

5-NITRO-2-THIENYLVINYLACTION. PREPARATION OF 2-SUBSTITUTED 1-(5-NITRO-2-THIENYL)ETHYLENES

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The preparation of 2-substituted 1-(5-nitro-2-thienyl)-ethylenes based on the reaction of (*Z*)-2-bromo-1-(5-nitro-2-thienyl)ethylene with aromatic or heteroaromatic compounds in the presence of aluminum chloride is described. The structure of the derivatives prepared was investigated by means of ^1H NMR and UV spectra and dipole moments measurement.

Reactions of nucleophilic vinyl(ic) substitution, as for example ketovinylation^{1,2}, cyanovinylation^{3,4}, sulfovinylation⁵, represent effective methods of synthesis of various aromatic and heteroaromatic compounds. In the preceding papers^{6,7} we found that (*Z*)- and (*E*)-2-bromo-1-(5-nitro-2-furyl)ethylene is capable of forming a complex with aluminum chloride and thus producing an electrophilic (alkenylating) reagent which with aromatic or heteroaromatic hydrocarbons gives (*E*)-2-substituted 1-(5-nitro-2-furyl)ethylenes. On the basis of a study of this reaction it may be assumed that the heteroaromatic nucleus affects the activation of the starting vinyl halogenide and the reaction course⁷. The aim of this study was to prepare 2-substituted 1-(5-nitro-2-thienyl)ethylenes on reaction of (*Z*)-2-bromo-1-(5-nitro-2-thienyl)ethylene with aromatic compounds in the presence of aluminum chloride and to study the structure of the compounds prepared. A further aim of the study was the preparation of (*E*)-2-bromo-1-(5-nitro-2-thienyl)ethylene, so far undescribed in literature, which would then be used for the study of the reactivity of activated vinyl halogenides.

Table I gives a survey of the products (*IIa–III*) of 5-nitro-2-thienylvinylation, prepared by reaction of (*Z*)-2-bromo-1-(5-nitro-2-thienyl)ethylene (*I*) with aromatics in the presence of aluminum chloride. For the reaction the (*Z*)-isomer of the starting vinyl halogenide was used preferentially, because much can already be predicted about the reaction course on the basis of the configuration of the isolated product (retention, inversion, convergence of the structure). The starting (*Z*)-2-bromo-1-(5-nitro-2-thienyl)ethylene was found to function as a reactive electrophile in reactions with O, S and N nucleophiles, under formation of products of nucleophilic substitution⁸ with biological activity. Thus, using debrominating decarboxylation 2,3-dibromo-3-(5-nitro-2-thienyl)propanoic acid⁸ was prepared. (*E*)-2-Bromo-1-

-(5-nitro-2-thienyl)ethylene was prepared by applying the reaction of the sodium salt of 3-(5-nitro-2-thienyl)-2-propenoic acid with N-bromosuccinimide⁹. The mixture of isomers (*Z*) and (*E*) formed in this reaction in a 1 : 1.75 ratio was separated by column chromatography.

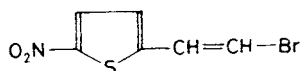
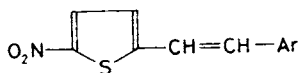
I, *Z*II α - II β

