

PREPARATION OF 5-NITRO-2-SUBSTITUTED FURANES FROM 5-NITRO-5-FURFURYL NITRATE*

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New O,O-dialkyl-S-(5-nitro-5-furfuryl)thiophosphates and -dithiophosphates were synthesized. A novel method for preparing these compounds, S-(5-nitro-2-furfuryl)dithiocarbamates and new O-alkyl-S-(5-nitro-2-furfuryl)dithiocarbamates from 5-nitro-2-furfuryl nitrate and alkali metal salts of O,O-dialkylthio(dithio)phosphorous, dithiocarbamic, and dithiocarbonic acids is reported.

Synthesis of nitrofuran derivatives has attracted attention in connection with biological activity of these compounds^{1,2}. S-(5-nitro-2-furfuryl)dithiocarbamates were prepared³⁻⁵ by reaction of a 5-nitro-2-furfuryl halogenide with an alkali metal salt of dithiocarbamic acid. These compounds proved useful as fungicides and bactericides. The synthesis of compounds *I-XXVI* described in this work was carried out with the aim of studying the biological activity of these substances.

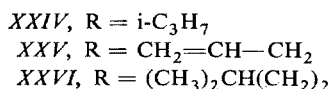
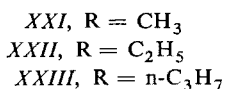
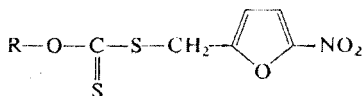
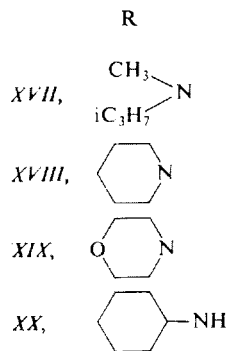
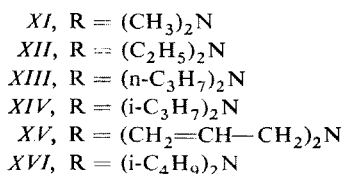
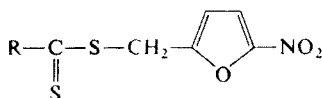
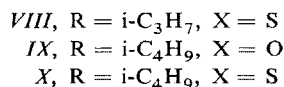
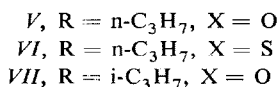
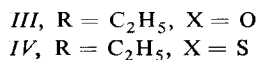
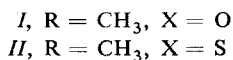
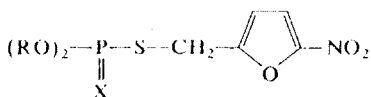
In preparing O,O-dialkyl-S-(5-nitro-2-furfuryl)thiophosphates and -dithiophosphates *I-X*, S-(5-nitro-2-furfuryl)-dithiocarbamates *XI-XX*, and S-(5-nitro-2-furfuryl)dithiocarbonates *XXI-XXVI* we used 5-nitro-2-furfuryl nitrate^{6,7} as a starting compound. This work continues our previous study⁸ which concerned with the use of 5-nitro-2-furfuryl nitrate in organic synthesis.

Preparation of compounds *I-X* was carried out in acetone and in ethyl acetate. On using chloroform as a solvent, compounds *I-IV* were not formed even after prolonged reaction time (6 h at a reflux of the solvent). In the above experiments only starting 5-nitro-2-furfuryl nitrate was recovered. Alkali metal salts of O,O-dialkylthiophosphorous acid were obtained from the appropriate O,O-dialkylphosphite, sulphur, and alkali metal alcoholate in benzene. When compared to the reported procedure^{3,5}, the advantage of the synthesis of compounds *XI-XX* reported in this work is that 5-nitro-2-furfuryl nitrate is starting compound also for preparing 5-nitro-2-furfuryl halogenides^{8,9}, so that one reaction step is saved. We found that the best yields are achieved at 10–20°C after 6–8 h, and at 50–60°C after 10–30 min. Alkali metal salts of dithiocarbamic acid were prepared by reported procedure¹⁰.

* Part LXI in the series Furan Derivatives; Part LX: Tetrahedron 30, 4123 (1974).

The optimum temperature for preparing compounds *XXI–XXVI* in acetone or ethyl acetate was found to be 0–20°C. The use of the higher temperature leads to formation of undesired polymeric substances in greater amounts. The addition of 5-nitro-2-furfuryl nitrate dissolved in acetone to an alkali metal salt of dithiocarbamic acid proved to be advantageous.

