, 48.43; H, 4.06; N, 18.83; S, 14.34. Found: C, 48.34; H, 4.03; N, 18.90; S, 14.32.

3,4,5-Trimethyl-1-[2'-(5'-nitrothienyl)]pyrazole (**3c**).

On elution of the reaction mixture with benzene-chloroform (5:5) 0.24 g (58%) of a yellow solid mp 145-146° was obtained and characterized as compound **3c**.

Anal. Calcd. for $C_{10}H_{11}N_3O_2S$: C, 50.63; H, 4.67; N, 17.72; S, 13.49. Found: C, 50.55; H, 4.67; N, 17.75; S, 13.44.

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