TABLE I
Products of 5-nitro-2-thienylvinylation of aromatic compounds

Compound substituents	Formula (mol. weight)	Calculated/found			M.p., °C yield, %
		% C	% H	% N	
<i>Ila</i> 4-CH ₃ O—C ₆ H ₄	C ₁₃ H ₁₁ NO ₃ S (261.3)	59.76 59.70	4.23 4.18	5.36 5.31	174—175 51.6
<i>Ilb</i> 4-HO—C ₆ H ₄	C ₁₂ H ₉ NO ₃ S (247.3)	58.28 58.24	3.67 3.65	5.66 5.63	240—243 40.4
<i>Ilc</i> 2-HO—C ₆ H ₄	C ₁₂ H ₉ NO ₃ S (247.3)	58.28 58.20	3.67 3.62	5.66 5.61	143—145 4.0
<i>Ild</i> 3-Cl-4-HO—C ₆ H ₃	C ₁₂ H ₈ ClNO ₃ S (281.7)	51.17 51.16	2.86 2.84	4.97 4.95	221—222 44.8
<i>Ile</i> 2-HO-3-Cl—C ₆ H ₃	C ₁₂ H ₈ ClNO ₃ S (281.7)	51.17 51.09	2.86 2.79	4.97 4.93	126—130 3.6
<i>Ilf</i> 2-Cl-4-HO—C ₆ H ₃	C ₁₂ H ₈ ClNO ₃ S (281.7)	52.17 51.06	2.86 2.77	4.97 4.95	208—210 43.4
<i>Ilg</i> 2-HO-5-Cl—C ₆ H ₃	C ₁₂ H ₈ ClNO ₃ S (281.7)	51.17 51.08	2.86 2.78	4.97 4.94	185—187 12.1
<i>Ilh</i> 2-HO-4-CH ₃ -5-Cl—C ₆ H ₂	C ₁₃ H ₁₀ ClNO ₃ S (293.7)	53.16 53.12	3.43 3.40	4.77 4.76	192—193 14.1
<i>Ili</i> 2-Thienyl	C ₁₀ H ₇ NO ₂ S ₂ (237.3)	50.62 50.48	2.97 2.86	5.90 5.80	102—103 59.4

To check the site of substitution and the steric effects we chose the following aromatic compounds: monosubstituted; 1,2-, 1,3-, 1,4-disubstituted; trisubstituted and heteroaromatic. Multiple substitution of the aromatics was not observed, because – probably as in the case of 5-nitro-2-furylvinylation – the 5-nitro-2-thienyl group deactivated the aromatic nucleus sufficiently for further substitution. While in the case of 5-nitro-2-furylvinylation the product of substitution in *ortho*-position with respect to the substituent with the highest activating effect on the aromatic nucleus was observed only when the *para*-position was occupied, in the case of 5-nitro-2-thienylvinylation both substitution products could be isolated, *i.e.* in position *para* and *ortho*. When thiophene or anisole were substituted, only one product of substitution in position 2 or 4 was isolated. In the case of phenol or 2-chlorophenol both substitution products were isolated. In the case of 3-chlorophenol three products of substitution can be formed theoretically, but only one was isolated. In the same way, in the case of 4-chloro-3-methylphenol, which gives theoretically the possibility of formation of two derivatives, only one was isolated. The products of substitution in position *ortho* to the activating substituent are formed in very low yields. In all instances the starting derivative with the retained configuration was also isolated in addition to the products.

The structure of the compounds prepared was determined by interpretation of the ^1H NMR and UV spectra and dipole moments. The values of the chemical shifts and the coupling constants are given under Experimental. The position of the bonding of the 5-nitro-2-thienyl group to the thiophene or benzene nucleus was determined on the basis of the chemical shift and the multiplicity of the corresponding protons. Almost in all instances, with the exception of thiophene and 3-chlorophenol, the ethylene protons give a singlet (7.23–7.57 δ), from which it could not be determined whether it is the (*Z*) or the (*E*) configuration. The ethylene protons of (*Z*) and (*E*)-stilbene also give a singlet and the only difference was in the chemical

TABLE II
Polarizations and dipole moments of 2-Ar-1-(5-nitro-2-thienyl)ethylene

Compound	Concentration range, 100 w_2	α^a	ε_{10}^b	β^c	v_{10}^d	$P_{2\infty}^3$ cm 3	R_D^3 cm 3	μ D
<i>Ila</i>	0.0340–0.2270	14.39	2.2701	–0.103	1.14464	746.72	71.9	5.74
<i>IId</i>	0.0021–0.0664	5.24	2.2738	–0.950	1.14497	293.81	71.7	3.27
<i>IIIi</i>	0.0300–0.4155	11.90	2.2624	–0.284	1.14468	594.47	64.1	5.09

