Synthesis and Antibacterial Activity of 5-Nitro-2-furfurylidene *p*-Sulfonyl- and *p*-Sulfamoylbenzoylhydrazides VII

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Abstract □ Thirteen 5-nitro-2-furfurylidene *p*-sulfonyl- and *p*-sulfamoylbenzoylhydrazides were synthesized. All compounds prepared were tested against 10 Gram-positive and Gram-negative bacteria and exhibited antibacterial activity.

Keyphrases □ 5-Nitro-2-furfurylidene *p*-sulfonyl- and *p*-sulfamoylbenzoylhydrazides—synthesis, antibacterial activity □ Antibacterial activity—evaluation of 13 5-nitro-2-furfurylidene *p*-sulfonyl- and *p*-sulfamoylbenzoylhydrazides

In continuation of studies on the preparation of new 5-nitro-2-furfurylidene derivatives (1) and on the synthesis and pharmacological activity of compounds related to alkylsulfonyl-, arylsulfonyl-, and sulfamoylbenzoylhydrazides(2–5), a series of 5-nitro-2-furfurylidene benzoylhydrazides having sulfonyl or sulfamoyl groups in the *para*-position was synthesized. *p*-Sulfonyl- and *p*-sulfamoylbenzoylhydrazides were prepared by interaction of hydrazine hydrate and an appropriate ethyl ester (3, 4). The new benzoylhydrazides prepared are summarized in Table I.

Benzoylhydrazides were allowed to react with 5-nitro-2-furaldehyde to give the 5-nitro-2-furfurylidene derivatives (Scheme I). The 5-nitro-2-furfuryli-

Table I—*p*-Sulfamoylbenzoylhydrazides $p\text{-RNHSO}_2\text{C}_6\text{H}_4\text{—CONHNH}_2$

R	Melting Point	Yield, %	Formula	Analysis, % Calc.	Found
CH_3	143°	65	$C_8H_{11}N_3O_3S$	C 41.92 H 4.80	41.88 4.71
C_2H_5	150–152°	50	$C_9H_{13}N_3O_3S$	C 44.44 H 5.34	44.54 5.28
$(CH_3)_2CH$	168–169°	80	$C_{10}H_{15}N_3O_3S$	C 46.69 H 5.83	46.73 5.81
C_6H_5	220–222°	57	$C_{13}H_{13}N_3O_3S$	C 53.60 H 4.46	53.66 4.52

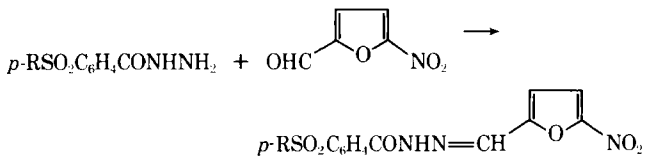
Table II—5-Nitro-2-furfurylidene *p*-Sulfonyl- and *p*-Sulfamoylbenzoylhydrazides $p\text{-RSO}_2\text{C}_6\text{H}_4\text{—CONHN=CH}$ (furan ring) NO_2

Compound	R	Melting Point	Yield, %	Formula	Analysis, % Calc.	Found
1	CH_3	265°	82	$C_{13}H_{11}N_3O_6S$	C 46.29 H 3.26	46.25 3.26
2	C_2H_5	240°	85	$C_{14}H_{13}N_3O_6S$	C 47.86 H 3.70	48.02 3.75
3	C_6H_5	237°	92	$C_{18}H_{13}N_3O_6S$	C 54.13 H 3.25	54.14 3.33
4	$p\text{-FC}_6H_4$	238–243°	90	$C_{18}H_{12}FN_3O_6S$	C 51.79 H 2.87	51.82 2.77
5	NH_2	285°	83	$C_{12}H_{10}N_4O_6S$	C 42.60 H 2.95	42.61 3.09
6	CH_3NH	297°	79	$C_{13}H_{12}N_4O_6S$	C 44.31 H 3.40	44.30 3.44
7	C_2H_5NH	258°	81	$C_{14}H_{14}N_4O_6S$	C 45.90 H 3.82	45.99 3.82
8	$(CH_3)_2CHNH$	254–259°	77	$C_{15}H_{16}N_4O_6S$	C 47.36 H 4.21	47.40 4.40
9	C_6H_5NH	275°	75	$C_{18}H_{14}N_4O_6S$	C 52.17 H 3.38	52.17 3.44
10	$(CH_3)_2N$	227°	89	$C_{14}H_{14}N_4O_6S$	C 45.90 H 3.82	45.80 3.70
11	$(C_2H_5)_2N$	243°	93	$C_{16}H_{18}N_4O_6S$	C 48.73 H 4.56	48.69 4.51
12	$(C_3H_7)_2N$	210°	89	$C_{18}H_{22}N_4O_6S$	C 51.18 H 5.21	51.18 5.23
13	$(CH_2)_5N$	250°	79	$C_{17}H_{18}N_4O_6S$	C 48.98 H 4.54	49.11 4.50

