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Spectrochimica Acta Part A 70 (2008) 641–645
SPECTROCHIMICA ACTA PART A
www.elsevier.com/locate/saa

Synthesis, characterization and antibacterial activity of new sulfonyl hydrazone derivatives and their nickel(II) complexes

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Received 6 June 2007; received in revised form 14 August 2007; accepted 18 August 2007

Abstract

Prophane sulfonic acid hydrazide (psh: $CH_3CH_2CH_2SO_2NHNH_2$) derivatives as salicylaldehydeprophanesulfonylhydrazone (salpsh), 5-methylsalicylaldehydeprophanesulfonylhydrazone (5-msalpsh), 2-hydroxyacetophenoneprophanesulfonylhydrazone (afpsh), 5-methyl-2-hydroxyacetophenoneprophanesulfonylhydrazone (5-mafpsh) and their Ni(II) complexes have been synthesized. The structure of these compounds has been investigated by using elemental analysis, FTIR, ^{1}H NMR, LC/MS, UV–vis spectrophotometric method, magnetic susceptibility and conductivity measurements. The complexes were found to have general compositions [NiL2]. Square-planer structures are proposed for the Ni(II) complexes on the basis of magnetic evidence, electronic spectra and TGA data. Bacterial activities of sulfonyl hydrazone compounds were studied against gram-positive bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus magaterium* and gram-negative bacteria: *Salmonella enteritidis*, *Escherichia coli* by using minimum inhibitory concentrations (MICs) method.

Keywords: Aroylsulfonylhydrazone; Ni(II) complexes; Sulfonamide derivatives; Antibacterial activity

1. Introduction

The chemistry of hydrazones has been intensively investigated in recent years, owing to their coordinating capability, pharmacological activity, antibacterial and antifungal properties [1]. Sulfonamide drugs are widely used chemotherapeutic agents with large spectrum of activity [2]. Methanesulfonamide residue has appeared as a suitable pharmacophoric equivalent to replace functional groups in drug design [3]. Methanesulfonamide derivatives possess DNA binding ability, show cytostatic effects, and some of them, like amsacrine, find application in cancer chemotherapy [4–7]. Having hydrophilic character, like the sulfonyl group is considered as a suitable pharmacophoric equivalent for replacing functional groups in drug design [8]. Transition metal complexes of hydrazides and sulfonamides also find application in chemotherapy [9] as well as their hyrazone derivatives. In previous paper, we reported the antibacterial and cytotoxic effect of methanesulfonic acid hydrazide, $CH_3SO_2NHNH_2$, (containing both a sulfonamide and a hydrazine fragment), and its hydrazone derivatives [10], as well as their transition metal carbonyl complexes [11–15] and also inhibition efficiency of some sulfonyl hydrazone on aluminium alloy [16].

In this work new prophane sulfonic acid hydrazide (psh: $CH_3CH_2CH_2SO_2NHNH_2$) and its derivatives as sulfonyl hydrazones and their Ni(II) complexes have been synthesized. The structure of psh will be submitted in sulfonic acid hydrazide series at further studies. The structures of all these compounds have been investigated by using elemental analysis, FTIR, ^{1}H NMR, LC/MS, UV–vis spectrophotometric method, magnetic susceptibility, TGA/DTA methods and conductivity measurements. Antibacterial activities were determined as MICs values using the microdilution broth method against to gram-positive bacteria: *Staphylococcus aureus* ATCC 25923, *Bacillus subtilis* RSKK 244, *Bacillus magaterium* RSKK 5117 and gram-negative bacteria: *Salmonella enteritidis* ATCC 13076, *Escherichia coli* ATCC 11230. The biological activity of these ligands and their metal chelates are reported in Table 4.

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doi:10.1016/j.saa.2007.08.012

2. Experimental

2.1. Physical measurements

Elemental analyses were performed according to standard microanalytical procedures (TÜBİTAK Laboratories, Ankara). ^{1}H NMR and ^{13}C NMR spectra of dimethylsulfoxide-d_6 (DMSO-d_6) solutions of the compounds were registered on a Bruker WM-400 spectrometer (400 MHz) using tetramethylsilane as internal standard. D_2O-exchange was applied to confirm the assignment of the NH- and OH-signals. The infrared spectra of the compounds as KBr-disks were recorded in the range of 4000–400 cm^{-1} with a Mattson 1000 FT spectrometer. Melting points of hydrazone derivative were determined with a Gallenkamp melting point apparatus. The solvents used were purified and distilled according to routine procedures [17]. Prophane sulfonyl chloride, hydrazine hydrate, salicylaldehyde, 5methylsalicylaldehyde, 2-hydroxyacetophenone, 5-methyl-2-hydroxyaceto phenone and anhydrous nickel chloride were commercial products (purum). Minimum inhibitory concentrations (MICs) method was used to determine the antibacterial activity of compounds against the bacteria: *E. coli* ATCC 11230, *B. subtilis* RSKK 244, *B. magaterium* RSKK 5117, *S. enteritidis* ATCC 13076, *S. aureus* ATCC 25923.

