

Nucleophilic vinyl substitution Reactions of pyridylvinyl bromides with sulfur and nitrogen nucleophiles

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The preparation of new activated vinyl halides of 2- and 3-(2-bromovinyl)-*N*-methylpyridinium iodides by the quaternization of corresponding 2-, resp. 3-pyridylvinyl bromides with methyl iodide is described. New arylthioethylenes of the pyridine series were obtained by the nucleophilic replacement of bromine with arylthiolate anions. Enamines of the pyridinium series were obtained by the reaction with secondary amines.

Описано получение новых активированных галоидных винилов типа иодидов 2- и 3-(2-бромвинил)-*N*-метилпиридиния посредством квартернизации соответствующих 2- или 3-пиридилвинилбромидов метилиодидом. Новые арилтиоэтилены пиридинового ряда были получены путем нуклеофильного замещения брома анионами арилтиолата. Енамины пиридинового ряда были получены путем реакции со вторичными аминами.

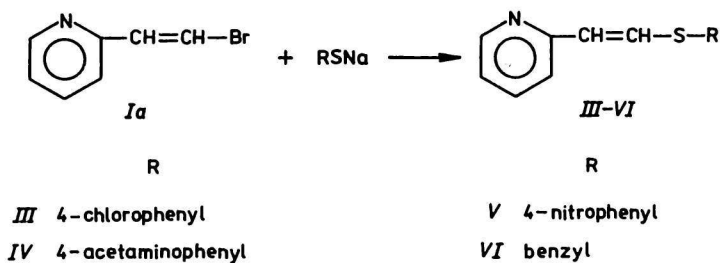
The reactions of the nucleophilic vinyl substitution — heteroarylvinylations [1, 2] represent very efficient methods of the synthesis of various not easy available heteroatomic compounds.

The preparation of basic 2-, 3-, and 4-pyridylvinyl bromides (*Ia—Ic*) by the debromination decarboxylation of corresponding pyridyl-substituted 2,3-dibromopropanoic acids with sodium carbonate was studied in the previous paper [3].

The aim of this paper was to study the reactions of 2- and 3-pyridylvinyl bromides (*Ia*, resp. *Ib*) with arylthiolate anions, and with secondary amines.

We have obtained corresponding 1-(2-pyridyl)-2-arylthioethylenes *III—VI* (Scheme 1) by the reaction of *Ia* with arylthiolates in dimethylformamide at the reflux temperature. Their structures were identified by ¹H NMR spectra (Table 3). The assignment of protons was determined on the basis of the values of the coupling constants and multiplicity. The prepared arylthioethylenes *III—VI* are in the *Z* configuration ($J_{AB} = 10.5—10.6$ Hz).

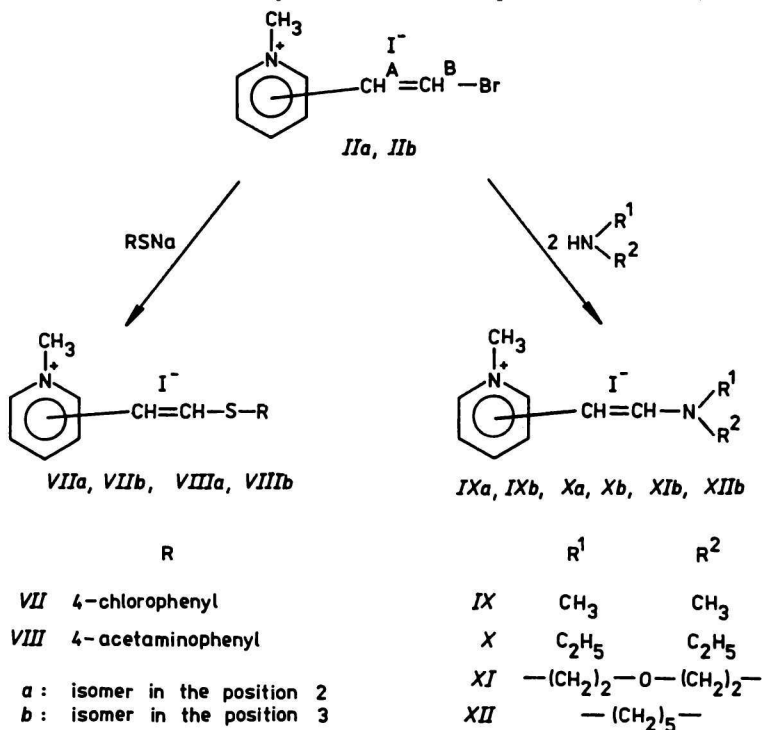
We have prepared corresponding bromovinylpyridinium salts *IIa*, *IIb* by the



