Synthesis, Characterization and Antimicrobial Activities of Organosilicon(IV) Complexes

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Received: 4 March 2018;

Accepted: 21 April 2018;

Published online: 30 June 2018;

AJC-18979

The new organosilicon(IV) complexes of vanillin and thiophene-2-carboxylic acid hydrazide were synthesized and characterized by elemental analyses, molar conductance, infrared and NMR (¹H, ¹³C and ²⁹Si) spectral analyses. The synthesized compounds were screened for antimicrobial activity against Gram-positive bacteria viz. *K. pneumoniae* and *S. aureus*, Gram-negative bacteria viz. *E. coli* and *E. aerogenes*, fungi viz. *A. niger* and *C. albicans*. The study revealed that some of compounds were found to be more active than the standard drugs used in the assay and further increase in antimicrobial activity was observed on coordination with silicon atoms as compared to their respective free ligands.

Keywords: Vanillin, Hydrazide, Organosilicon complexes, Antimicrobial activity.

INTRODUCTION

Due to various applications in chemical, industrial and medicinal fields [1-5], chemistry of organosilicon complexes have gained a major importance in daily life. Schiff bases have aggravated wide interest for their interesting biological and pharmacological activities like anticancer [6], antimalarial [7], anti-inflammatory [8], anti-HIV, antifertility [9], anticonvulsant [10] and antimicrobial activities [11]. Recently, many research papers have been published on Schiff bases as they contain different bonding site to coordinate with metal centers to form variety of the complexes. Hence, in the pursuit for biologically active antimicrobial agents, we targeted to synthesize the Schiff bases derived from vanillin and hydrazide and further the synthesis of their complexes with silicon metal. All the synthesized compounds were characterized with the help of conductance measurements, elemental analyses, IR, ¹H, ¹³C and ²⁹Si NMR spectroscopy. Further these were evaluated for antimicrobial activity to study their biological effect on different microbes.

EXPERIMENTAL

The chemicals procured from Aldrich were used as such without any further purification but the solvents used were purified according to the standard procedures. The IR spectra were recorded using Spectrum BX Series FT-IR spectrophotometer in the range 4000-400 cm⁻¹ as KBr pellets. The NMR (¹H, ¹³C, ²⁹Si) spectra were recorded on Bruker Avance II 400 MHz NMR spectrometer and the chemical shifts (δ)

are reported in part per million (ppm) relative to tetramethyl silane (TMS) as an internal standard in CDCl₃ and DMSO.

Synthesis of Schiff base ligands: Synthesis of ligands (HL₁-HL₃) were carried out in the following two steps:

(i) Synthesis of 4-benzyloxy-3-methoxy-benzaldehyde and 3-methoxy-4-(4-bromo/nitro-benzyloxy)-benzaldehyde (I): A mixture of hydroxy benzaldehyde (10 mmol), alkyl halide (benzyl bromide and *para* bromo/nitro benzyl bromide) 10 mmol and K₂CO₃ (20 mmol) were taken in 30 mL of DMF and the reaction mixture was stirred overnight. The progress of reaction was monitored through thin layer chromatography and the visualization was accomplished with UV light. The reaction mixture was then quenched with approx. 25 g of ice followed by the addition of 50 mL of water. The solid product obtained was filtered over the vacuum pump and dried.

(ii) Synthesis of Schiff base ligands (HL₁-HL₃): The Schiff base were synthesized by dissolving 4-benzyloxy-3-methoxy-benzaldehyde and 3-methoxy-4-(4-bromo/nitro-benzyloxy)-benzaldehyde (I) and thiophene-2-carboxylic acid hydrazide (II) in equimolar ratio in methanol (**Scheme-I**). The reaction mixture was refluxed for 3-4 h. The solid product so obtained was filtered and recrystallized from hot methanol.

Synthesis of complexes: The organosilicon(IV) complexes were prepared under dry nitrogen atmosphere. The weighed amount of Schiff base ligand (20 mmol) and sodium (20 mmol) was dissolved in dry methanol and refluxed the reaction mixture for 3 h. Further weighed amount of dichlorodiorganosilicon (20 mmol) was added slowly to the above reaction

mixture (**Scheme-II**). The final resulting mixture was refluxed for 6 h and salt (Et_3NHCl) formed during the course of reaction was removed by filtration. The target compound was obtained by the removal of the excess solvent under vacuum. The compound was washed several times with dry hexane and finally dried under reduced pressure. The entire series of organosilicon(IV) complexes with Schiff base ligands were synthesized by adopting the same procedure.