IR spectra of compounds *I–XXVI* show bands characteristic for the nitro group: $\nu(\text{NO}_2)_{\text{sym}}$ 1356 cm^{-1} and $\nu(\text{NO}_2)_{\text{asym}}$ 1505–1510 cm^{-1} . Compounds *I, III, V, VII,* and *IX* exhibit strong $\nu(\text{P}=\text{O})$ band at 1277 cm^{-1} ; Compounds *XI–XXVI* have the $\nu(\text{C}=\text{S})$ band located in 1152–1140 cm^{-1} . The spectra of compounds *I–XXVI*



show the bands due to out-of-plane deformation vibration of the furan ring^{11,12} in the 885–870 cm⁻¹ region.

As to their effectiveness on *Musca domestica* L., compounds *I*, *III*, and *IV* were almost as efficient as the standard Malation. The other substances were essentially inactive. The compounds prepared were all essentially inefficient on *Calandra granaria* L., *Macrosyphoniella sanborni* THEOB., and on *Aphis fabae* SCOP. When investigating acaricide efficiency on *Tetranychus urticae* KOCH we found that compounds *I*, *III*, and *IV* are almost three times as active as the standard substance, Malation (It for *I*: 285, *III*: 305, and *IV*: 320). Compounds *II*, *V*, *XI*, *XII*, *XIV*, *XV*, *XIX*, *XXI*, *XXII*, *XXIII*, and *XXV* were by about one order of magnitude less

TABLE I

O,O-Dialkyl-S-(5-nitro-2-furfuryl)thiophosphates and -dithiophosphates

Compd.	Formula (m.wt.)	Calculated/Found		n_D^{20} (yield, %)	R_F
		% P	% S		
<i>I</i> ^a	C ₇ H ₁₀ NO ₆ PS (267.3)	11.62	11.98	— (41.3)	0.385
		11.32	12.21		
<i>II</i>	C ₇ H ₁₀ NO ₅ PS ₂ (283.3)	10.95	22.60	1.5938 (60.7)	0.661
		11.16	22.09		
<i>III</i>	C ₉ H ₁₄ NO ₆ PS (293.3)	10.60	10.92	1.5417 (77.0)	0.532
		10.34	11.09		
<i>IV</i>	C ₉ H ₁₄ NO ₅ PS ₂ (309.4)	10.03	20.66	1.5749 (78.7)	0.711
		9.91	20.45		
<i>V</i>	C ₁₁ H ₁₈ NO ₆ PS (323.3)	9.60	9.88	1.5330 (87.0)	0.623
		9.30	9.49		
<i>VI</i>	C ₁₁ H ₁₈ NO ₅ PS ₂ (339.3)	9.13	18.86	1.5628 (83.9)	0.720
		8.85	18.68		
<i>VII</i>	C ₁₁ H ₁₈ NO ₆ PS (323.3)	9.60	9.88	1.5268 (80.8)	0.607
		9.84	9.71		
<i>VIII</i>	C ₁₁ H ₁₈ NO ₅ PS ₂ (339.3)	9.13	18.86	1.5561 (74.0)	0.728
		8.92	18.64		
<i>IX</i>	C ₁₃ H ₂₂ NO ₆ PS (351.4)	8.82	9.12	1.5231 (83.0)	0.673
		8.58	8.82		
<i>X</i>	C ₁₃ H ₂₂ NO ₅ PS ₂ (367.5)	8.45	17.43	1.5485 (79.5)	0.760
		8.17	17.51		

^a M.p. 83–84°C (ethanol).

active, the other substances were inactive. The efficiency, tested against *T. urticae* KOCH ovides of compounds XII, XIV, XVII, and XXII was about one order of magnitude less than that of the standard; the other substances were not active. Their efficiency as fungicides and herbicides was insignificant with respect to that of the standard.