Scheme 1

quaternization of *Ia*, *Ib* with methyl iodide in order to enhance the reactivity of halogen. These compounds retain the *Z* configuration ($J_{AB} = 8.3\text{--}8.5$ Hz). In the case of *IIa* the splitting of the signal of the methyl group was observed in ^1H NMR spectrum. In the case of *IIb* the singlet is a signal of the methyl group.

The assumption that quaternized bromovinylpyridinium iodides *IIa*, *IIb* are more reactive than *Ia*, *Ib* was proved by the accomplishment of their reactions with arylthiolates and secondary amines in the aqueous medium (Scheme 2).



Scheme 2

Table 1

Characterization of the compounds II—XII

Compound	Formula M_r	$w_i(\text{calc.})/\%$ $w_i(\text{found})/\%$				Yield %	M.p. °C
		C	H	N	S		
<i>Ila</i>	C_8H_9BrIN	29.48	2.78	4.30	—	80	178—180
	325.98	29.56	2.49	4.20	—		
<i>Ilb</i>	C_8H_9BrIN	29.48	2.78	4.30	—	86	124—126
	325.98	29.53	2.59	4.16	—		
<i>III</i>	$C_{13}H_{10}ClNS$	63.02	4.07	5.65	12.94	30	90—91
	247.75	63.00	3.98	5.58	12.81		
<i>IV</i>	$C_{15}H_{14}N_2OS$	66.64	5.22	10.36	11.86	25	Oil
	270.36	66.58	5.36	10.28	11.75		
<i>V</i>	$C_{13}H_{10}N_2O_2S$	60.45	3.90	10.85	12.41	23	108—111
	258.30	60.33	3.80	10.68	12.28		
<i>VI</i>	$C_{14}H_{13}NS$	73.98	5.76	6.16	14.11	18	Oil ^a
	227.33	73.94	5.66	6.05	13.98		
<i>VIIa</i>	$C_{14}H_{13}ClINS$	43.15	3.36	3.59	—	60	148—151
	389.69	43.02	3.15	3.42	—		
<i>VIIb</i>	$C_{14}H_{13}ClINS$	43.15	3.36	3.59	—	58	268—270
	389.69	43.05	3.28	3.50	—		
<i>VIIIa</i>	$C_{16}H_{17}IN_2OS$	46.61	4.16	6.79	—	51	136—140
	412.29	46.50	3.98	6.65	—		
<i>VIIIb</i>	$C_{16}H_{17}IN_2OS$	46.61	4.16	6.79	—	52	207—210
	412.29	46.58	4.10	6.81	—		
<i>IXa</i>	$C_{10}H_{15}IN_2$	41.40	5.21	9.66	—	68	196—198 d
	290.15	41.21	5.18	9.54	—		
<i>IXb</i>	$C_{10}H_{15}IN_2$	41.40	5.21	9.66	—	65	204—207 d
	290.15	41.25	5.15	9.60	—		
<i>Xa</i>	$C_{12}H_{19}IN_2$	45.30	6.02	8.80	—	60	Oil
	318.20	45.25	5.95	8.82	—		
<i>Xb</i>	$C_{12}H_{19}IN_2$	45.30	6.02	8.80	—	58	Oil
	318.20	45.18	5.89	8.68	—		
<i>XIb</i>	$C_{12}H_{17}IN_2O$	43.39	5.16	8.43	—	55	154—156
	332.19	43.28	5.10	8.40	—		
<i>XIIb</i>	$C_{13}H_{19}IN_2$	47.29	5.80	8.48	—	50	Oil
	330.21	47.20	5.65	8.31	—		

a) Ref. [4] gives m.p. = 42—45°C. d = decomposition.