Test microorganism: Gram-positive bacteria (*viz.* *K. pneumoniae* [NCDC No. 138], *S. aureus* [MTCC No. 3160]) Gram-negative bacteria (*viz.* *E. coli* [MTCC No. 443], *E. aerogenes* [NCDC No. 106] and fungi (*viz.* *A. niger* [MTCC No. 282], *C. albicans* [MTCC No. 227] were used for antimicrobial assay.

in vitro antimicrobial activity: The synthesized compounds were screened for *in vitro* antimicrobial activity against bacterial and fungal strains by using serial dilution technique to find their minimum inhibitory concentration. The medium was prepared by dissolving weighed amount of nutrient broth/

sabouraud dextrose broth in 1 L of distilled water and 1 mL of nutrient medium was transferred to each test tube. The test tubes having nutrient medium were autoclaved for 30 min at 120 °C. The solution of test compounds was prepared by dissolving 1.0 mg of synthesized compounds in dry DMSO, which was further diluted to give a stock solution of 100 µg/mL. The solution of test compounds was transferred to test tubes having sterilized nutrient medium to get a set of five dilutions of test compounds having concentrations 50, 25, 12.5, 6.25 and 3.125 µg/mL. The inoculation of test strains was done with the help of micropipette with sterilized tips as 100 µL of freshly cultured strain was transferred in to test tubes and incubated at 37 °C for 24 h for bacterial strains, 48 h for *C. albicans* and 7 days at 25 °C for *A. niger*. The efficacy of ligands and their organotin(IV) complexes against the tested microbes was compared with standard drugs norfloxacin and fluconazole for antibacterial and antifungal activity, respectively. Each sample was assayed in triplicate and the concordant values were reported.

RESULTS AND DISCUSSION

All the ligands (HL₁-HL₃) and their complexes were synthesized using the same synthetic procedure as predicted in **Scheme-I**. The ligands were prepared by the reaction of substituted vanillin derivatives with thiophene-2-carboxylic acid hydrazide. The final organosilicon(IV) complexes were synthesized by reaction of R₂SiCl₂ with the sodium salt of Schiff base ligands in equimolar ratio in the dry methanol. The elemental analyses data of the synthesized compounds were well in agreement with their corresponding molecular formulae (Table-1). The molar conductance values of these complexes in the range of 7.18–12.4 Ω⁻¹ cm² mol⁻¹ suggested non-electrolytic nature of complexes.

Electronic spectra: The electronic spectra of ligands and their silicon complexes were recorded in dimethyl formamide. The Schiff base ligands HL₁₋₃ exhibited a maxima at 394-398 nm, respectively, which may be assigned to the n-π* transition of the azomethine group and these bands showed blue shift in the complexes suggesting the involvement of azomethine nitrogen in complex formation. Some medium intensity bands were also appeared at 238, 244 and 263 nm due to π-π* transition of benzene ring of Schiff base ligands, which remains almost unchanged on complex formation.

IR spectra: The infrared spectra of compound were recorded in the range of 4000-400 cm⁻¹ using KBr pellets. The IR spectrum of the ligands showed strong bands at 1698-1690 cm⁻¹ [12] and 3392-3371 cm⁻¹ due to ν(C=O) and ν(N-H) stretching, respectively. These bands were disappeared in the spectra of complexes indicating the involvement of these groups in bond formation with silicon after deprotonation. Another sharp band appeared at 1568-1565 cm⁻¹ due to azomethine ν(C=N) group of Schiff base ligands was shifted to lower frequency in the complexes due to the decrease in the electron density over nitrogen of azomethine group suggested the participation of nitrogen of this group in coordination with silicon atom. Other new bands appeared in the range 466-453 and 561-530 cm⁻¹ were assigned to ν(Si-N) and ν(Si-O) modes, respectively which confirmed the involvement of oxygen and nitrogen as donor atoms to form bond with metal [13].

¹H NMR spectra: The ¹H NMR spectra of the synthesized compounds were recorded in DMSO using TMS as internal standard. In the ¹H NMR spectra of the free ligands the signals appeared at δ 8.70-9.11 ppm due to the NH proton, which completely disappeared from the spectra of the complexes indicating the participation of NH group. Another sharp singlet due to azomethine proton appeared at δ 11.90-12.03 ppm which was shifted in the complexes indicating the participation of azomethine proton in bond formation [14]. The aromatic protons of the ligands appeared in the range δ 7.05-8.72 ppm and OCH₃ and OCH₂ protons appeared in the range δ 3.82-5.05 ppm. The signals due to OCH₃ and OCH₂ groups remains unchanged in the spectra of complexes suggested the non-involvement of these protons in bond formation. Further formation of complexes was confirmed by the appearance of new signals at δ 1.20-1.23, 1.18-3.10, 1.20-3.11 and 6.52-7.45 ppm due to methyl, ethyl, butyl and phenyl protons attached to silicon atom.

