

PREPARATION OF TETRASUBSTITUTED α,β -UNSATURATED SULFONES OF 5-NITROFURAN SERIES*

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Received February 19th, 1976

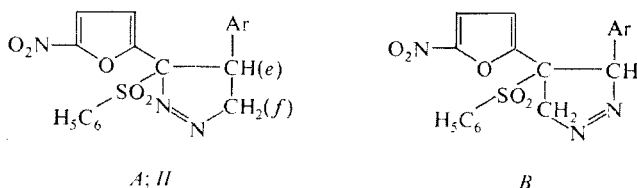
By addition of diazomethane to 1-(5-nitro-2-furyl)-1-phenylsulfonyl-2-(4-X-phenyl)ethylenes *I* ($X = H, OCH_3, N(CH_3)_2, F, NO_2$) or 1-(5-nitro-2-furyl)-1-phenylsulfonyl-2-furylethylene in tetrahydrofuran corresponding 3-(5-nitro-2-furyl)-3-phenylsulfonyl-4-(4-X-phenyl-; or 2-furyl)-1-pyrazolines *II* were prepared which on thermal decomposition afforded tetrasubstituted derivatives of ethylene *III*. The same products are formed from unsaturated sulfones when these are reacted with CH_2I_2 under catalytic effect of Zn/Cu and traces of I_2 . The IR, UV and 1H -NMR spectra of the synthesized substances are also interpreted.

The rules on the addition of diazomethane to α,β -unsaturated compounds activated by electron-accepting substituents have been studied on a large number of derivatives^{1,2}. Less attention has so far been paid to the addition of CH_2N_2 to α,β -unsaturated sulfones³⁻⁹. Parham and coworkers⁵ mention that during the addition of diazomethane to sulfones of the $R^1SO_2CH=CHR^2$ type, where R^2 is aryl, a normal product is formed in which the carbon of diazomethane is bound to the β -C, or also an abnormal product with the diazocarbon atom bound to the α -C of the ethylene bond. If R^2 was alkyl or hydrogen the authors⁵ describe the formation of normal products. More recently Helder and coworkers⁹ made some conclusions published by Parham and coworkers⁵ more exact.

The aim of our work was the investigation of the addition of CH_2N_2 to non-planar trisubstituted ethylene derivatives – unsaturated sulfones of 5-nitrofurans series¹⁰. In all substances investigated equal structural groupings were on $C_{(1)}$ of the ethylene bond, *i.e.* 5-nitro-2-furyl and phenylsulfonyl residues, and on $C_{(2)}$ 4-X-phenyl and furyl residues were present, where X represents electron-accepting and electron-donating substituents. The newly synthesized 1-(5-nitro-2-furyl)-1-phenylsulfonyl-2-(4-fluorophenyl)ethylene was prepared in the same manner as other unsaturated sulfones¹⁰. From the analysis of the reaction mechanism¹¹, UV spectra and molecular models^{10,11} it follows that the initial α,β -unsaturated sulfones *I* have probably the configuration *E* and that they are considerably sterically compressed.

* Part LXXVI in the series Furan Derivatives; Part LXXV: This Journal *41*, 3085 (1976).

In consequence of the weak solubility of *I* the addition of CH_2N_2 took place in dry tetrahydrofuran at 0°C over 7 to 14 days, or at room temperature over 48 to 72 hours. For the reaction freshly prepared CH_2N_2 was always used, in a 3 to 5 fold excess. In dependence on the orientation of the CH_2N_2 two types of 1-pyrazolines may be formed theoretically, A or B, which can isomerize to corresponding 2-pyrazolines (Scheme 1).



