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Xiaorong Li
Shaanxi Teachers University

Zoumin Sun
Shaanxi Teachers University

James C. Chang
University of Northern Iowa

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Synthesis and Antibacterial Studies of Some 2-Furanthiocarboxyhydrazones

XIAORONG LI[1], ZUOMIN SUN[1] and JAMES C. CHANG[2]

[1]Department of Chemistry, Shaanxi Teachers University, Xian, Shaanxi, People's Republic of China

[2]Department of Chemistry, University of Northern Iowa, Cedar Falls, Iowa 50614

Seven 2-furanthiocarboxyhydrazones were prepared, 5-nitro-furaldehyde-2-furanthiocarboxyhydrazone from the reaction of 2-furanthiocarboxyhydrazide with 5-nitro-2-furaldiacetate and the others from the condensation of 2-furanthiocarboxyhydrazide with aldehydes: 2-furaldehyde, benzaldehyde, *p*-hydroxybenzaldehyde, *o*-methoxybenzaldehyde, *o*-vanillin, and salicylaldehyde. The seven 2-furanthiocarboxyhydrazones were tested for their antibacterial activities against *Staphylococus aureus* and *Bacillus subtilis*. 5-Nitro-2-furaldehyde-2-furanthiocarboxyhydrazone was found to display the strongest bacterotoxicity.

INDEX DESCRIPTORS: 2-Furanthiocarboxyhydrazones, antibacterial studies

Thiosemicarbazones have been found to exhibit remarkable antitumor,[1] antiviral,[2] and antimalarial[3] activities. Since thiosemicarbazones and thioacylhydrazones have similar structures, both having the $-\overset{|}{N}-\overset{||}{C}=S$ group, it is reasonable to expect that the latter will also have biological activities. The only work on 2-furanthiocarboxyhydrazones reported in the literature are the syntheses of 2-furaldehyde-2-furanthiocarboxyhydrazone,[4] *p*-acetamidobenzaldehyde-2-furanthiocarboxyhydrazone,[4] and salicylaldehyde-2-furanthiocarboxyhydrazone.[5] Now we report the synthesis of five new aldehyde-2-furanthiocarboxyhydrazones and a study of their antibacterial activities.

EXPERIMENTAL

All chemicals used in this work were analytical reagent grade or of equivalent quality.

2-Furanthiocarboxyhydrazine and 2-furaldehyde-2-furanthiocarboxyhydrazone were prepared as described by Jensen and Pedersen.[4] Salicylaldehyde-2-furanthiocarboxyhydrazone was prepared by the method of Singh *et al.*[5] 5-nitro-2-furaldiacetate was prepared by the method of Wang *et al.*[6]

5-nitrofuraldehyde-2-furanthiocarboxyhydrazone was prepared by condensing 5-nitro-2-furaldiacetate with 2-furanthiocarboxyhydrazine in the presence of sulfuric acid. To 15 mL of 73% H_2SO_4 was added 1.0 g of 5-nitro-2-furaldiacetate. The solution was heated to boiling for 5 minutes, and 0.5 g of 2-furanthiocarboxyhydrazine was added. The mixture was heated with stirring for an additional 20 minutes. The product appeared as yellow precipitate and was suction-filtered, washed with water and ethanol, and dried *in vacuo*. The yield was 97%. It is insoluble in water, soluble in acetone, and slightly soluble in methanol and ethanol.

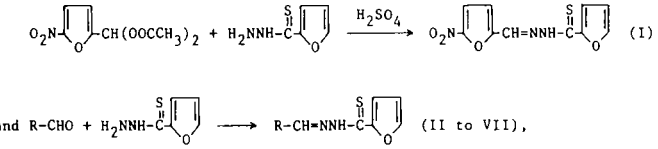
All other 2-furanthiocarboxyhydrazones were prepared by condensing the appropriate aldehyde with 2-furanthiocarboxyhydrazine in ethanol. In a typical preparation, 0.68 g (5 mmol) of *o*-methoxybenzaldehyde and 0.71 g (5 mmol) of 2-furanthiocarboxyhydrazine were added to 5mL of ethanol. The mixture was stirred at 50°C for 1 hour and left overnight at room temperature. Then water was added dropwise to the ethanol mixture to precipitate the yellow product. The product was filtered, washed with ethanol, and recrystallized from 50% ethanol. The yields are given in Table 1. These compounds are all soluble in methanol and ethanol.

Carbon, hydrogen, and nitrogen were determined by microanalyses. IR spectra were measured, as KBr pellets, by a Perkin-Elmer Model 983 spectrophotometer. UV spectra were measured by a UV-260 spectrophotometer, using ethanol as the solvent.

The antibacterial activities of the 2-furanthiocarboxyhydrazones were evaluated against *Staphyloccocus aureus* and *Bacillus subtilis* by the agar plate technique,[7] using fine suspensions of the compounds in water at concentrations of 128, 64, 32, 16, 8, 4, 2, and 1 μg mL^{-1}. The culture medium was MPA, and furalcilinum was used as a control. After incubation at 32 ± 1°C for 24 hours, the plates were examined and the minimum inhibitory concentration (MIC) of each compound was recorded. Each assay was done in triplicate.