¹³C NMR: The ¹³C NMR spectra of ligands exhibited signals at 160.3-164.2 and 152.0-154.1 ppm due to carbon of carbonyl and azomethine groups, respectively, which was shifted to the lower values in the spectra of complexes, indicating the participation of these carbons in bond formation. The aromatic carbons of ligands were observed in the range 114.0-152.1 ppm while OCH₃ and OCH₂ carbons appeared at 55.5 and 73.7 ppm, respectively. The extra signals in the complexes due to the carbons of methyl, ethyl and *n*-butyl groups attached to the silicon atom appeared in the range of 8.52-8.61 ppm, 8.47-12.89 ppm and 8.25-27.11 ppm, respectively and signals due to the carbons of phenyl ring attached to the silicon atom appeared at 128.19-129.21 ppm.

²⁹Si NMR spectra: The ²⁹Si NMR spectra of the complexes were recorded in CDCl₃ with small amount of dimethyl sulfoxide (DMSO-*d*₆) and chemical shift values for all the organosilicon(IV) complexes were appeared in the range -74.13 to -125.31 ppm with reference to TMS, indicated penta coordinated geometry around silicon atom [15].

Antimicrobial evaluation: The Schiff base ligands and their silicon complexes were evaluated for *in vitro* antimicrobial activity against two Gram-positive bacteria *viz.* *Klebsiella*

TABLE-1
PHYSICO-CHEMICAL CHARACTERIZATION AND ELEMENTAL ANALYSIS OF
SYNTHESIZED SCHIFF BASES AND THEIR COMPLEXES

Comp. No.	Compounds	m.f.	<i>m/z</i>	Yield (%)	Elemental analysis (%): Calcd. (found)			
					C	H	N	Si
1	HL ₁	C ₂₀ H ₁₈ N ₂ O ₃ S	366.10	81	65.55 (65.46)	4.95 (4.69)	7.64 (7.34)	–
2	HL ₂	C ₂₀ H ₁₇ BrN ₂ O ₃ S	444.01	84	53.94 (53.98)	3.85 (3.78)	6.29 (6.27)	–
3	HL ₃	C ₂₀ H ₁₇ N ₃ O ₃ S	411.09	78	58.38 (58.24)	4.16 (4.32)	10.21 (10.36)	–
4	Me ₂ Si(L ₁)Cl	C ₂₂ H ₂₅ ClN ₂ O ₃ SSi	460.10	86	57.31 (57.48)	5.47 (5.34)	6.08 (6.21)	6.09 (6.11)
5	Et ₂ Si(L ₁)Cl	C ₂₄ H ₂₉ ClN ₂ O ₃ SSi	488.14	85	58.94 (58.73)	5.98 (5.88)	5.73 (5.62)	5.74 (5.65)
6	Bu ₂ Si(L ₁)Cl	C ₂₆ H ₃₃ ClN ₂ O ₃ SSi	516.17	84	60.38 (60.62)	6.43 (6.64)	5.42 (5.34)	5.43 (5.15)
7	Ph ₂ Si(L ₁)Cl	C ₃₂ H ₂₉ ClN ₂ O ₃ SSi	584.14	87	65.68 (65.32)	5.00 (5.23)	4.79 (4.63)	4.80 (4.68)
8	Me ₂ Si(L ₂)Cl	C ₂₂ H ₂₄ BrClN ₂ O ₃ SSi	538.01	85	48.94 (48.65)	4.48 (4.44)	5.19 (5.34)	5.20 (5.34)
9	Et ₂ Si(L ₂)Cl	C ₂₄ H ₂₈ BrClN ₂ O ₃ SSi	566.05	74	50.75 (50.90)	4.97 (4.88)	4.93 (4.72)	4.94 (4.67)
10	Bu ₂ Si(L ₂)Cl	C ₂₆ H ₃₂ BrClN ₂ O ₃ SSi	594.08	86	52.39 (52.45)	5.41 (5.35)	4.70 (4.49)	4.71 (4.34)
11	Ph ₂ Si(L ₂)Cl	C ₃₂ H ₂₈ BrClN ₂ O ₃ SSi	662.05	77	57.88 (57.36)	4.25 (4.48)	4.22 (4.34)	4.23 (4.64)
12	Me ₂ Si(L ₃)Cl	C ₂₂ H ₂₄ ClN ₃ O ₃ SSi	505.09	89	52.22 (52.34)	4.78 (4.74)	8.30 (8.44)	5.55 (5.46)
13	Et ₂ Si(L ₃)Cl	C ₂₄ H ₂₈ ClN ₃ O ₃ SSi	533.12	78	53.97 (53.78)	5.28 (5.21)	7.87 (7.82)	5.26 (5.48)
14	Bu ₂ Si(L ₃)Cl	C ₂₆ H ₃₂ ClN ₃ O ₃ SSi	561.15	82	55.55 (55.68)	5.74 (5.35)	7.47 (7.32)	5.00 (5.11)
15	Ph ₂ Si(L ₃)Cl	C ₃₂ H ₂₈ ClN ₃ O ₃ SSi	629.12	89	60.99 (60.78)	4.48 (4.32)	6.67 (6.44)	4.46 (4.52)