EXPERIMENTAL

Measurements

IR spectra in the $3600-800\text{ cm}^{-1}$ region of $2 \cdot 10^{-2}\text{ M}$ chloroform solutions of the compounds were recorded a double-beam Model UR-20 spectrophotometer, using 1.0 mm NaCl cells. The

TABLE II
S-(5-Nitro-2-furfuryl)dithiocarbamates

Compd.	Formula (m.wt.)	Calculated/Found		M.p., °C (yield, %)	R_F (n_D^{20})
		% N	% S		
XI	$\text{C}_8\text{H}_{10}\text{N}_2\text{O}_3\text{S}_2$ (246.3)	11.39	26.00	113–115 ^a (89.3)	0.334 —
		11.17	25.89		
XIII	$\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_3\text{S}_2$ (274.4)	10.21	23.37	75–76 ^a (84.1)	0.466 —
		10.52	23.63		
XIII	$\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}_3\text{S}_2$ (302.4)	9.26	21.20	42–43 ^a (87.2)	0.558 —
		9.44	21.54		
XIV	$\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}_3\text{S}_2$ (302.4)	9.26	21.20	85–86 ^a (79.4)	0.525 —
		9.31	21.33		
XV	$\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_3\text{S}_2$ (298.4)	9.38	21.43	— (86.1)	0.492 (1.6338)
		9.40	21.73		
XVI	$\text{C}_{14}\text{H}_{22}\text{N}_3\text{O}_3\text{S}_2$ (330.4)	8.47	19.35	44–45 ^a (90)	0.600 —
		8.44	19.38		
XVII	$\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_3\text{S}_2$ (274.4)	10.20	23.40	59–61 ^b (91)	0.475 —
		10.26	23.35		
XVIII	$\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3\text{S}_2$ (286.4)	9.78	22.38	84–85 ^a (97.7)	0.458 —
		9.70	22.48		
XIX	$\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_4\text{S}_2$ (288.3)	9.71	22.21	135–137 ^c (64.4)	0.284 —
		9.60	22.02		
XX	$\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_3\text{S}_2$ (288.4)	9.72	22.20	— (41.6)	— (1.5721)
		9.70	21.85		

Crystallized from ^a ethanol, ^b cyclohexane, and ^c toluene.

instrument was calibrated with 25 μm polystyrene film. Electronic absorption spectra in the 200–480 mm region of $6 \cdot 10^{-5} \text{M}$ ethanolic solutions of compounds *I–XXVI* were recorded on a Specord UV VIS instrument (Zeiss, Jena, GDR) at room temperature. Cells were 1 cm thick.

R_F values listed in Tables *I–III* were determined on silica gel plates (Silufol, Kavalier), using acetone–light petroleum (4 : 6) for *I–X* and cyclohexane–ethyl acetate (7 : 3) for *XI–XXVI*.

O,O-Dialkyl-S-(5-nitro-2-furfuryl)thiophosphates and -dithiophosphates

A mixture of 0,05 mol of 5-nitro-2-furfuryl nitrate and 0,05 mol of alkali O,O-dialkylthio(or dithio)phosphate in acetone (100 ml) was refluxed with stirring for 4 h. After cooling, benzene (100 ml) was added, the mixture was washed successively with water, 5% sodium carbonate, and water. After drying over sodium sulphate, the solvents were distilled off, the temperature and pressure at the end of the distillation being 70°C and 0,1 Torr, respectively.

S-(5-Nitro-2-furfuryl)dithiocarbamates

A total of 0,05 mol of 5-nitro-2-furfuryl nitrate was added portionwise (15 min) at room temperature to a stirred solution of 0,055 of alkali dithiocarbamate in acetone (100 ml). The mixture was stirred at room temperature for another 1 h or at 40°C for 20 min. After cooling to 15°C, the mixture was poured onto 400 ml of ice water. If the product formed is precipitate, this is filtered

TABLE III
S-(5-Nitro-2-furfuryl)dithiocarbonates

Compd.	Formula (m.wt.)	Calculated/Found		M.p., °C (yield, %)	R_F (n_D^{20})
		% N	% S		
<i>XXI</i>	$\text{C}_7\text{H}_7\text{NO}_4\text{S}_2$ (233.3)	5.99	27.43	43–45 ^a	0.405
		6.12	27.52	(61.2)	—
<i>XXII</i>	$\text{C}_8\text{H}_9\text{NO}_4\text{S}_2$ (247.3)	5.66	25.93	29.5–30.5 ^a	0.446
		5.51	25.69	(86.8)	—
<i>XXIII</i>	$\text{C}_9\text{H}_{11}\text{NO}_4\text{S}_2$ (261.3)	5.36	24.52	29–31 ^b	0.504
		5.40	24.82	(82.5)	—
<i>XXIV</i>	$\text{C}_9\text{H}_{11}\text{NO}_4\text{S}_2$ (261.3)	5.36	24.52	39–41 ^b	0.496
		5.32	24.76	(53.7)	—
<i>XV</i>	$\text{C}_9\text{H}_9\text{NO}_4\text{S}_2$ (259.3)	5.40	24.72	—	0.480
		5.43	24.68	(81.4)	(1.5412)
<i>XVI</i>	$\text{C}_{11}\text{H}_{15}\text{NO}_4\text{S}_2$ (289.3)	4.84	22.16	—	0.546
		4.92	22.41	(88.2)	(1.5863)