SCHEME 1

A; II

B

TABLE I

Physical Properties and Elemental Analyses of the Synthesized Substances

Compound X	M.p., $^\circ\text{C}$ (yield, %)	Formula (m.w.)	Calculated/Found		
			% C	% H	% N
3-(5-Nitro-2-furyl)-3-phenylsulfonyl-4-(4-X-phenyl)-1-pyrazoline					
V	131–132 ^a	$\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_5\text{S}$	57.43	3.78	10.58
H	(74)	(397.5)	57.40	3.67	10.43
VI	146 ^a	$\text{C}_{19}\text{H}_{14}\text{FN}_3\text{O}_5\text{S}$	54.94	3.37	10.12
F	(76)	(415.5)	54.87	3.27	10.12
VII	163 ^a	$\text{C}_{19}\text{H}_{14}\text{N}_4\text{O}_7\text{S}$	51.58	3.17	12.67
NO_2	(75.5)	(442.5)	51.56	3.09	12.41
3-(5-Nitro-2-furyl)-3-phenylsulphonyl-4-(2-furyl)-1-pyrazoline					
VIII	152–153 ^a	$\text{C}_{17}\text{H}_{13}\text{N}_3\text{O}_6\text{S}$	52.65	3.36	10.84
	(75)	(387.4)	52.49	3.31	10.73
1-(5-Nitro-2-furyl)-1-phenylsulfonyl-2-methyl-2-(4-X-phenyl)ethylene					
IX	184	$\text{C}_{19}\text{H}_{15}\text{NO}_5\text{S}$	59.22	3.64	3.63
H	(93)	(369.4)	59.09	3.54	3.58
X	201–202	$\text{C}_{19}\text{H}_{14}\text{FNO}_5\text{S}$	61.79	3.62	3.79
F	(96)	(387.4)	61.71	3.56	3.74
XI	226–227	$\text{C}_9\text{H}_{14}\text{N}_2\text{O}_7\text{S}$	55.07	3.38	6.76
NO_2	(97)	(414.4)	54.93	3.22	6.69

^a Decomposes at m.p.

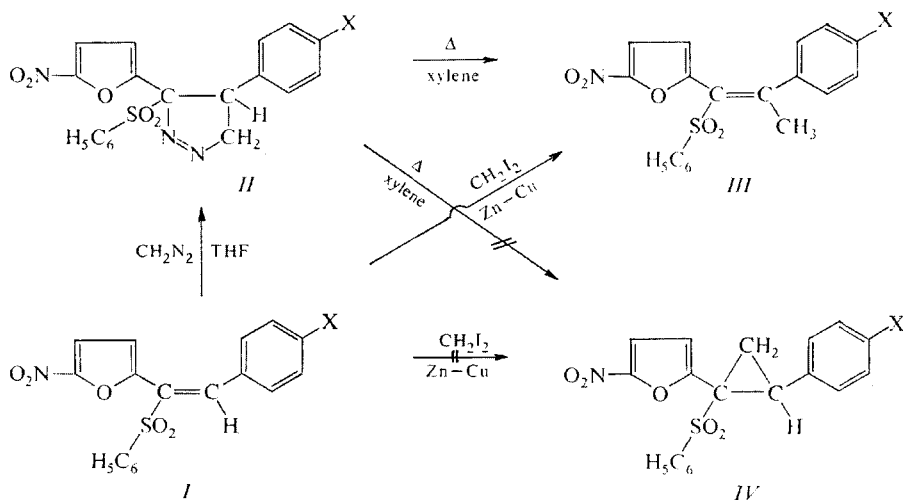
From the elemental analysis and the analysis of IR and $^1\text{H-NMR}$ spectra it follows that the products which are formed in about a 75% yield are unambiguously 3-(5-nitro-3-furyl)-3-phenylsulfonyl-4-(4-X-phenyl)-1-pyrazolines, *II*. The orientation of CH_2N_2 during the addition to the strongly polarized >C=C< bond of such systems follows the polar effects, *i.e.* the nucleophilic carbon of CH_2N_2 adds to the $\text{C}_{(2)}$ carbon of the ethylene bond, carrying a considerable positive charge in consequence of the strongly electron-accepting phenylsulfonyl and 5-nitrofuran residue, probably from the less hindered side. It was found that the stability of products *II* depends on the character of the substituent X. If X is H, NO_2 , F, or if a furyl residue is bound to $\text{C}_{(2)}$ of the ethylene bond, the 1-pyrazolines formed are stable and they can be crystallized and characterized by elemental analysis (Table I) and spectral data (Table II). If X is an electron-donating substituent (OCH_3 , $\text{N}(\text{CH}_3)_2$) the derivatives *II*, after their isolation, are very unstable in air and change to tars. Therefore, these 1-pyrazolines were characterized by mass spectroscopy only, and the presence of nitrogen was determined by elemental analysis. Attempts at the isomerization of stable 1-pyrazolines *II* to 2-pyrazolines in tetrahydrofuran and acetonitrile, under the catalytic effect of triethylamine, were in no case successful. In all instances the

