Journal of Organometallic Chemistry 794 (2015) 223–230

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Diorganotin(IV) complexes with 2-furancarboxylic acid hydrazone derivative of benzoylacetone: Synthesis, X-ray structure, antibacterial activity, DNA cleavage and molecular docking

Tahereh Sedaghat [a, *], Yahya Ebrahimi [a], Lucia Carlucci [b], Davide M. Proserpio [b, c], Valiollah Nobakht [a], Hossein Motamedi [d], Mohammad Reza Dayer [d]

[a] Department of Chemistry, College of Sciences, Shahid Chamran University, Ahvaz, Iran
[b] Dipartimento di Chimica, Università degli Studi di Milano, Via C. Golgi 19, 20133 Milano, Italy
[c] Samara Center for Theoretical Materials Science (SCTMS) Samara State University, Samara 443011, Russia
[d] Department of Biology, College of Sciences, Shahid Chamran University, Ahvaz, Iran

ARTICLE INFO

Article history:
Received 1 March 2015
Received in revised form
26 June 2015
Accepted 29 June 2015
Available online 4 July 2015

Keywords:
Organotin(IV)
Hydrazone
Diketone
Antibacterial activity
DNA cleavage
Molecular docking

ABSTRACT

Two new diorganotin(IV) complexes, Me_2SnL and Ph_2SnL, have been synthesized from the reaction of Me_2SnCl_2 and Ph_2SnCl_2 with the hydrazone H_2L [H_2L = (Furan-2-yl) (5-hydroxy-3-methyl-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-methanone] derived from furan-2-carbohydrazide and benzoylacetone. The new compounds have been characterized by elemental and spectroscopic analyses. The crystal structures of the monohydrate form of the ligand and of the Me_2SnL derivative have been also determined by X-ray crystallography. Experimental evidences confirm the existence of the hydrazone ligand exclusively in cyclic form in both solution and solid state. On coordination to tin the hydrazone undergoes a ring opening reaction and a doubly deprotonation to act as a tridentate ligand via imine nitrogen and enolic oxygens. The tin atom in the complexes is five coordinate with geometry between square-pyramidal and trigonal-bipyramidal. The *in vitro* antibacterial activity of ligand and its complexes has been evaluated against Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria. The interaction between compounds with bacterial DNA was also studied by molecular docking. Our findings indicate that diphenyltin(IV) complex, by binding to DNA via minor groove to TATA sequence in genes upstream, has good activities along with the standard antibacterial drugs. Our agarose-gel electrophoresis experiments show that the ligand exert DNA cleavage, while Me_2SnL and Ph_2SnL did not.

1. Introduction

1,3-Diketones constitute an important class of compounds, which is used in organic chemistry for the synthesis of heterocycles [1,2] and in coordination chemistry as ligand [3]. Moreover, Imines (Schiff bases) can be obtained from condensation of these dicarbonyl compounds and primary amines. The derived Schiff bases have keto-enol tautomerism with strong intramolecular hydrogen bonds (N–H…O or N…H–O). They are of biological interest, play as synthetic intermediates in organic reactions and act as sensor materials [4–6]. These compounds can also be used as coordination ligands for transition and non-transition metals; however, less attention has been paid to this type of systems. Recently we have reported synthesis, structural and theoretical studies and antibacterial activities of several Schiff bases derived from condensation of β-diketones with aminophenol derivatives and their complexes with transition metals and organotins [7–12]. In continuation of our earlier work, we are herein reporting a hydrazonic derivative of a 1,3-diketone and its organotin(IV) complexes. Hydrazone-based Schiff base ligands, and their metal complexes have received much attention because of their potential pharmacological applications [13,14]. Facile keto-enol tautomerization and the availability of several potential donor sites in these ligands allows and encourages chemists to construct complexes with large structural varieties [15]. Along this line, organotin(IV) complexes of hydrazones have received considerable attention for both structural and

* Corresponding author.
E-mail address: tsedaghat@scu.ac.ir (T. Sedaghat).

http://dx.doi.org/10.1016/j.jorganchem.2015.06.034
0022-328X/

biological importance: many of these compounds may interact with biological systems in different ways as bactericides, fungicides, acaricides and industrial biocides [16–21]. Recently these compounds have been used in new contexts as in cancer chemotherapy [22,23]. In view of a few reports on organotin(IV) complexes of hydrazones derived from 1,3-diketones [24–28], it was considered worthwhile to investigate the synthesis, structural aspects and biological properties of hydrazonic derivatives of 1,3-diketones and their organotin complexes. In the present paper, 2-furancarboxylic acid hydrazone derivative of benzoyl acetone and its dimethyl- and diphenyltin complexes have been synthesized. The solution and solid state structures as well as biological properties of ligand and complexes are reported. In order to elucidate the interaction mechanisms for these compounds, we performed *In Silico* experiments using molecular dynamic and docking.

2. Experimental

2.1. Materials and methods

All starting materials were purchased from Merck while diphenyltin dichloride was supplied from Acros Company and were all used as received. All solvents were of reagent grade and used without further purification. IR spectra were obtained using a FT BOMEM MB102 spectrophotometer. The ^{1}H, ^{13}C and ^{119}Sn NMR spectra were recorded with Bruker Avance Ultrashield spectrometers using TMS and $SnMe_4$ as references, respectively.