RESULTS AND DISCUSSION

The formation of the 2-furanthiocarboxyhydrazones followed the reactions below:



where R = 2-furyl (II), *p*-hydroxyphenyl (III), *o*-methoxyphenyl (IV), phenyl (V), 2-hydroxy-3-methoxyphenyl (VI), and *o*-hydroxyphenyl (VII).

The analytical results, melting points, and the percentage yields of the five new 2-furanthiocarboxyhydrazones are given in Table 1. All the compounds exhibit IR bands at 3136-3278 cm^{-1}, 1599-1620 cm^{-1}, and 600-710 cm^{-1}, attributed to the N-H,[8] C=N,[9] and C=S[10] vibrations, respectively. All the compounds prepared showed a maximum near 320 nm in their UV spectra. This may be attributed to the π-π* transition originated from the $-C=S$ group.[5] The similarities in the IR and UV spectra of these compounds indicated that they all have similar structure.

In Table 2 are listed the minimum inhibitory concentrations of the seven compounds studied, as compared to the control, furalcilinum (VIII). It can be seen that 5-nitro-2-furaldehyde-2-furanthiocarboxyhydrazone has strong inhibitory ability to the two bacteria tested. Among the substituted benzaldehyde-2-furanthiocarboxyhydrazones, the inhibitory abilities decreases in the following sequence, in terms of the substituents:

o-methoxy = unsubstituted > *o*-hydroxy > 2-hydroxy-3-methoxy > *p*-hydroxy.

This sequence shows that a hydroxy group on the benzene ring decreases the antibacterial activity. This may be explained by the reduced polarity of the compound without the hydroxy group, increasing the hydrophobic character of the compounds. The increased hydrophobic nature will favor the permeation of the com-

Table 1. Analytical Results of New 2-Furanthiocarboxyhydrazones

No.	R	Analyses, Found (Calcd.) C	H	N	m.p., °C	Percentage Yield
I	5-nitro-2-furyl	45.00(45.28)	2.66(2.66)	15.49(15.84)	157-158	97%
III	*p*-hydroxyphenyl	58.80(58.52)	4.15(4.09)	11.26(11.37)	174-175	96%
IV	*o*-methoxyphenyl	60.50(59.98)	4.73(4.65)	10.89(10.76)	142-143	95%
V	phenyl	63.04(62.59)	4.35(4.38)	13.10(12.16)	99-100	74%
VI	2-hydroxy-3-methoxyphenyl	56.76(56.51)	4.34(4.38)	10.03(10.14)	164-165	98%

pounds through the lipoid layer of the bacteria membrane.[11]

Cu(II), Ni(II), and Zn(II) complexes of some of the 2-furanthiocarboxyhydrazones have been prepared and tested against several organisms.[12] It was found that, for example, Cu(II) complexes of *o*-methoxybenzaldehyde-2-furanthiocarboxyhydrazone and 5-nitro-2-furaldehyde-2-furanthiocarboxyhydrazone exhibit strong antibacterial activity. The 2-furanthiocarboxyhydrazones and their transition-metal complexes may also be antifungal, and further work in this respect is in progress.

Table 2. Minimum Inhibitory Concentration ($\mu g\ mL^{-1}$) of the 2-Furanthiocarboxyhydrazones

No.	R	*S. aureus*	*B. subtilis*
I	5-nitro-2-furyl	16	4
II	2-furyl	NI[a]	32
III	*p*-hydroxyphenyl	NI	NI
IV	*o*-methoxyphenyl	32	32
V	phenyl	32	32
VI	2-hydroxy-3-methoxyphenyl	NI	128
VII	*o*-hydroxyphenyl	128	64
Furalcilinum		16	4

[a]NI = no inhibition.

REFERENCES

[1] BROCKMAN, R.W., THOMSON, J.R., BELL, M.J., SKIPPER, H.E. 1956. *Cancer Res., 16,* 167.

[2] MINTON, S.A., OFFICER, J.E., THOMPSON, R.L. 1953. *J. Immunol., 70,* 222.

[3] KLAYMAN, D.L., BARTOSEVICH, J.E., GRIFFIN, T.S., MASON, C.J., SCOVILL, J.P. 1979. *J. Med. Chem.,* 22, 855.

[4] JENSEN, K.A., PEDERSEN, C. 1961. *Acta Chem. Scand., 15,* 1097.

[5] SINGH, N.K., AGRAWAL, S., AGGARWAL, R.C. 1985. *Synth. React. Inorg. Met.-Org. Chem. 15,* 75.

[6] WANG, H., SONG, S., SONG, D., YANG, Z. 1986. *Linchan Huaxue Yu Gongye, 6(2),* 29.

[7] DAI, Z. 1985. "Clinical Antimicrobial Materia Medica," People's Health Press, Beijing, PRC, p. 9.

[8] NAKANISHI, K., SOLOMON, P.H. 1977. "Infrared Absorption Spectroscopy," 2nd ed., Holden-Day, San Francisco, p. 33.

[9] KOVACIC, J.E. 1967. *Spectrochim. Acta, 23A,* 183.

[10] DESSEYN, H.O., AARTS, A.J., HERMAN, M.A. 1980. *Spectrochim. Acta, 36A,* 59.

[11] SINGH, H., YADAV, L.D.S., MISHRA, S.B.S. 1981. *J. Inorg. Nucl. Chem., 43,* 1701.

[12] LI, X., SUN, Z., CHANG, J.C. 1988. *Synth. React. Inorg. Met.-Org. Chem., 18,* 657.