

## PREPARATION AND REACTIONS OF *Z* AND *E* ISOMERS OF 5-NITRO-2-FURYLVINYL AZIDE

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Nucleophilic displacement of bromine or trimethylammonium group of 5-nitro-2-furylvinyl bromide (*I*) or 5-nitro-2-furylvinyltrimethylammonium bromide (*II*) afforded *Z* and *E* isomers of 5-nitro-2-furylvinyl azide (*III*). The *Z* and *E* isomers of *III* react with triphenylphosphine to give *Z* and *E* isomers of P=N-ylide *IV*.

The activating effect of 5-nitro-2-furyl group onto ethylene grouping and the possibility to substitute the properly selected substituents at the end of the ethylene functionality enable to obtain new substances possessing an antibacterial effect<sup>1-4</sup>. The 5-nitro-2-furyl substituted vinyl azides *III* or P=N-ylides *IV* represent a new group of 5-nitro-2-furan compounds which can be used as convenient starting intermediates for synthetic purposes.

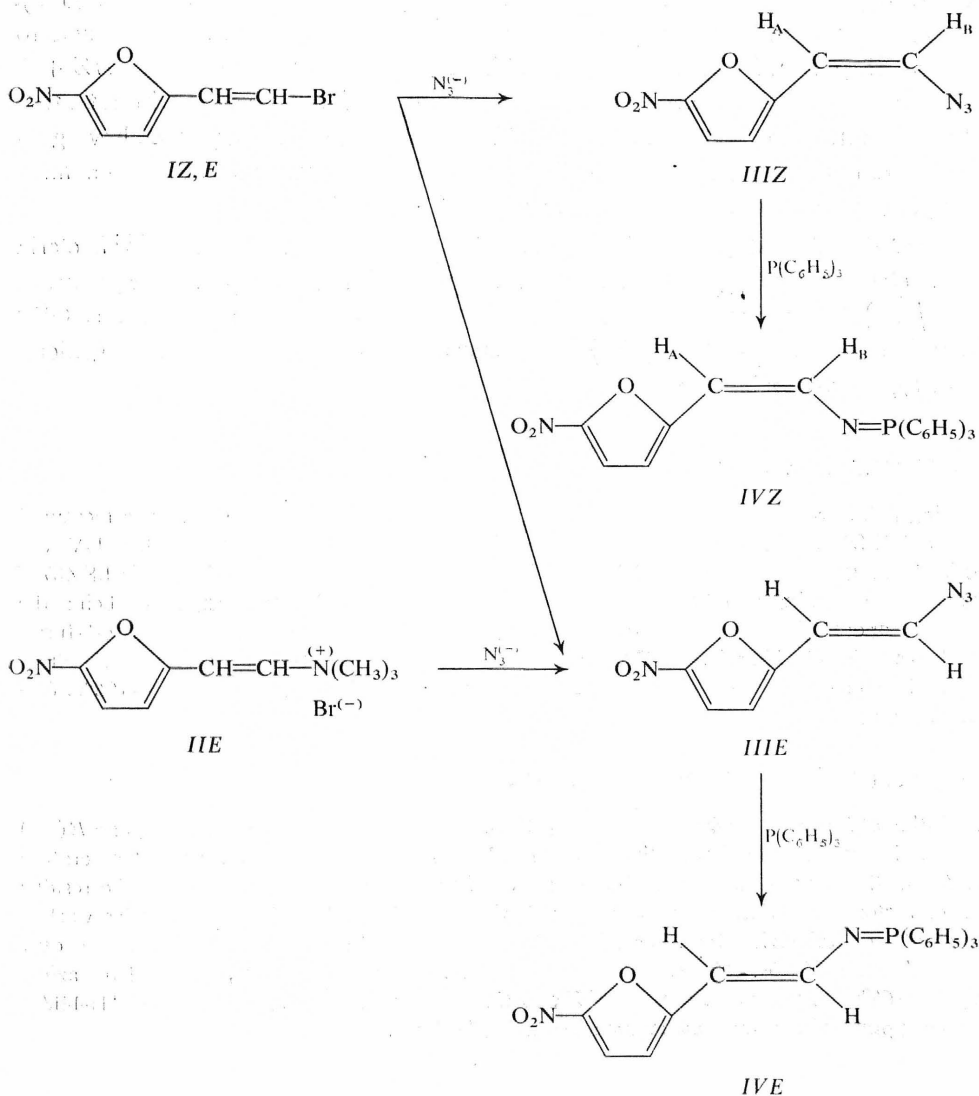
5-Nitro-2-furylvinylene bromide<sup>2</sup> (*I*) and 5-nitrofurylvinyltrimethylammonium bromide<sup>5</sup> (*II*) undergo an easy reaction with an azide anion in organic solvents, in water, or mixtures thereof to furnish 5-nitro-2-furylvinyl azide (*III*).

