Synthesis and antibacterial activity of Schiff Base Complexes of Si (IV)

S. DHAKA and PRATIBHA CHOUDHARY*
Department of Chemistry, S.K. Government P.G. College, Sikar - 332001, India
*Corresponding author E-mail:- nikiphd86@gmail.com

Abstract

In the present work, synthesis, characterization, and antibacterial evaluation of organosilicon (IV) complexes of a class of amino-acid-based Schiff base which have been prepared by the interaction of ethoxytrimethylsilane with the Schiff bases (N OH) in 1:1 molar ratio have been studied which have been characterized on the basis of elemental analyses, molecular weight determinations and conductivity measurements. A few representative complexes have also been screened for their bactericidal activity and found to be quite active in this respect against bacteria (Bacillus subtilis, Escherichia coli, Streptococcus albedencus, and Staphylococcus aureus. Pseudomonas aeroginosa). The complexes were found to be more potent as compared to the ligands.

Key words- Organosilicon (iv) complexes, Schiff base complexes N OH donar, Antibacterial activity.

Introduction

Recently, the research relating with metal complexes of heteronuclear Schiff bases has expanded enormously and now comprising their interesting aspects in coordination chemistry with a special emphasis in bioinorganic chemisty. A use of organosilicon compounds as reagents or intermediates in the inorganic synthesis has further strengthened their applications [1,2]. The biological activity of Schiff bases was significantly enhanced on chelation [3]. It has been reported that chelation is the cause and cure of many diseases including cancer. Schiff base complexes [3–7] have found antibacterial, antifungal, anticancer, tuberculostatic, and herbicidal activities [8–12]. It is known that the presence of metal ions bonded to biologically active compounds may enhance their activity [13–16]. Heteronuclear Schiff base complexes have found applications as magnetic materials, catalysts and in the field of bioengineering [17, 18]. Organosilicon compounds of nitrogen and sulphur containing ligands are well known for their anticarcinogenic, antibacterial, tuberculostatic, antifungal, insecticidal, and acaridial activities [19–22]. The interest in organosilicon(IV) compounds [23–25] is due to their versatile applicability in the pharmaceutical industries. Generally, organosilicon compounds seem to owe their antitumour properties to the immunodefensive system of the organism. The medical applications and effectiveness of the silatrines in the treatment of wounds and tumours are thought to be related to the role of silicon in the growth of epithelial and connective tissues and hair, where their function is to impart strength, elasticity, and impermeability to water [26].

In view of this, the synthesis of organosilicon(IV) complexes of Schiff bases derived from the condensation of chloroisatin and isatin with different amino acids derivatives is reported herein. Their antibacterial activities were screened against various bacteria.

Experiment

Adequate care was taken to keep the organosilicon(IV) complexes, chemicals, and glass apparatus free from moisture clean and well dried glass apparatus fitted with quickfit interchangeable standard ground joints was used throughout the experimental work. All the chemicals and solvents used were dried and purified by standard methods. The ligands were prepared by the condensation of isatins with amino acids as described earlier [27, 28].

Physical Measurements and Analytical Methods.

Silicon was determined gravimetrically as SiO₂. Nitrogen and sulphur were estimated by Kjeldahl's and Mezenger's methods, respectively. Molecular weights were determined by the Rast camphor method (freezing point depression method) using resublimed camphor (MP178°C). The conductance measurements were carried out in dry dimethylformamide (DMF) at room temperature using a systronics conductivity bridge (model 305) in conjunction with a cell having a cell constant of 1.0. The electronic spectra were recorded on a Thermo UV-visible spectrophotometer in the range 200–800 nm, using dry methanol as the solvent. Infrared spectra were recorded on a Perkin Elmer, FT-IR SP-2 spectrophotometer in KBr pellets. Multinuclear magnetic resonance spectra were recorded on BRUKER AVANCE II FTNMR 400MHz spectrometer. ¹H NMR spectra were recorded in deuterated dimethylsulphoxide (DMSO-d6) at 400MHz using tetramethylsilane (TMS) as an internal standard. ¹³ C and ²⁹Si NMR spectra were recorded in dry dimethylsulphoxide using TMS as the internal standard.

Synthesis of the Organosilicon(IV) Complexes.