Ib does not react with arylthiolates. Obtained *N*-methylpyridinium salts of arylthioethylenes *VIIa*, *VIIb* and *VIIIa*, *VIIIb* have retained the *Z* configuration of the protons at the double bond ($J_{AB} = 10.6$ Hz) according to 1H NMR spectra (Table 2). *Ila*, *Ilb* react with secondary amines under the formation of corre-

Table 2

¹H NMR spectra (δ /ppm) of *II*, *VII*—*XII* in hexadeuterodimethyl sulfoxide

Compound	H ^A	H ^B	⁺ N—CH ₃	J _{AB} /Hz	Others
<i>IIa</i>	7.73 (d) 7.90 (d)	7.55 (d) 7.78 (d)	4.25 (s) 4.30 (s)	8.5 8.5	9.13 (d, 1H, H-6), 8.0—8.88 (m, 3H, H-3, H-4, H-5)
<i>IIb</i>	7.49 (d)	7.26 (d)	4.41 (s)	8.3	9.21 (s, 1H, H-2), 8.81—9.06 (m, 2H, H-4, H-6), 8.18 (dd, 1H, H-5)
<i>VIIa</i>	7.91 (d)	7.73 (d)	4.40 (s)	10.5	9.13 (d, 1H, H-6), 7.5—8.75 (m, 3H, H-3, H-4, H-5), 8.25 (d, 2H, H _{arom} -2, H _{arom} -6), 7.97 (d, 2H, H _{arom} -3, H _{arom} -5)
<i>VIIb</i>	7.26 (d)	6.79 (d)	4.35 (s)	10.6	9.18 (d, 1H, H-2), 8.6—9.0 (m, 2H, H-4, H-6), 8.0—8.5 (m, 1H, H-5), 7.5 (s, 4H, H _{arom}), 2.10 (s, 3H, CH ₃)
<i>VIIIa</i>	7.82 (d)	7.63 (d)	4.32 (s)	10.5	9.17 (d, 1H, H-6), 7.45 (s, 4H, H _{arom}), 7.5—8.75 (m, 3H, H-3, H-4, H-5)
<i>VIIIb</i>	7.17 (d)	6.72 (d)	4.41 (s)	10.5	9.13 (s, 1H, H-2), 9.03 (d, 1H, H-6), 8.63 (d, 1H, H-4), 8.11 (dd, 1H, H-5), 7.7 (d, 2H, H _{arom} -2, H _{arom} -6), 7.43 (d, 2H, H _{arom} -3, H _{arom} -5), 2.06 (s, 3H, CH ₃), 10.1 (s, 1H, NH)
<i>IXa</i>	5.09 (d)	8.16 (d)	3.84 (s)	12.5	8.25 (d, 1H, H-6), 7.8—8.3 (m, 2H, H-3, H-4), 6.7—7.1 (m, 1H, H-5), 3.0 (s, 3H, >N—CH ₃), 3.23 (s, 3H, >N—CH ₃)
<i>IXb</i>	5.05 (d)	7.59 (d)	4.19 (s)	12.5	8.71 (d, 1H, H-2), 8.0—8.4 (m, 2H, H-4, H-6), 7.69 (dd, 1H, H-5), 2.89 (s, 6H, —N(CH ₃) ₂)
<i>Xa</i>	5.23 (d)	8.21 (d)	3.90 (s)	12.5	7.62—8.44 (m, 3H, H-3, H-4, H-6), 6.96 (dd, 1H, H-5), 2.96 (q, 4H, N—X ₂), 1.25 (t, 6H, CH ₃)
<i>Xb</i>	5.20 (d)	7.67 (d)	4.25 (s)	12.5	8.68 (d, 1H, H-2), 7.95—8.4 (m, 2H, H-4, H-6), 7.78 (dd, 1H, H-5), 2.90 (q, 4H, N—X ₂), 1.3 (t, 6H, CH ₃)

Table 2 (Continued)

Compound	H ^A	H ^B	⁺ N—CH ₃	J _{AB} /Hz	Others
<i>XIb</i>	5.34 (d)	7.53 (d)	4.21 (s)	12.5	8.78 (d, 1H, H-2), 8.13—8.5 (m, 2H, H-4, H-6), 7.76 (dd, 1H, H-5), 3.7 (m, 4H, O—X ₂), 3.14 (m, 4H, N—X ₂)
<i>XIIb</i>	5.25 (d)	7.50 (d)	4.20 (s)	12.5	8.75 (d, 1H, H-2), 8.0—8.38 (m, 2H, H-4, H-6), 7.69 (dd, 1H, H-5), 3.13 (m, 4H, N—X ₂), 1.54 (m, 6H, CH ₂ —X ₂)

s — singlet, d — doublet, dd — doublet of doublets, t — triplet, q — quartet, m — multiplet.