5-Nitro-2-furylvinylation of an azide anion with 5-nitro-2-furylvinyl bromide (*I*) in organic solvents, or aqueous organic solvents at room temperature is, according to reaction conditions more or less stereospecific. The bromide *I* can be obtained as an almost pure *Z* isomer<sup>2</sup> and therefore, we investigated the 5-nitro-2-furylvinylation of an azide anion with a mixture consisting of 95% *Z* and 5% *E* 5-nitrofurylvinyl bromides in an aqueous acetone solution. In acetone-water (4 : 1) at room temperature a mixture of *Z* and *E* isomers of 5-nitro-2-furylvinyl azide was obtained in a 2 : 3 ratio after 5 h and a 30–40 min illumination by sunlight. 5-Nitro-2-furylvinylation of the azide anion with 5-nitro-2-furylvinyltrimethylammonium bromide (*II*) occurs in the moment of mixing the aqueous solutions of components together; the resulting azide *III* has, according to <sup>1</sup>H-NMR spectrum, the *E* configuration. The yield of 5-nitro-2-furylvinyl azide is almost 100%.

The structure of *III* was elucidated by elemental analysis, infrared, ultraviolet, mass and <sup>1</sup>H-NMR spectral methods. It is noteworthy that compound *III* reveals

the peak of molecular ion ( $m/e$  180, 35%), although the most part of citations<sup>6</sup> report the loss of molecular nitrogen from the molecular ion.

The pure (*E*)-5-nitro-2-furylvinyl azide shows a higher stability than the mixture of both. Azides *IIIE* and *Z* + *E* undergo a gradual decomposition in the light to furnish a polymer of m.p. 350–450°C (decomposition). Heating of azides *III* above their melting point results in an intense decomposition accompanied with the loss of nitrogen, and, according to reaction conditions (solvent, heat, light) a wealth



SCHEME 1

of 5-nitro-2-furan compounds is formed; these are under investigation at the time being.

5-Nitro-2-furylvinyl azides *Z* and *E* react with triphenylphosphine at room temperature to give the red 5-nitro-2-furylvinyl-N-iminotriphenylphosphorane (*IV*). This reaction is accompanied by liberation of  $N_2$ . The azide *III* can be determined in ethereal solution by titration with an ethereal solution of triphenylphosphine (the indication being the evolution of nitrogen, thin layer chromatography, infrared spectroscopy in the  $2128\text{ cm}^{-1}$  region, ultraviolet spectroscopy in the 390 nm region). Reactions of azides with triphenylphosphine<sup>7,8</sup> offer an important approach to reactive vinyl  $P=N$ -ylide intermediates. The reaction of azides *IIIZ* and *IIIZ + E* with triphenylphosphine proceeds, as evidenced by  $^1\text{H-NMR}$  spectra, with retention of configuration to give *IVE* and *IVE + Z*. The latter are red compounds having an intense ultraviolet maximum at 497 nm, this being characteristic of an enamine grouping in 5-nitro-2-furylethylene compounds<sup>4</sup>.

The azide *III* displays a high biological activity against both  $G^{(-)}$  and  $G^{(+)}$  bacteria (*Escherichia coli* 50  $\mu\text{g}/\text{disc}$ , *Bacillus subtilis* 12.5  $\mu\text{g}/\text{disc}$ , *Staphylococcus pyogenes* 50  $\mu\text{g}/\text{disc}$ ). The phosphorane *III* reveals a greater biological activity against  $G^{(-)}$  bacteria (*Escheria coli* 50  $\mu\text{g}/\text{disc}$ ). Both compound *III* and *IV* evolve mutagenicity of *S. typhimurium* TA100.

## EXPERIMENTAL

Melting points were determined on a Kofler micro hot-stage. Infrared spectra were measured with a UR-20 (Zeiss, Jena) spectrophotometer in  $\text{CHCl}_3$ , ultraviolet spectra with a UV VIS (Zeiss Jena) apparatus in methanol. The  $^1\text{H-NMR}$  spectra were recorded with a Tesla BS 487 C instrument operating at 80 MHz in deuteriochloroform at  $25^\circ\text{C}$ , tetramethylsilane being the internal standard. Mass spectrum was measured with an AEI 902 S spectrometer. 5-Nitro-2-furylvinyl bromides (*I*) *Z* and *Z + E* were prepared according to<sup>2</sup>, 5-nitro-2-furylvinyltrimethylammonium bromide according to<sup>5</sup> by reacting *I* with trimethylamine. M.p.  $193\text{--}195^\circ\text{C}$  (decomposition).