Crystallized from ^aethanol, ^bcyclohexane.

off and recrystallized. In the event of formation of liquid product, it is extracted with benzene, the extract is dried and condensed under vacuum (finally at 40°C and 0.1 Torr).

S (5-Nitro-2-furfuryl)dithiocarbonates

A solution of 0.05 mol of 5-nitro-2-furfuryl nitrate in acetone was added to a stirred and cooled (0°C) solution of 0.055 mol of potassium dithiocarbonate in acetone (30 ml). The mixture was stirred at 15–20°C for 4 h, poured onto water and extracted with benzene. The benzene extract

TABLE IV
UV Spectra (in nm) of Compounds I–XXVI

Compound	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$
I	210	4.08	—	—	—	—	318	4.16
II	209	4.07	—	—	—	—	319	4.06
III	209	3.90	—	—	—	—	314	4.06
IV	210	3.97	—	—	—	—	317	4.12
V	210	3.83	—	—	—	—	316	4.04
VI	212	3.98	—	—	—	—	319	4.06
VII	212	4.13	—	—	—	—	320	4.09
VIII	213	3.93	—	—	—	—	320	4.03
IX	211	3.97	—	—	—	—	326	4.12
X	209	3.93	—	—	—	—	314	4.12
XI	215	4.24	244	4.08	275	4.08	323	4.09
XII	216	4.22	244	4.08	281	4.19	325	4.16
XIII	216	4.20	248	4.06	282	4.22	325	4.16
XIV	218	4.18	249	4.00	272	4.19	316	4.13
XV	215	4.24	248	4.06	284	4.20	325	4.12
XVI	216	4.22	251	4.04	287	4.23	326	4.16
XVII	219	4.23	244	4.08	282	4.12	325	4.09
XVIII	215	4.18	250	4.08	286	4.25	324	4.16
XIX	215	4.22	250	4.08	286	4.27	323	4.18
XX	216	4.21	251	4.10	284	4.24	322	4.16
XXI	210	4.13	—	—	279	4.10	319	4.16
XXII	213	4.18	—	—	280	4.12	311	4.18
XXIII	213	4.18	—	—	279	4.11	321	4.18
XXIV	212	4.16	—	—	281	4.10	321	4.15
XXV	206	4.08	—	—	246	3.85	319	4.06
XXVI	216	4.15	—	—	281	4.10	319	4.15

was dried, then the solvent was distilled off under vacuum (at the end 40°C and 0.1 Torr). Solid substances were purified by crystallization.

Investigation of Pesticidal Effectiveness

The methods used to examine the action of prepared compounds as pesticides were following^{13,14}: insecticide action was tested on *Musca domestica* L., *Calandra granaria* L.; system insecticide effectiveness on *Macrosyphoniella sanborni* THEOB.; acaricide effectiveness on *Tetranychus urticae* KOCH, Ovicidal effectiveness on *T. urticae* KOCH ovidices, and contact insecticide effectiveness on *Aphis fabae* SCOP.

The action as fungicides was determined both *in vitro* and *in vivo*. The inherent effectiveness was examined with the use of spores of following fungies: *Sclerotinia fructicola* (WINT.) and *Aspergillus niger* TIEGH, *Fusarium nivale* (FR.) ces., *Alternaria* sp., *Stemphylium sarcinoformae* (CAV.), WITHSHIRE, using the method by Sharvell. The antiwheat effectiveness was examined by using living plant of the "Dunajský trh" spring sort barley (*Erysiphe graminis* DC), the Znojenský sort cucumbers (*Erysiphe cichoracearum* DC) and tomatoes (*Phytophthora infestans* DE BY).

To estimate herbicide effectiveness, we used both the method of preemergent application into the soil and of postemergent application (on the leaf) using *Avena sativa*, *Polygonum persicaria*, *Fagopyrum sagittatum*, and *Sinapis alba*.

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