TABLE-2
MINIMUM INHIBITORY CONCENTRATION (MIC) VALUES OF SCHIFF
BASE LIGANDS AND THEIR ORGANOSILICON(IV) COMPLEXES

Comp. No.	Compounds	Minimum inhibitory concentration (µg/mL)					
		Gram-positive bacteria		Gram-negative bacteria		Fungus	
		<i>S. aureus</i>	<i>K. pneumonia</i>	<i>E. coli</i>	<i>E. aerogenes</i>	<i>C. albicans</i>	<i>A. niger</i>
1	HL ₁	50	25	25	50	50	50
2	HL ₂	50	25	25	50	50	50
3	HL ₃	25	12.5	12.5	25	25	25
4	Me ₂ Si(L ₁)Cl	50	25	25	25	50	12.5
5	Et ₂ Si(L ₁)Cl	25	12.5	25	25	25	12.5
6	Bu ₂ Si(L ₁)Cl	12.5	12.5	12.5	25	12.5	6.25
7	Ph ₂ Si(L ₁)Cl	6.25	12.5	12.5	12.5	6.25	6.25
8	Me ₂ Si(L ₂)Cl	12.5	12.5	25	25	12.5	12.5
9	Et ₂ Si(L ₂)Cl	12.5	6.25	12.5	12.5	12.5	6.25
10	Bu ₂ Si(L ₂)Cl	12.5	6.25	12.5	12.5	12.5	6.25
11	Ph ₂ Si(L ₂)Cl	6.25	6.25	6.25	12.5	6.25	6.25
12	Me ₂ Si(L ₃)Cl	12.5	12.5	25	25	12.5	12.5
13	Et ₂ Si(L ₃)Cl	12.5	12.5	12.5	12.5	12.5	6.25
14	Bu ₂ Si(L ₃)Cl	6.25	6.25	6.25	12.5	6.25	6.25
15	Ph ₂ Si(L ₃)Cl	6.25	6.25	6.25	12.5	6.25	6.25
16	Fluconazole	–	–	–	–	12.5	3.12
17	Norfloxacin	12.5	12.5	12.5	25	–	–

pneumoniae and *Staphylococcus aureus*, two Gram-negative bacteria viz. *Escherichia coli* and *Enterobacter aerogenes* and two fungal strains *Aspergillus niger* and *Candida albicans*. The antimicrobial behaviour of compounds was assessed by serial dilution method and minimum inhibitory concentrations (MIC) were recorded as µg/mL (Table-2). The negative and positive controls were taken as dimethyl sulphoxide (DMSO) and standard drugs (norfloxacin and fluconazole), respectively.

The antimicrobial activity data generalized that almost all the compounds showed significant efficiency against all the tested strains. The biological activity of these compounds might be due to the presence of azomethine group in Schiff bases, which express some transformation reaction in the biological system [16]. Another important effect observed in the study was that biological activity of Schiff base ligands got enhanced on complexation with metal and this enhancement in activity was explained on the basis of Overtone's concept of cell permeability and chelation theory [12,17]. Second remarkable observation in the biological study of the compounds was that in the entire series phenyl derivatives were found to be more potent antimicrobial agent in comparison to the other derivatives and this effect was explained on the basis of lipophilicity and effective binding of the molecules to the membrane through additional π -cation interactions.

Conclusion

A series of 15 compounds was synthesized and characterized using elemental analyses and various spectral techniques like UV, IR and (¹H, ¹³C and ²⁹Si) NMR. All the compounds were screened for antimicrobial activity and the test compounds were found to be active against all the tested bacterial and fungal strains. The complexes were found to be more active antimicrobial agent in comparison to the Schiff bases.

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