### (*Z*) and (*E*)-5-Nitro-2-furylvinyl Azides (*III*)

A solution of 5-nitro-2-furylvinyl bromide (*I*) (2.18 g, 10 mmol), consisting of *Z* (95%) and *E* (5%) isomers, in acetone (45 ml) was stirred with  $\text{NaN}_3$  (0.7 g) in water (5 ml) at room temperature for 5 h in the dark. Acetone was then distilled off under diminished pressure and the residue was extracted after addition of water (10 ml) with ether. The ethereal layer was twice washed with water (10 ml each), the organic layer distilled off and the residue chromatographed over silica gel column (150–250 mesh, eluent benzene, chloroform). Yield 1.35 g (75%) of the azide, m.p.  $62\text{--}65^\circ\text{C}$  obtained as a mixture of *Z* and *E* isomers in a 2 : 3 ratio (according to  $^1\text{H-NMR}$  analysis); physical constants are summarized in Tables I and II.

*(E)*-5-Nitro-2-furylvinyl Azide (*IIIE*)

A solution of  $\text{NaN}_3$  (1 g) in water (15 ml) was added to a solution of bromide *II* (2.77 g, 10 mmol) in water (50 ml). The reaction proceeds immediately under separation of a yellow azide *IIIE*. Yield 1.66 g (92%) m.p. 84–86°C (ether, chloroform). This product is sufficiently pure even without further crystallization.

TABLE I

Physical Data of Compounds *III* and *IV*

Formula (mol. weight)	M.p., °C (yield, %)	IR $\text{cm}^{-1}$	UV $\lambda_{\text{max}}$ $\log \epsilon$	Calculated/Found		
				% C	% H	% N
<i>III</i>						
$\text{C}_6\text{H}_4\text{N}_4\text{O}_3$ (180.1)	62–65 <sup>a</sup>	1 320 <sup>c</sup>	393( <i>E</i> )	40.01	2.24	31.11
	(75)	1 530 <sup>c</sup>	(4.03)	39.83	2.18	30.98
	84–86 <sup>b</sup>	1 642 <sup>d</sup>	378( <i>Z</i> )			
		2 135 <sup>e</sup>				
<i>IV</i>						
$\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_2\text{P}$ (415.4)	137–140 <sup>a</sup>	1 320 <sup>c</sup>	497	69.56	4.42	6.75
	(80)	1 370 <sup>c</sup>	(4.39)	69.32	4.28	6.57
	144–146 <sup>b</sup>	1 555 <sup>c</sup>				
	(90)	1 615 <sup>d</sup>				

<sup>a</sup> *Z* : *E* (2 : 3) Isomer; <sup>b</sup> *E* isomer; <sup>c</sup>  $\nu(\text{NO}_2)$ ; <sup>d</sup>  $\nu(\text{C}=\text{C})$ ; <sup>e</sup>  $\nu(\text{N}_3)$ .

TABLE II

<sup>1</sup>H-NMR Data of Stereoisomers *IIIZ* and *IIIE*

Com- pound	Parameter <sup>a</sup>	<i>Z</i>				<i>E</i>			
		H <sub>A</sub>	H <sub>B</sub>	H <sub>3</sub>	H <sub>4</sub>	H <sub>A</sub>	H <sub>B</sub>	H <sub>3</sub>	H <sub>4</sub>
<i>III</i>	$\delta$ , ppm	6.65	5.70	6.89	7.31	7.13	6.07	6.35	7.30
	<i>J</i> , Hz		8.0		4.0		13.6		4.0
<i>IV</i> <sup>b</sup>	$\delta$ , ppm	6.83	7.14	5.50	7.29	5.92	7.97	5.95	7.25
	<i>J</i> , Hz		7.2		4.05		12.5		4.05

<sup>a</sup> Measured in  $\text{CDCl}_3$  (tetramethylsilane); <sup>b</sup> 7.56 ppm (15 Hz).

## Reaction of 5-Nitro-2-furylvinyl Azides with Triphenylphosphine

a) *Z* and *E* isomers *IV*: Triphenylphosphine (2.62 g) in ether (30 ml) was added under stirring to a solution of 5-nitro-2-furyl azides *Z* : *E* (2 : 3) in ether (30 ml). The reaction is indicated both by the red colouration of the solution coming from the formed P=N-ylide *IV* and the evolution of nitrogen. Evaporation of the solvent to a half of its volume afforded the crystalline *IV*, red in colour and metal-lustrous in nature (3.3 g, 80%), m.p. 137–140°C. The starting ratio of isomers remained approximately unchanged. Physical constants are listed in Tables I and II.

b) *E* Isomer *IV*: Triphenylphosphine (2.62 g) in ether (30 ml) was gradually added to a solution of azide *IIIE* (1.8 g, 10 mmol) in ether (30 ml) while stirring. A successive precipitation of a metal-lustrous red compound takes place. Yield 3.72 g (90%), m.p. 144–146°C of an *E* isomer (according to <sup>1</sup>H-NMR analysis).

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