The complexes were prepared under anhydrous conditions by the slow addition of a dry, hot methanol solution of the ethoxytrimethylsilane (0.47 g; 3.385mmole) in a 1 : 1 molar ratio to a solution of the Schiff bases (0.691–1.127 g;
3.385 mmol (60 mL). The mixture was refluxed with constant stirring, giving a clear solution in half an hour; refluxing was then continued for 10–12 hr. Excess solvent was removed under reduced pressure, and the compound was finally dried in vacuum at a bath temperature of 40 ± 5°C on rotary evaporator after being repeatedly washed with a mixture of methanol and n-hexane (1 : 1 v/v). The crystalline solids were separated out and purified by recrystallization from the same solvent. The purity of the compounds was checked by TLC using silica gel-G as adsorbent. Their physical properties and analytical data are recorded in Table 1.

Antibacterial Assay
Synthesized compounds were screened for their antibacterial activity against Bacillus subtilis, Escherichia coli, Streptococcus albulencus, and Staphylococcus aureus, Pseudomonas aeroginosa. at the concentrations of 100 μg/mL by the agar well diffusion method [29]. An aliquot (5 mL) of nutrient broth was inoculated with the test organisms and incubated at 37°C for 24 hr. Sterile nutrient agar plates were also prepared, and holes of 6 mm diameter were cut using a sterile cork borer ensuring proper distribution. The test organisms after 24 hr of incubation were spread onto separate agar plates. The compounds were dissolved in DMSO and were poured into appropriately labeled holes using a pipette in aseptic conditions. DMSO served as control with Streptomycin (100 μg/mL) used as a standard antibiotic. Whole determination was made in triplicate for each of the compounds. An average of three independent readings for each compound was recorded. The zone of inhibition was calculated in millimeters carefully.

Results and Discussion
The 1 : 1 molar reactions of Me₃Si (OCH₃) with Schiff base of amino acids have led to the formation of Me₃Si(L) type of complexes. The reactions have been carried out in dry methanolic medium. These reactions can be represented by the general equations in Scheme 1.

All the newly synthesized organosilicon(IV) complexes were coloured solids soluble in DMSO, DMF, and methanol. The compounds were dissolved in DMF and molar conductance 10⁻³ M of solution at 45°C was measured. The molar conductance values of the complexes fall in the range 08–16 ohm⁻¹ cm² mol⁻¹, indicating that these compounds are nonelectrolytic nature. The analytical data were in the good agreement with the proposed stoichiometry of the complexes.

Scheme 1: Representative equation illustrating the formation of Me₃Si(L) complexes.

\[(\text{CH}_3)_3\text{SiOCH}_2\text{CH}_3 + \text{N OH} \rightarrow \text{Dry methanol} \quad (\text{CH}_3)_3\text{Si(N O) + CH}_3\text{CH}_2\text{OH} \quad 10–12\text{hr}\]

Where N OH represents the donor system of the Schiff bases

Antimicrobial Activity
In vitro antibactericidal activity of the ligands, silicon complexes, and standard drugs was screened separately for their antibacterial activity against Gram-positive and Gram-negative bacteria (Bacillus subtilis, Escherichia coli, Streptococcus albulencus, and Staphylococcus aureus. Pseudomonas aeroginosa). Streptomycin was used as a reference compound for antibacterial activities. These bacterial strains are used because they are known as common pathogens of human beings. The antimicrobial studies suggested that the Schiff bases are biologically active and their silicon complexes showed significantly enhanced antibacterial activity against microbial strains in comparison to the free ligands. It has been observed that the silicon complexes showed increased zone of inhibition against the bacterial strains (Table 1) as compared to ligands. On the basis of zone of inhibition produced against the test bacterium, compound 3 was found to be most effective Bacillus subtilis, Escherichia coli, Streptococcus albulencus, and Staphylococcus aureus. Pseudomonas aeroginosa with zone of inhibition of 12.6 mm, 12.7 mm, 12.9 mm, 9.5 mm, 9.9 mm, and 8.7 mm, respectively (Table 1). This also showed that the antibacterial activity of ligands is greatly enhanced when it is coordinated to silicon ions.