2.2. Synthesis of the ligand (*1*)

A solution of furan-2-carbohydrazide (0.630 g, 5 mmol) and benzoylacetone (0.81 g, 5 mmol) in ethanol (30 mL) was refluxed for 4 h. Cubic white single crystals were obtained after standing the solution for 3 days at room temperature (**1a**). Yield: 1.152 g (80%), m.p. 128–132 °C; Anal. Calcd. For $C_{15}H_{14}N_2O_3$: C, 62.49; H, 5.59; N, 9.71; Found: C, 62.22; H, 5.61; N, 9.83; FT-IR (KBr, cm^{-1}): ν(OH), 3396; ν(C=O), 1640; ν (C=N), 1626; ν(CH_2), 1434; ν(C–O), 1318; ν(OH), 1163; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.16 (s, 3H, H_9), 3.00 (d, 1H, H_7, $^{2}J_{HH}$ = 18.7 Hz), 3.34 (d, 1H, H_7, $^{2}_{HH}J$ = 18.7 Hz), 5.30 (s, 1H, OH), 6.57 (m, 1H, H_2), 7.30 (d, 1H, H_3, $^{3}J_{HH}$ = 4.0 Hz), 7.32–7.46 (m, 4H, H_1, 3ArH), 7.62 (m, 2H, 2ArH) (See Fig. 3 for numbering). Synthesis of **1** in methanol gives the hydrated form of this compound as bright yellow crystals suitable for X-ray crystallography (**1b**).

2.3. Synthesis of Me_2SnL (*2*)

H_2L (0.067 g, 0.25 mmol) was dissolved in ethanol (5 mL) and triethylamine (0.5 mmol) was added. This solution was stirred for 30 min and then $SnMe_2Cl_2$ (0.055 g, 0.25 mmol) in ethanol (5 mL) was added. The mixture was refluxed for 2 h. The yellow-orange crystals suitable for X-ray crystallography were obtained after standing the solution for 2 days at room temperature.

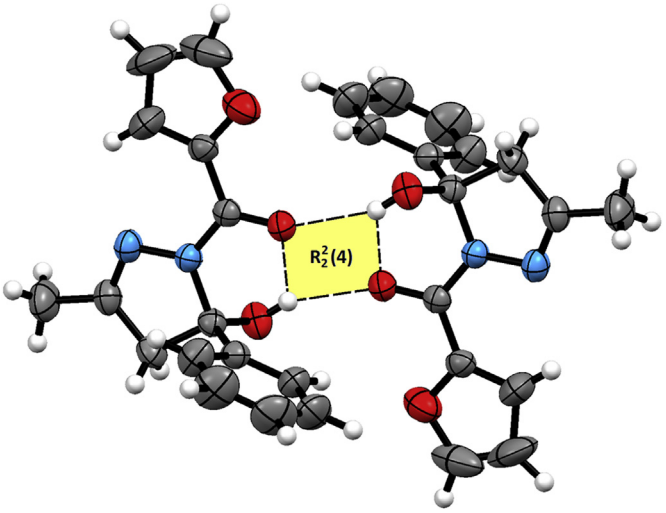

Fig. 2. An ORTEP view with a representation of intra- and intermolecular hydrogen bonds and formation of $R_2^2(4)$ ring in **1a.**

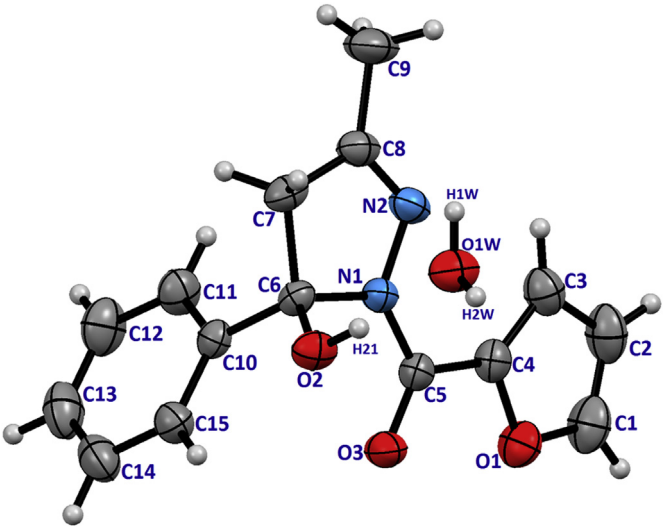

Fig. 3. An ORTEP view with the atomic numbering scheme for **1b.**

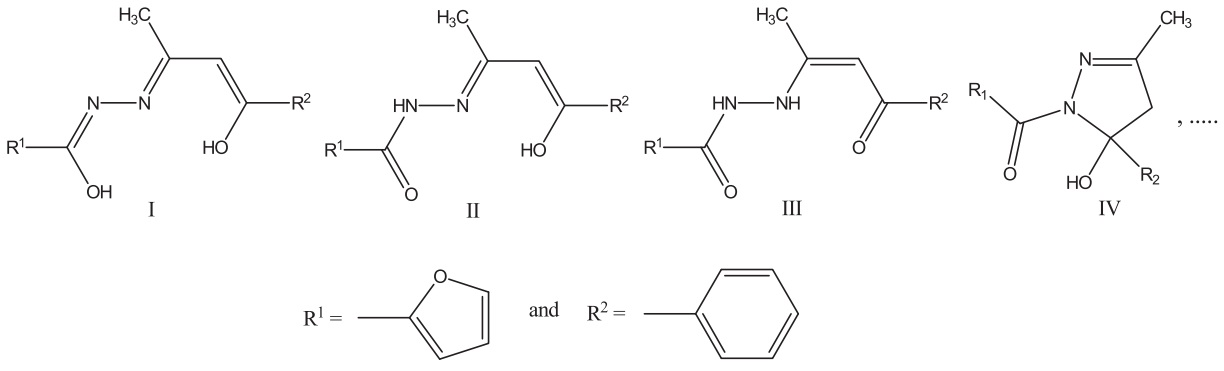

Fig. 1. Tautomeric forms for **1.**