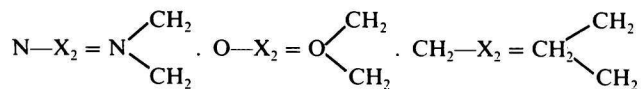


Table 3

¹H NMR spectra (δ/ppm) of *III—VI* in deuteriochloroform

Compound	H ^A	H ^B	H _{arom} ⁻² , H _{arom} ⁻⁶	H _{arom} ⁻³ , H _{arom} ⁻⁵	J _{AB} /Hz	Others
<i>III</i>	6.78 (d)	6.55 (d)	7.52 (d)	7.34 (d)	10.5	8.71 (d, 1H, H-6), 7.0—7.75 (m, 3H, H-3, H-4, H-5)
<i>IV</i>	6.77 (d)	6.52 (d)		7.5 (s)	10.5	8.71 (d, 1H, H-6), 7.0—7.88 (m, 3H, H-3, H-4, H-5), 2.18 (s, 3H, CH ₃)
<i>V</i>	6.88 (d)	6.69 (d)	8.19 (d)	7.60 (d)	10.6	8.72 (d, 1H, H-6), 7.06—7.88 (m, 3H, H-3, H-4, H-5)
<i>VI</i>	6.58 (d)	6.40 (d)			10.6	8.62 (d, 1H, H-6), 7.45—7.70 (m, 1H, H-4), 7.12 (d, 1H, H-3), 7.01 (dd, 1H, H-5), 7.0—7.45 (m, 5H, H _{arom}), 3.92 (s, 2H, —CH ₂ —)

sponding enamines *IX—XII*. By the analysis of ^1H NMR spectra we have proved that enamines *IX—XII* are in the *E* configuration ($J_{\text{AB}} = 12.6$ Hz).

Experimental

Melting points were measured on a Kofler block. ^1H NMR spectra were taken with a Tesla BS 487 C spectrometer (80 MHz) in deuteriochloroform and hexadeuterodimethyl sulfoxide using tetramethylsilane as an internal standard.

2- and 3-Pyridylvinyl bromides (*Ia*, *Ib*) were prepared according to the literature [3].

2- and 3-(2-Bromovinyl)-N-methylpyridinium iodides (IIa, IIb)

Corresponding pyridylvinyl bromide *Ia*, resp. *Ib* (0.92 g; 5 mmol) is mixed with methyl iodide (0.71 g; 5 mmol). The reaction mixture turns to a solid after 0.5 h standing at room temperature. The product is crystallized from the methanol—ether mixture. The physicochemical constants are given in Tables 1 and 2.

1-(2-Pyridyl)-2-arylthioethylenes III—VI

To a solution of *Ia* (0.92 g; 5 mmol) in 20 cm³ of dimethylformamide corresponding sodium arylthiolate (7.5 mmol) is added. The reaction mixture is heated at the reflux temperature for 8 h. After completion of the reaction, the reaction mixture is poured into water, and the product is extracted with ether. The extract is dried over anhydrous sodium sulfate, thickened, and the residue is crystallized or purified by column chromatography (aluminium oxide, chloroform as an eluent). The physicochemical constants are listed in Tables 1 and 3.

2- and 3-(2-Arylthiovinyl)-N-methylpyridinium iodides VII, VIII

To a solution of *Iia* and *Iib* (0.67 g; 2 mmol), respectively, in 10 cm³ of water corresponding sodium arylthiolate (3 mmol) in 5 cm³ of water is added. Then the mixture becomes cloudy and the elimination of pure *VII* and *VIII*, respectively, takes place. The product is filtered off and crystallized from the methanol—ether mixture. The physicochemical constants are summarized in Tables 1 and 2.

2- and 3-(2-R¹,R²-Aminovinyl)-N-methylpyridinium iodides IX—XII

To a solution of corresponding *Iia* and *Iib* (0.67 g; 2 mmol), respectively, in 10 cm³ of water a secondary amine (4 mmol) is added. After evaporating of the solvent the

products obtained are isolated by the fraction crystallization from the methanol—ether mixture or by the chromatography on a very short column of neutral aluminium oxide (ethyl acetate, methanol as an eluent). The physicochemical constants are set out in Tables 1 and 2.

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