Table 1: Antibacterial activity of ligands and their organosilicon(IV) complexes.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Bacillus subtilis</th>
<th>Streptomyces albulencus</th>
<th>Staphylococcus aureus</th>
<th>E. coli</th>
<th>Pseudomonas aeroginosa</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Inhibition zone (mm)</td>
<td>Inhibition zone (mm)</td>
<td>Inhibition zone (mm)</td>
<td></td>
<td>Inhibition zone (mm)</td>
</tr>
<tr>
<td></td>
<td>and activity index</td>
<td>and activity index</td>
<td>and activity index</td>
<td></td>
<td>and activity index</td>
</tr>
<tr>
<td>L1H</td>
<td>100 (0.556)</td>
<td>100 (0.556)</td>
<td>100 (0.556)</td>
<td>100 (0.556)</td>
<td>100 (0.556)</td>
</tr>
<tr>
<td>Me₂SiL1</td>
<td>7.9 (0.556)</td>
<td>8.9 (0.616)</td>
<td>8.2 (0.554)</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>L2H</td>
<td>11.3 (0.795)</td>
<td>10.4 (0.712)</td>
<td>11.2 (0.756)</td>
<td>7.8 (0.598)</td>
<td>8.4 (0.785)</td>
</tr>
<tr>
<td></td>
<td>7.0 (0.495)</td>
<td>7.2 (0.523)</td>
<td>7.9 (0.534)</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

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The newly synthesized Schiff bases act as bidentate ligands coordinating to silicon ion through azomethine nitrogen and carboxylate oxygen atom. Thus, on the basis of the previously mentioned spectral features, as well as the analytical data, the penta-coordinated trigonal bipyramidal geometries have been suggested for the organosilicon (IV) complexes. The Schiff bases and their silicon complexes were found to be highly active against some of the antibacterial species. The activity is significantly increased on coordination. The coordination compounds have been found to be most active against *B. subtilis* and the *S. abudencus*. Thus, the formation of the coordination compounds can be used as the future prospective antibiotic agents against some known pathogenic organisms and can be used as marketed drugs.

### Conclusions

The newly synthesized Schiff bases act as bidentate ligands coordinating to silicon ion through azomethine nitrogen and carboxylate oxygen atom. Thus, on the basis of the previously mentioned spectral features, as well as the analytical data, the penta-coordinated trigonal bipyramidal geometries have been suggested for the organosilicon (IV) complexes. The Schiff bases and their silicon complexes were found to be highly active against some of the antibacterial species. The activity is significantly increased on coordination. The coordination compounds have been found to be most active against *B. subtilis* and the *S. abudencus*. Thus, the formation of the coordination compounds can be used as the future prospective antibiotic agents against some known pathogenic organisms and can be used as marketed drugs.

### References


<table>
<thead>
<tr>
<th>Schiff Base</th>
<th>Inhibition Zone (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me₂SiL₂</td>
<td>10.5 (0.739)</td>
</tr>
<tr>
<td>L₃H</td>
<td>9.6 (0.676)</td>
</tr>
<tr>
<td>Me₂SiL₃</td>
<td>12.6 (0.887)</td>
</tr>
<tr>
<td>L₄H</td>
<td>9.5 (0.669)</td>
</tr>
<tr>
<td>Me₂SiL₄</td>
<td>12.6 (0.887)</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>14.2 (1.831)</td>
</tr>
</tbody>
</table>

(Al): inhibition zone of test compounds/inhibition zone of standard.


A. Doddi, J. V. Kingston, V. Ramkumar, M. Suzuki, M. Hojo, and M. N. S. Rao, “Synthesis and characterization of dianionic hexacoordinate silicon(IV) complexes of substituted catechols, flavones, and fluorene: X-ray crystal structures of \([\text{n–}\text{(H}_2\text{C})_3\text{H}_2\text{NH}_3\text{]}\{(\text{C}_6\text{H}_5\text{C}_2\text{O}_2)\text{Si}\}_3\ \text{CH}_3\text{CN}\) and \([\text{n–}\text{(H}_2\text{C})_3\text{H}_2\text{NH}_3\text{]}\{(\text{Br}_3\text{C}_6\text{O}_2)\text{Si}\}_2\ \text{(CH}_3\text{)}_2\text{SO}\),” *Phosphorus, Sulfur and Silicon and the Related Elements*, vol. 187, no. 3, pp. 343–356, 2012.