TABLE II
IR, UV and $^1\text{H-NMR}$ Spectra of the Synthesized Compounds

Com- pound	$\nu(\text{C}=\text{C})$ alif.	$\nu(\text{NO}_2)_s$	δH , p.p.m.		λ_{max} , nm (log ϵ) ^a		
			He	Hf			
<i>V</i>	—	1 362 1 389	m 4.56—4.75	m 5.25—5.45	210(4.58)	221(4.57)	313(4.23)
<i>VI</i>	—	1 358 1 390	m 4.33—4.51	m 5.23—5.43	210(4.62)	220(4.60)	312(4.25)
<i>VII</i>	—	1 359 1 389	m 4.35—4.56	m 5.24—5.35	207(4.64)	218(4.62) 276(4.25)	303(4.13)
<i>VIII</i>	—	1 357 1 385	m 4.53—4.73	m 5.15—5.33	208(4.45)	i220(4.46)	311(4.18)
<i>IX</i>	1 630	1 358 1 387	—	—	211(4.46)	220(4.64)	315(4.20)
<i>X</i>	1 625	1 355 1 385	—	—	211(4.60)	223(4.58)	317(4.26)
<i>XI</i>	1 640	1 360 1 390	—	—	208(4.47)	218(4.46) 278(4.26)	304(4.18)

^a i inflexion, sh shoulder, m multiplet.

initial compound *II* was recovered unchanged. In acid medium (tetrahydrofuran with hydrogen chloride) degradation of phenylsulfonyl residue took place, followed by other chemical changes, under formation of a substance the structure of which is still not elucidated. The characteristic property of stable 1-pyrazolines *II* is their decomposition at melting point. During heating in xylene these compounds set free nitrogen even below the boiling point of the solvent and they do not afford cyclopropane derivatives *IV*, but the insertion of the CH_2 group between the $\text{C}-\text{H}$ bond of the ethylene takes place under formation of corresponding tetrasubstituted ethylenes *III* (Scheme 2; Table I, derivatives *IV-VI*).



SCHEME 2

The yields of this reaction are high (93–97%). It could be expected that the formation of the cyclopropane ring would be unfavourable in this case, owing to the steric bulkiness of the substituents and their strong electron-accepting effect. In order to check this fact we applied the Simmons–Smith reaction which permits a synthesis of even strongly strained cyclopropane derivatives¹². However, even when sulfones *I* were heated with diiodomethane on tetrahydrofuran with zinc activated with copper cyclopropane derivatives could not be obtained, but only corresponding tetrasubstituted ethylenes *III*, identical with the products obtained by thermal decomposition of 1-pyrazolines *II*. Such tetrasubstituted derivatives cannot be prepared by condensation of 5-nitrofuryl phenyl sulfone under the conditions of the synthesis of α,β -unsaturated sulfones *I* (ref.^{10,11}), because – as we have checked – neither acetophenone nor 4-nitroacetophenone undergo condensation reaction with this sulfone.

In IR spectrophotometry the use of $\nu_{(N=N)}$ in the $1550-1600\text{ cm}^{-1}$ region for the identification of 1-pyrazolines *II* can be auxiliary only, because in this type of substance $\nu(\text{NO}_2)_{\text{as}}$ also occur in this region, which overlap with the preceding bands. In unsaturated sulfones (*I*) a single absorption band appears¹⁰ in the 1535 to 1550 cm^{-1} region for $\nu(\text{NO}_2)_{\text{as}}$, and in the pyrazolines investigated two bands appear in the $1529-1603\text{ cm}^{-1}$ region, of which one corresponds to NO_2 and the other to the $\text{N}=\text{N}$ group. The absorption band corresponding to $\nu(\text{NO}_2)_{\text{s}}$ (Table II) is split for all substances *V-XI* into two bands, in the same manner as in the starting unsaturated sulfones¹⁰. The bands of $\nu(\text{SO}_2)_{\text{as}}$ of 1-pyrazolines *V-VIII* appear in the $1321-1328\text{ cm}^{-1}$ region, and in tetrasubstituted ethylenes at 1318 cm^{-1} . The absorption bands corresponding to $\nu(\text{SO}_2)_{\text{s}}$ appear in the $1157-1160\text{ cm}^{-1}$ region for all substances. In addition to these bands the vibrations of the furan nucleus and other substituents can also be seen in the IR spectra.

