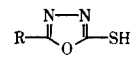
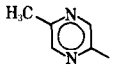
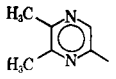
Table IV—2-(2-Pyrazinyl)-5-mercapto-1,3,4-oxadiazoles



Sample Number	R	Yield, %	Melting Point	Formula	Analysis, % Calc.	Analysis, % Found	Hypoglycemic Activity at 50 mg./kg. Mice[a]	Hypoglycemic Activity at 50 mg./kg. Rats[b]
1		30.5	213°	$C_6H_4N_4OS$	C 40 H 2.24 N 31.1 S 17.78	39.8 2.4 31 17.6	Rejected	—
2		33.4	230°	$C_7H_6N_4OS$	C 43.3 H 3.1 N 28.85 S 16.51	43.38 3.15 28.6 16.41	Rejected	—
3		43	198°	$C_8H_8N_4OS$	C 46.12 H 3.87 N 26.93 S 15.36	46 3.72 26.1 15.43	Rejected	—

[a] Accepted = hypoglycemic activity > then that of tolbutamide at the same dosage. [b] Maximal hypoglycemic activity as percent decrease in comparison to controls. Tolbutamide activity = 38%.

compounds synthesized by the above-mentioned authors but, under our conditions, found no hypoglycemic activity.

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Synthesis and Antimicrobial Activity of Thiocarbohydrazide-1,5-dicarboxylic Acid Diesters

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Abstract □ Eight thiocarbohydrazide-1,5-dicarboxylic acid diesters were prepared and found to be active against some pathogenic microorganisms.

Keyphrases □ Thiocarbohydrazide-1,5-dicarboxylic acid diesters—synthesis, evaluation of antimicrobial activity □ Antimicrobial activity—eight thiocarbohydrazide-1,5-dicarboxylic acid diesters

Recently the synthesis and antiviral and antibacterial activities of *N*-thiadiazolylcarbamic acid esters (1, 2) were reported. In the present work, a series of thiocarbohydrazide-1,5-dicarboxylic acid diesters was syn-

Table I—Thiocarbohydrazide-1,5-dicarboxylic Acid Diesters ROOCNHNHCSNHNHCOOR

Compound	R	Melting Point	Yield, %	Formula[a]	Analysis, % Calc.	Found
1	CH_3	170°	67	$C_5H_{10}N_4O_4S$	C 27.02	27.10
					H 4.50	4.55
2	C_2H_5	150°	73	$C_7H_{14}N_4O_4S$	C 33.60	33.65
					H 5.60	5.51
3	iso-C_3H_7	150°	71	$C_9H_{18}N_4O_4S$	C 38.84	38.72
					H 6.47	6.52
4	*n*-C_4H_9	90°	65	$C_{11}H_{22}N_4O_4S$	C 43.13	43.08
					H 7.18	7.23
5	iso-C_4H_9	90°	72	$C_{11}H_{22}N_4O_4S$	C 43.13	43.16
					H 7.18	7.12
6	$CH_2CH{=}CH_2$	120°	57	$C_9H_{14}N_4O_4S$	C 39.41	39.36
					H 5.10	5.08
7	$C_6H_5CH_2$	160°	53	$C_{17}H_{18}N_4O_4S$	C 55.54	55.50
					H 4.81	4.90
8	C_6H_5	210°	80	$C_{15}H_{14}N_4O_4S$	C 52.02	51.89
					H 4.04	4.10

[a] All compounds were subjected to IR, NMR, and mass spectroscopy and the results were as expected.

Table II—Antimicrobial Activity

Compound	Concentration, mcg./ml.	Zones of Inhibition, Average Size, mm. E.c.[a]	P.v.	K.p.	B.s.	B.a.	S.a.	St.a.	Ps.a.
1	5000	50	45	50	48	42	33	38	45
	500	36	17	28	18	22	—	18	17
2	5000	20	20	—	20	22	—	—	—
	500	—	—	—	—	—	—	—	—
3	5000	34	34	47	36	36	35	25	43
	500	—	23	26	28	25	20	—	23
6	5000	22	—	22	25	28	35	22	—
	500	—	—	—	—	—	16	—	—
7	5000	—	—	—	36	40	38	32	—
	500	—	—	—	16	16	18	—	—

[a] E.c. = *E. coli*, P.v. = *P. vulgaris*, K.p. = *K. pneumoniae*, B.s. = *B. subtilis*, B.a. = *B. anthracis*, S.a. = *S. aureus*, St.a. = *S. albus*, and Ps.a. = *P. aeruginosa*. Microbial cultures were obtained from Pahlavi Medical Center of Tehran University.

thesized by interaction of the appropriate chloroformic ester and thiocarbohydrazide. The physical data of the compounds prepared are reported in Table I.

EXPERIMENTAL[1]

Antimicrobial Activity—All compounds were tested against *Escherichia coli*, TUHP12; *Proteus vulgaris*, TUF21; *Pseudomonas aeruginosa*, TUF41; *Klebsiella pneumoniae*, TUHP35; *Bacillus anthracis*, TU25; *Bacillus subtilis*, W; *Staphylococcus aureus*, TU200; and *Staphylococcus albus*, TUMA201.

Aqueous solutions of 5000 mcg./ml. of each compound were prepared and filtered through a seitz filter. Dilutions were made with sterile, distilled water to obtain 500 and 50 mcg./ml. Nutrient agar was used as a culture medium. There were six replicates for each dilution.

Caves of 14 mm. were removed from the center of each plate, and 0.4 ml. of each solution was placed in the well. After incubation at 37 ± 0.5° for 58 hr., the inhibition zone was measured. Compounds 4, 5, and 8 were found to be inactive on all microorganisms tested. All other compounds were also inactive at concentrations of 50 mcg./ml.

[1] Melting points were taken on a Kofler hot-stage microscope and are uncorrected. The IR spectra were determined with a Leitz model III spectrograph. NMR spectra were obtained on a Varian A60A instrument. The mass spectra were recorded on a Varian Mat 111 instrument.

The antimicrobial activity of the compounds are reported in Table II.

Thiocarbohydrazide-1,5-dicarboxylic Acid Di-*n*-butyl Ester—Powdered thiocarbohydrazide and twice its weight of chloroformic acid *n*-butyl ester were mixed and allowed to stand at 50° for 2.5 hr. The pasty reaction mixture was then mixed with 10 parts of hot distilled water. The excess of chloroformic ester was decomposed, and the diester was dissolved. On cooling, white crystals were separated and recrystallized from water. The IR (KBr) spectrum revealed bands characteristic of the N—H groups in the regions 3260 and 1205 $cm.^{-1}$ and the C=O groups at 1700 and 1760 $cm.^{-1}$. NMR ($CDCl_3$): 1.12 (t, 6, $2CH_3$), 1.7 (m, 8, $4CH_2$), 4.3 (t, 4, $2CH_2$), 7.87 (bs, 2, 2NH), and 8.8 (bs, 2, 2NH). Mass *m/e* 306.

The other compounds were prepared similarly.

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