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5-NITRO-2-THIENYLVINYLATION. NUCLEOPHILIC SUBSTITUTION ON 2-(2-BROMOVINYL)- 5-NITROTHIOPHENE, NEW ONE-STEP METHOD FOR PREPARATION OF NEW BIOLOGICALLY ACTIVE ETHYLENIC DERIVATIVES OF 5-NITRO-2-THIOPHENE

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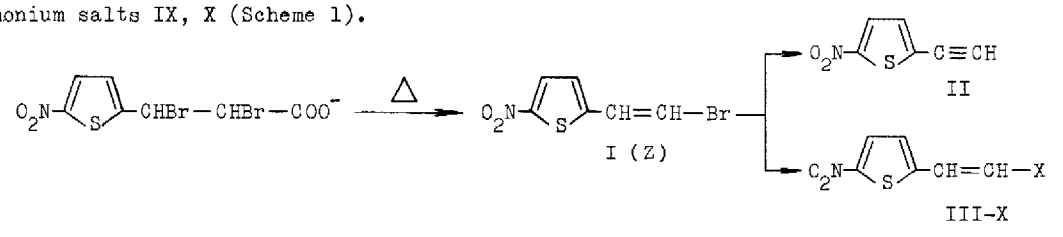
A facile method for preparing 2-(2-X-vinyl)-5-nitrothiophenes has been established by the reaction of (Z)-2-(2-bromovinyl)-5-nitrothiophene with O, S and N nucleophiles.

Previously[1] we reported the activating effect of 5-nitro-2-furyl group on the ethylene group and the possibility to introduce properly selected substituents at the end of the ethylene group via 5-nitro-2-furylvinylation to form new substances having an antibacterial effect.

Aiming at the synthesis of new nitrothiophene derivatives we investigated the preparation of the previously not known 2-(2-bromovinyl)-5-nitrothiophene (I), which is formed in the debrominative decarboxylation[2] of the alkali salt of 2,3-dibromo-3-(5-nitro-2-thienyl)propionic acid[3]. When the reaction was carried out in organic solvents such as acetone or methylethyl ketone, only the (Z) isomer I was obtained[4]. The successful synthesis of (Z)-2-(2-bromovinyl)--5-nitrothiophene containing a sufficiently reactive bromine has opened the path for a new synthesis of new groups of biologically active 2-(2-X-vinyl)-5-nitrothiophenes, e.g. vinyl ethers III, vinyl thioethers IV, vinyl sulphones V, vinyl azides VI, enamines VII, VIII and enammonium salts IX, X (Scheme 1).

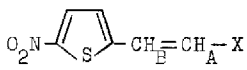


X= O-C6H4-CH3 (III), S-C6H4-CH3 (IV), SO2-C6H4-CH3 (V), N3 (VI), N(CH3)2 (VII), N(CH2)2O (VIII), +N(CH3)3Br⁻ (IX), +N(C5H5)Br⁻ (X)

Scheme 1

2-(2-bromovinyl)-5-nitrothiophene reacts with a large group of nucleophiles from which the O, S and N nucleophiles were studied. Using strong bases such as the CH_3O^- anion, elimination of HBr preferentially[5] proceeds to form 5-nitro-2-thienylacetylene (II). While preservation of the (Z) configuration of the vinyl group has been observed with enammonium salts IX, X, vinyl sulphones V and enamines VII, VIII had the opposite (E) configuration. The vinyl

group of vinyl ethers III, vinyl thioethers IV and vinyl azide VI according to reaction conditions partially retained its original configuration.

TABLE 1. 2-(2-X-Vinyl)-5-Nitrothiophene Derivatives 

Compound	Formula	m.p. °C	Yield %	isomer	^{1}H NMR H_A	H_B	$J_{A,B}$	Z:E
I	$C_6H_4BrNO_2S$	79-81	75	Z	6.57	7.31	8.0	1:0
III	$C_{13}H_{11}NO_3S$	75-80	70	Z E	6.82 7.30	5.93 6.24	6.3 12.3	3:1
IV	$C_{13}H_{11}NO_2S_2$	oil	85	Z E	6.72 7.01	6.65 6.34	10.5 15.4	1:1
V	$C_{13}H_{11}NO_4S_2$	138-140	85	E	6.85	7.66	15.2	0:1
VI	$C_6H_4N_4O_2S$	82-87	70	Z E	5.94 6.31	6.60 6.82	7.8 13.7	2:1
VII	$C_8H_{10}N_2O_2S$	124-127	80	E	7.02	5.23	13.2	0:1
VIII	$C_{10}H_{12}N_2O_3S$	165-168	80	E	6.87	5.44	13.6	0:1
IX	$C_9H_{13}BrN_2O_2S$	160-165	80	Z	6.70	6.96	10.0	1:0
X	$C_{11}H_9BrN_2O_2S$	215-220	75	Z	6.89	7.15	8.6	1:0

The structure of the compounds prepared and the ratio Z:E were confirmed by means of ^{1}H NMR spectroscopy.
Solvent: $CDCl_3$ (I-VIII), DMSO-d_6 (IX), CF_3COOH (X).

Typical synthetic procedures are given below:

1. II - VI. 2-(2-Bromovinyl)-5-nitrothiophene (I) (0.01 mole) is treated with alkali salts of O, S nucleophiles and N_3^- anion (0.01 mole) in acetone-water or dimethoxyethane-water mixture at room temperature for 1-4 hours. The solvent was distilled off and the residue chromatographed over silica gel column.
2. VII - X. 2-(2-Bromovinyl)-5-nitrothiophene (I) (0.01 mole) is treated with secondary amines (0.02 mole) or tertiary amines (0.01 mole) in benzene or dimethoxyethane at room temperature for several hours. Enamines VII, VIII after filtration of ammonium salts were concentrated and crystallised from a benzene-ether solution[6]. Quaternary enammonium salts IX, X were separated by filtration and crystallised from methanol- ether.

References and Notes

1. D. Végh, J. Kováč and F. Považanec, Collection Czech. Chem. Commun., 43, 3404 (1978) and references cited therein.
2. Ch.A. Kingbury and G. Max, J. Org. Chem., 43, 3131 (1978) and references cited therein.
3. H. Saikachi and Y. Taniguchi, Yakugaku Zasshi, 87, 704 (1967); Chem. Abstr., 68, 21762 (1968).
4. Analogously prepared as 2-(2-bromovinyl)-5-nitrofurane (Z) in 75-85 % yield as the pure Z isomer, cit. D. Végh, J.Kováč and B. Hasová, Collection Czech. Chem. Commun., 41, 614 (1976).
5. Reaction of 2-(2-bromovinyl)-5-nitrothiophene with CH_3O^- in methanol gave 5-nitro-2-thienyl acetylene in 60-65 % yield, m.p. 67-70 °C (sublimation). ^{1}H NMR ($CDCl_3$) δ 7.16 (H_3, d, $J_{3,4}$ = 4.3 Hz), 7.78 (H_4, d), 3.57 (CH, s).
6. The strong band observed in the region of 490-510 nm in the UV spectra is characteristic for synthetised enamines VII, VIII.

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