$$^a \alpha = d\varepsilon_{12}/dw_2; ^b \varepsilon_{10} = \lim_{w_2 \rightarrow 0} \varepsilon_{12}; ^c \beta = dv_{12}/dw_2; ^d v_{10} = \lim_{w_2 \rightarrow 0} v_{12}.$$

shift value (6.55δ ; 7.10δ)¹⁰, the same as in (*E*)-2-phenyl-1-(5-nitro-2-thienyl)ethylene¹¹ which also displays a singlet (7.10δ). For the purpose of configuration determination we also measured the dipole moments of some derivatives (see Table II). The dipole moments of possible configurations and conformations were determined by mathematical summation of vectors¹². The calculation gave the following values of the dipole moments (μ_{cal}) for the anisole derivative *Ila*: (*Z*), *s-trans* = 5.67 D; (*Z*), *s-cis* = 4.60 D and (*E*), *s-trans* = 3.27 D. A comparison of μ_{cal} with μ_{exp} (5.74 D) shows that derivative *Ila* is in (*Z*), *s-trans* configuration. The difference between the experimental and the calculated value may be due to the mesomeric dipole moment. On the basis of these results the phenol derivative *Iib* was assigned by analogy the configuration (*Z*). For the derivative of 2-chlorophenol (*Iid*) the following values of the dipole moments (μ_{cal}) were determined in dependence on the spatial orientation of the chlorine atom: (*Z*), *s-trans* = 6.35, 5.69 D; (*Z*), *s-cis* = 5.83, 3.61 D; (*E*), *s-trans* = 2.40, 4.18 D. Comparison of μ_{cal} with μ_{exp} (3.27) indicates that derivative *Iid* is in (*E*), *s-trans* configuration. In the case of the derivative of 3-chlorophenol (*Iif*) the ethylene protons were identified as a doublet (16.5 Hz) which confirms the configuration (*E*). On the basis of this fact, further on the basis of the configuration of derivative *Iid*, confirmed by the dipole moment, and the comparison of the chemical shifts of the ethylene protons of derivatives *Iic*, *Iie*, *Iig*, and *Iih*, it may be assumed that these derivatives are in (*E*) configuration. From the coupling constant value of ethylene protons (10.1 Hz) of thiophene derivative *Iii* it follows that the derivative isolated is in (*Z*) configuration.

EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. The ¹H NMR spectra were measured on a Tesla NMR BS 487 C, 80 MHz instrument, in hexadeuterioacetone, unless stated otherwise, using tetramethylsilane as internal reference. The UV spectra were measured on a Specord UV VIS spectrophotometer in methanol. The dielectric constants of benzene solutions were measured on a Dipolmeter WTW DM01 instrument (G.F.R.) at $25^\circ \pm 0.05^\circ\text{C}$. The total polarization $P_{2\infty}$ was obtained by extrapolation, using the Halverstadt-Kumler method¹³. Polarization ($P_e + P_a$) was determined as $1.05 R_D$ (molar refraction) which was calculated by adding together the additive increments¹⁴. The following moments of the bonds and groups¹⁵ were used: $\mu_{\text{NO}_2} = 4.00$ D, $\mu_{\text{C}_A-\text{O}} = 1.04$ D, $\mu_{\text{C}_{A1}-\text{O}} = 1.06$ D, $\mu_{\text{H}-\text{O}} = 1.5$ D, $\mu_{\text{C}-\text{H}} = 0.4$ D, $\mu_{\text{Cl}} = 1.59$ D and for thiophene 0.53 D (ref.¹⁶).