Table III—Antibacterial Activity

Compound	Zone of Inhibition, Average Size, mm					
	Staph. aureus	*Staph. albus*	*K. pneumoniae*	*S. fecalis*	*B. cereus*	*B. subtilis*
1	—	9.9	—	—	—	12.4
2	13	13.8	—	—	—	13
3	11	12	10.1	—	—	12
4	9.11	9.9	—	—	10.8	11.5
5	—	—	—	—	—	—
6	10.6	—	—	—	—	—
7	11.2	10.3	—	—	—	10.7
8	11.1	11.3	11.1[a]	—	—	10.7
9	10.8	11.8	—	—	11	11.4
10	9.5	11.3	—	—	—	11.3
11	13.3[a]	12.3	—	—	11.8[a]	14.3
12	—	11.9	—	—	—	10.4
13	11.2	13.9	—	—	11.8	13.8
Furazolidone	23.3	22.7	20.2	13.1	23.4	25.5

[a] Hazy zones.



1: R = CH_3 5: R = NH_2 9: R = NHC_6H_5
2: R = C_2H_5 6: R = $NHCH_3$ 10: R = $N(CH_3)_2$
3: R = C_6H_5 7: R = NHC_2H_5 11: R = $N(C_2H_5)_2$
4: R = p-FC_6H_4 8: R = $NHCH(CH_3)_2$ 12: R = $N(C_3H_7)_2$
13: R = $N(CH_2)_5$

Scheme I

dene *p*-sulfonyl and *p*-sulfamoyl derivatives are summarized in Table II.

PHARMACOLOGY

The compounds listed in Table II were tested against 10 Gram-positive and Gram-negative bacteria. Furazolidone was used as a control. The compounds were dissolved in acetone and diluted with water or phosphate buffer (pH 8) to a final concentration of 250 μg/ml. The solvent mixture was acetone–water (0.5:1.5) for Compounds 1, 11, and 17; acetone–buffer (1:1) for Compounds 5 and 6; and acetone–water (1:1) for all other compounds. Paper disks of 9-mm diameter were immersed in the solutions and put on the inoculated surface of penicillin assay seed agar.

All compounds and furazolidone were inactive against *Bordetella bronchiseptica* (ATCC 4617), *Sarcina lutea* (ATCC 341a), and *Proteus vulgaris*[1]. None of the compounds prepared showed significant activity against *Escherichia coli* (0128) at the test concentration. The antibacterial activities of other compounds against *Staphylococcus aureus* (ATCC 6538-P), *Staphylococcus albus* (ATCC 12228), *Klebsiella pneumoniae* (ATCC 10031), *Streptococcus faecalis* (ATCC 8043), *Bacillus cereus* (ATCC 1178), and *Bacillus subtilis* (NCTC 3610) are reported in Table III.

[1] Obtained from S. S. Pfizer Laboratories, Tehran, Iran.

EXPERIMENTAL[2,3]

***para*-Substituted Benzoylhydrazides**—A *para*-substituted benzoyl ethyl ester (0.02 mole) was dissolved in 25 ml of ethanol, and then 0.025 mole of 99% hydrazine hydrate was added to the hot solution. After refluxing the reaction mixture for 1 hr, the solvent was distilled off and the residue was crystallized from aqueous ethanol (Table I).

5-Nitro-2-furfurylidene *p*-Sulfonyl- and *p*-Sulfamoylbenzoylhydrazides—To a hot solution of 0.01 mole of the appropriate benzoylhydrazide in 25 ml of alcohol, a solution of 0.01 mole of 5-nitro-2-furaldehyde in 5 ml of alcohol was added. After standing for 3 hr at room temperature, the crystalline mass was filtered and recrystallized from alcohol (Table II).

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[2] Melting points were taken on a Kofler hot stage microscope and are uncorrected. The IR spectra were recorded using a Leitz spectrograph. NMR spectra were obtained with a Varian A-60A instrument. The mass spectra were recorded on a Varian Mat 111 spectrograph.

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