2.2. Synthesis of sulfonyl hydrazones

The procedure of preparation of hydrazone derivatives 1–4 is similar to that applied by us [10] Thus, solution of 1.10 g (10 mmol) Prophane sulfonic acid hydrazide in 5 mL of ethanol was mixed with hot solution of 12 mmol of the corresponding carbonyl compound (salicylaldehyde, 5-methylsalicylaldehyde, 2-hydroxyacetophenone, 5-methyl-2-hydroxyacetophenone, respectively) in 10 mL of ethanol and stirred for 1 h. Upon cooling, the obtained crystalline precipitates were filtered, washed with ethanol-ether, recrystallized from water and dried in vacuo over P_2O_5. They are colourless and light yellow crystalline solids, stable at normal conditions and soluble in methanol, ethanol, acetonitrile, dimethylformamide, DMSO; poorly soluble in benzene and water.

2.3. Synthesis of Ni(II) complexes

All complexes are prepared by the following general method. A sample of anhydrous $NiCl_2$ (0.07 g, 0.53 mmol) was dissolved in a mixture of methanol and acetonitrile (25 mL), and solution of hydrazone derivatives (0.20 g, 1.60 mmol) in a mixture of acetonitrile (25 mL) and NaOH solution in methanol (0.06 g, 1.60 mmol) was added. The reaction mixture was heated at 40 °C for 30 min and left in ice bath for 3 h. The greenly solid complexes formed were collected by filtration, washed with a small volume of methanol and ether, and then, dried in a desiccator over $CaCl_2$.

2.4. Procedure for antibacterial activity

The in vitro antibacterial activity of the free ligands and their complexes were tested against the gram-positive bacteria: *S. aureus* ATCC 25923, *B. subtilis* RSKK 244, *B. magaterium* RSKK 5117 and gram-negative bacteria, *S. enteritidis* ATCC 13076, *E. coli* ATCC 11230. Minimum inhibitory concentrations (MICs) were determined by the microdilution broth method following the procedures recommended by the National Committee for Clinical Laboratory Standards [18,19]. MICs were defined as the lowest concentrations of compounds which inhibit the growth of microorganisms. All tests were performed in Nutrient Broth (NB) solved in DMSO which lacked antibacterial activity against any of the test bacteria. The microplates were incubated at 37 °C and read visually after 24 h for MIC's [20]. The results were recorded according to the presence and absence of growth. The MIC values of the sulfonyl hydrazone compounds are presented in Table 4.

3. Results and discussion

Analytical data and some physical properties of the sulfonyl hydrazones derivatives and their Ni^{2+} complexes are listed in Table 1.

3.1. Characterization of ligands

The main vibration frequencies and chemical shifts of sulfonyl hydrazones are listed in Tables 2 and 3. Bands in the region of 3140–3218 cm^{-1} may be due to ν_{NH} modes, respectively. The former stretching vibrations indicate the formation of sulfonyl hydrazones. The –CH=N– stretching modes in the spectra of all ligands are observed in the range of 1618–1628 cm^{-1}. Salpsh and 5-msalpsh show signals at 8.22–8.25 ppm which are attributed to the imine protons

Table 1
Analytical and physical data for sulfonyl hydrazone derivatives and their nickel(II) complexes

Compound	Empirical formula (formula weight)	Colour	mp (°C)	Yield (%)	Found (calculated)			
					%C	%H	%N	%S
Salpsh	$C_{10}H_{14}N_2SO_3$ (242.28)	White	80–81	50	49.35 (49.57)	5.65 (5.82)	11.78 (11.56)	12.86 (13.23)
5m-salpsh	$C_{11}H_{16}N_2SO_3$ (256.31)	White	117–118	60	52.12 (51.54)	5.96 (6.29)	10.68 (10.93)	11.90 (12.51)
Afpsh	$C_{11}H_{16}N_2SO_3$ (256.31)	White	115–116	50	51.32 (51.54)	5.95 (6.29)	10.14 (10.93)	12.35 (12.51)
5-mafpsh	$C_{12}H_{18}N_2SO_3$ (270.33)	White	92–95	55	52.93 (53.31)	6.50 (6.71)	10.28 (10.36)	11.52 (11.86)
Ni(salpsh)$_2$	$C_{20}H_{26}N_4S_2O_6Ni$ (541.01)	Green	>205	40	43.86 (44.39)	4.80 (4.80)	10.04 (10.35)	11.46 (11.85)
Ni(5-msalpsh)$_2$	$C_{22}H_{30}N_4S_2O_6Ni$ (569.03)	Green	>210	45	46.38 (46.43)	5.24 (5.27)	9.75 (9.84)	11.12 (11.26)
Ni(afpsh)$_2$	$C_{22}H_{30}N_4S_2O_6Ni$ (569.03)	Green	>200	38	45.78 (46.43)	5.17 (5.27)	9.78 (9.84)	11.05 (11.26)
Ni(5-mafpsh)$_2$	$C_{24}H_{34}N_4S_2O_6Ni$ (597.05)	Green	>155	49	48.05 (48.27)	5.33 (5.69)	9.30 (9.38)	10.70 (10.73)