2-Bromo-1-(5-nitro-2-thienyl)ethylene (*I*, *E*)

A mixture of 10 g (0.05 mol) of 3-(5-nitro-2-thienyl)-2-propenoic acid, water (25 ml), and 5 g (0.05 mol) of sodium carbonate was heated at 90°C , and 9.7 g (0.05 mol) of N-bromosuccinimide were added to it in small portions. The mixture was stirred at 90°C for 3 h, extracted with three 100 ml portions of benzene, and the extract was dried over sodium sulfate and evaporated in a vacuum. Yield, 3.7 g (30%) of a mixture of (*Z*) and (*E*) isomer in a 1 : 1.75 ratio. Chromatography on a silica gel column (elution with n-hexane) gave the (*E*) isomer with m.p. $79-80^\circ\text{C}$

For $C_6H_4BrNO_2$ (234.1) calculated: 5.98% N; found: 6.02% N. 1H NMR spectrum (δ , ppm, hexadeuteriodimethyl sulfoxide, tetramethylsilane): 8.14 (d, H_4), 7.51 (d, H_3), $J_{3,4} = 4.1$ Hz, 7.63 (d, H_A), 7.44 (d, H_B), $J_{A,B} = 13.75$ Hz.

2-Ar-1-(5-nitro-2-thienyl)ethylenes IIa–III

Aluminum chloride (2 g, 0.015 mol) was added under stirring to a solution of 2.34 g (0.01 mol) of (*Z*)-2-bromo-1-(5-nitro-2-thienyl)ethylene in 1,2-dichloroethane (30 ml). A solution of a corresponding aromatic compound (0.01 mol) was added to the above mixture, while keeping the temperature at 0°C. After 30 min stirring the mixture was poured onto ice (50 g), the organic layer was separated, washed with water and dried. The residue after vacuum evaporation of the solvent was chromatographed on a column of silica gel, using benzene for elution, or also chloroform, depending on the polarity of the substances.

(*Z*)-2-(4-Methoxyphenyl)-1-(5-nitro-2-thienyl)ethylene (IIa), from anisole. 1H NMR spectrum (δ , ppm, deuteriochloroform, tetramethylsilane): 7.81 (d, H_4), 6.92 (d, H_3), $J_{3,4} = 4.4$ Hz, 7.03 (s, $H_{A\equiv B}$), 7.44 (d, $H_{2',6'}$), 6.90 (d, $H_{3',5'}$), $J_{2',3'} = 8.7$ Hz; (δ , ppm, deuterioacetone, tetramethylsilane): 7.94 (d, H_4), 7.21 (d, H_3), $J_{3,4} = 4.4$ Hz, 7.60 (d, $H_{2',6'}$), 6.96 (d, $H_{3',5'}$), $J_{2',3'} = 9.33$ Hz, 3.84 (s, CH_3), 7.31 (s, $H_{A\equiv B}$). UV spectrum λ_{max} (nm, $\log \epsilon$ ($m^2 mol^{-1}$)): 286 (3.23), 430 (3.56).

(*Z*)-2-(4-Hydroxyphenyl)-1-(5-nitro-2-thienyl)ethylene (IIb), from phenol. 1H NMR spectrum (δ , ppm): 7.89 (d, H_4), 7.16 (d, H_3), $J_{3,4} = 4.35$ Hz, 7.23 (s, $H_{A\equiv B}$), 7.48 (d, $H_{2',6'}$), 6.87 (d, $H_{3',5'}$), $J_{2',3'} = 8.6$ Hz. UV spectrum λ_{max} (nm, $\log \epsilon$ ($m^2 mol^{-1}$)): 293 (3.03), 444 (3.27).

(*E*)-2-(2-Hydroxyphenyl)-1-(5-nitro-2-thienyl)ethylene (IIc), from phenol. 1H NMR spectrum (δ , ppm): 7.93 (d, H_4), 7.22 (d, H_3), $J_{3,4} = 4.3$ Hz, 7.53 (s, $H_{A\equiv B}$), 7.63–6.78 (m, $H_{3',-6'}$).

(*E*)-2-(3-Chloro-4-hydroxyphenyl)-1-(5-nitro-2-thienyl)ethylene (II d), from 2-chlorophenol. 1H NMR spectrum (δ , ppm): 7.96 (d, H_4), 7.24 (d, H_3), $J_{3,4} = 4.31$ Hz, 7.32 (s, $H_{A\equiv B}$), 7.68 (d, $H_{2'}$), 7.48 (dd, $H_{6'}$), 7.06 (d, $H_{5'}$), $J_{2',6'} = 2.18$ Hz, $J_{5',6'} = 8.5$ Hz. UV spectrum λ_{max} (nm, $\log \epsilon$ ($m^2 mol^{-1}$)): 287 (3.10), 427 (3.37).