The proof that substances *V-VIII* are 1- and not 2-pyrazolines consists in the absence in the IR spectra of NH vibration in the 3200 cm^{-1} region. This fact is also corroborated by $^1\text{H-NMR}$ spectra in which the singlet of N-H , CH_2 and CH protons does not appear, but two multiplets corresponding to the resonance signals of protons in the $-\text{CH}-\text{CH}_2-$ grouping do (theoretically a three-spin system ABC or a higher order ABX system), which is characteristic of 1-pyrazolines only. The dependence of these multiplets was proved by the technique of double resonance Indor. In tetrasubstituted ethylenes *III* the singlet at 3.33 to 3.55 p.p.m. appears in the $^1\text{H-NMR}$ spectrum, corresponding to three protons of the CH_3 group bound to the ethylene bond.

In the UV spectra (Table II) of 1-pyrazolines *V-VIII* and tetra-substituted ethylenes *IX-XI* three absorption bands appear in the majority of cases, of which the last appears in the $303-317\text{ nm}$ region, *i.e.* in the region that is weakly bathochromically shifted with respect to the starting unsaturated sulfone¹⁰. From this it follows that the disappearance of the multiple bond in sulfones *I* due to the formation of the pyrazoline cycle, or the substitution of H bound to the ethylene bond by CH_3 (by insertion of the methylene carbene), does not result in a substantial modification of the UV spectra of these substances. This represents a further proof that the investigated α,β -unsaturated sulfones *I* represent strongly non-planar systems in which the conjugation between the 5-nitrofurane and the aryl residue of the molecule, immediately bound to the ethylene bond^{10,11}, is interrupted.

EXPERIMENTAL

1-Pyrazolines *II*

A three to five-fold amount of freshly prepared ethereal diazomethane solution was added to a solution of the unsaturated sulfone *I* (0.02 mol) in a minimum amount of tetrahydrofuran and the mixture was allowed to stand at room temperature for 48–72 hours, or at 0°C for 7–14 days.

The solvents were evaporated in a vacuum without heating and the residue was dissolved in cold acetone, charcoal was added, the suspension filtered and the filtrate concentrated. The precipitated material was washed with ether (Table II). Unstable pyrazolines were obtained from the concentrated mixture by addition of the required amount of ether in which *II* are less soluble than in tetrahydrofuran. On standing in air they are rapidly converted to tars. The mass spectra of these substances were measured in ether which was evaporated during the spectrometry.

Tetrasubstituted Ethylenes *III*

These substances were prepared by thermal decomposition of 1-pyrazolines *II* (*A*) or by methylation of unsaturated sulfones *I* (*B*).

A. 1-Pyrazolines were refluxed in xylene. During the gradual heating of solid substances nitrogen escaped and the tetrasubstituted ethylenes formed passed into solution. When the development of nitrogen has ceased at the boiling point of xylene and all the precipitate passed into solution the reaction is over. Xylene was evaporated *in vacuo* and the products crystallized from acetone (Table II).

B. A mixture of CH_2I_2 (2 g; 0.0075 mol), iodine (0.1 g) and activated¹³ Zn—Cu catalyst (0.612 g; 0.012 mol) in dry tetrahydrofuran (15 ml) was heated and stirred on a water bath for 30 minutes. Unsaturated sulfone *I* (0.0025 mol) in tetrahydrofuran (10 ml) was then added to the solution and the mixture was refluxed for 30 hours. After filtration off of the catalyst the mixture was separated on a silica gel column (20 cm; 2 cm diameter). Unpolar solvents (hexane, CCl_4) eluted unreacted CH_2I_2 and I_2 , while the polar ones (ethanol, acetone) eluted the products *III* and a part of the unreacted sulfone *I*. The products *III* obtained were identical with the products of thermal decomposition of 1-pyrazolines (Table II).

Spectral Measurements

The infrared spectra were measured on a UR-20 Zeiss (Jena) spectrophotometer in KBr pellets, or in the form of saturated solutions in chloroform. The NaCl cell was 1.02 mm thick. Electron absorption spectra were measured on a Specord UV VIS Zeiss spectrophotometer in ethanol. The concentration of the substances measured was $2-6 \cdot 10^{-5}$ M. Cell thickness 1 cm, accuracy $\pm \pm 1$ nm. The ¹H-NMR spectra were measured on a Tesla BS 487 B, 80 MHz spectrometer, at 25°C, using deuterated dimethyl sulfoxide as solvent and hexamethyldisiloxan as internal reference. The δ_{H} values (Table II) are calculated with reference to tetramethylsilane.

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Translated by Ž. Procházka.