(*E*)-2-(2-Hydroxy-3-chlorophenyl)-1-(5-nitro-2-thienyl)ethylene (IIe), from 2-chlorophenol. 1H NMR spectrum (δ , ppm): 7.97 (d, H_4), 7.29 (d, H_3), $J_{3,4} = 4.35$ Hz, 7.56 (s, $H_{A\equiv B}$), 7.36 (dd, $H_{4'}$), 6.92 (t, $H_{5'}$), 7.62 (dd, $H_{6'}$), $J_{4',6'} = 1.75$ Hz, $J_{4',5'} = 7.9$ Hz.

(*E*)-2-(2-Chloro-4-hydroxyphenyl)-1-(5-nitro-2-thienyl)ethylene (II f), from 3-chlorophenol. 1H NMR spectrum (δ , ppm): 7.96 (d, H_4), 7.27 (d, H_3), $J_{3,4} = 4.4$ Hz, 7.57 (d, H_A), 7.28 (d, H_B), $J_{A,B} = 16.5$ Hz, 6.96 (d, $H_{3'}$), 6.87 (dd, $H_{5'}$), 7.73 (d, $H_{6'}$), $J_{3',5'} = 2.4$ Hz, $J_{5',6'} = 8.55$ Hz. UV spectrum λ_{max} (nm, $\log \epsilon$ ($m^2 mol^{-1}$)): 287 (1.94), 421 (3.18).

(*E*)-2-(2-Hydroxy-5-chlorophenyl)-1-(5-nitro-2-thienyl)ethylene (II g), from 4-chlorophenol. 1H NMR spectrum (δ , ppm): 7.97 (d, H_4), 7.28 (d, H_3), $J_{3,4} = 4.25$ Hz, 7.54 (s, $H_{A\equiv B}$), 6.96 (d, $H_{3'}$), 7.18 (dd, $H_{4'}$), 7.61 (d, $H_{6'}$), $J_{3',4'} = 8.67$ Hz, $J_{4',6'} = 2.5$ Hz. UV spectrum λ_{max} (nm, $\log \epsilon$ ($m^2 mol^{-1}$)): 272 (3.03), 303 (2.94), 420 (3.35).

(*E*)-2-(2-Hydroxy-4-methyl-5-chlorophenyl)-1-(5-nitro-2-thienyl)ethylene (II h), from 3-methyl-4-chlorophenol. 1H NMR spectrum (δ , ppm): 7.94 (d, H_4), 7.23 (d, H_3), $J_{3,4} = 4.3$ Hz, 7.48 (s, $H_{A\equiv B}$), 6.91 (s, $H_{3'}$), 7.57 (s, $H_{6'}$), 2.29 (s, CH_3). UV spectrum λ_{max} (nm, $\log \epsilon$ ($m^2 mol^{-1}$)): 279 (3.06), 308 (2.97), 431 (3.38).

(*Z*)-2-(9-Thienyl)-1-(5-nitro-2-thienyl)ethylene (II i), from thiophene. 1H NMR spectrum (δ , ppm, deuteriochloroform): 7.81 (d, H_4), 6.95 (d, H_3), $J_{3,4} = 4.0$ Hz, 7.32 (d, H_A), 6.87

(d, H_B), $J_{A,B} = 10.12$ Hz, 7.17 (d, H_{3'}), 7.04 (dd, H_{4'}), 7.32 (d, H_{5'}), $J_{3',4'} = 3.6$ Hz, $J_{3',5'} = 1.3$ Hz, $J_{4',5'} = 4.9$ Hz. UV spectrum λ_{\max} (nm, log ϵ (m² mol⁻¹)): 288 (3.02), 426 (3.20).

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