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Methyl Silicon (IV) Schiff base Complexes: Synthesis, Coordination Behavior and their Pharmacologically Significance as Antioxidant, Anti-inflammatory and Anti-diabetic agents

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ABSTRACT

Schiff bases exhibit many pharmacological and biological properties. Here, methyl silicon (IV) complexes are formed by reacting methyl silicon alkoxides with alanine based ligand. Later, the pharmacological characteristics of these ligand and associated methyl silicon (IV) Schiff base complexes were assessed. The ligand and methyl silicon (IV) complexes underwent physical and spectral characterization, including IR, ^{1}H-NMR, and ^{13}C-NMR. Pharmacological activities show an increase in the number of organic groups as well as in the coordinating environment of silicon. All compounds exhibited antioxidant, anti-inflammatory, and anti-diabetic activities, but the methyl silicon (IV) Schiff base complexes demonstrated superior activities relative to the ligand.

Keywords: Methyl Silicon (IV) Schiff base complexes, Spectral studies, Antioxidant, Anti-inflammatory, Anti-diabetic activities.

INTRODUCTION

The design of Schiff base is widely recognized as versatile ligand due to its easy synthesis and diverse applications in synthesizing metal complexes. Among these, Schiff base amino acid complexes have acquired attention for their inorganic significance and potential physiological and pharmacological activities[1,2]. The combination of Schiff bases derived from o-hydroxy aromatic aldehydes with amino acids holds relevance to various biological processes like transamination, racemization, and carboxylation, highlighting their importance[3]. Organosilicon (IV) complexes are renowned for their diverse pharmacological effects, including anticarcinogenic, antibacterial, antifungal, tuberculostatic, insecticidal, and acaricidal properties[4-7]. These properties highlight their potential for various therapeutic applications, making them subjects of continued research and exploration in

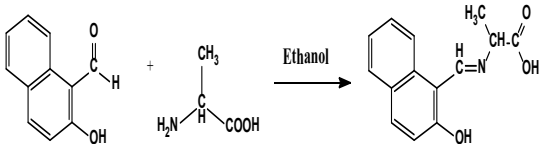
medicinal chemistry. Keeping this in view, we have synthesized new methyl silicon (IV) complexes and evaluated their pharmacological activities.

MATERIALS AND METHOD

All chemicals used in the present work were acquired from Sigma Aldrich. Elemental analyses were obtained using Thermo Scientific (FLASH 2000) CHN elemental analyzer at SAIF Punjab University, while silicon was determined gravimetrically as SiO_2. A Bruker Advance neo 500 MHz NMR spectrometer at SAIF Punjab University was utilized to acquire the multinuclear (^1H and ^{13}C NMR) spectra. Using TMS as the internal reference, the chemical shift (δ) was measured and expressed in parts per million. Infrared data were obtained using an RZX (Perkin Elmer) spectrophotometer, Model SAIF Punjab University, considering the wave numbers from 4000 to 400 cm^{-1}. A UV-Visible spectrophotometer was used to measure absorbance to determine pharmacological activity at GBPUAT, Pantnagar, Uttarakhand.

Preparation of ligand (LH_2) (1)

The ligand was synthesized through the reaction of 2-hydroxy-1-naphthaldehyde (2.24 g, 13mmol) with a hot aqueous solution (25 mL) of alanine (1.16 g, 13mmol) dissolved in ethanol (50 mL) (Scheme 1)[8]. After the completion of the addition, the solution was refluxed for 3 to 4 h in a round bottom flask. After standing overnight, the polycrystalline precipitate was produced. Following multiple washes in aqueous ethanol, the substance underwent vacuum drying to attain purification.



Scheme 1. Synthesis of ligand

Synthesis of methyl silicon (IV) Schiff base complexes (1a, 1b, 1c)

For the preparation of complexes, a calculated amount of the trimethoxymethylsilane and ligand **(1)** were dissolved separately in 30 mL of benzene and mixed with constant stirring. The mixture was stirred magnetically for 20-22 h using a $CaCl_2$ guard tube. Excess solvent was removed under distillation, and the compound was finally dried. The crystalline solids were separated and purified by re-crystallization from benzene.

Pharmacological activities

Formula to calculate percentage inhibition of pharmacological activities:

Percentage Inhibition (IC_{50}) = [1- (sample/control)] × 100

Evaluation of antioxidant activity

To assess the antioxidant properties of ligand and methyl silicon (IV) Schiff base complexes, three *in-vitro* assays were used: metal chelating, DPPH, and H_2O_2 radical scavenging activity. In metal chelating activity, the absorbance was measured at 560 nm. For this, 0.1 mL of 2 mM $FeCl_2 \bullet 4H_2O$, 0.2 mL of 5 mM ferrozine, and 4.7 mL of MeOH were mixed into samples (5 µg/mL-25 µg/mL), followed by incubation for ten minutes at ambient temperature. After mixing the solution thoroughly and subsequently incubating it for thirty minutes at ambient temperature, the absorbance at 562 nm was measured using a UV-Visible spectrophotometer. As a standard, ascorbic acid was employed[9].

In DPPH radical scavenging activity, various amounts (5 µg/mL - 25 µg/mL) of the ligand and methyl silicon (IV) Schiff base complexes were mixed into five milliliters of MeOH solution containing four milligrams of DPPH. BHT was utilized as an antioxidant standard at equivalent concentrations to those of the samples. A UV-Visible spectrophotometer was utilized to measure the absorbance in triplicate at 517nm, after incubation for 30 min in darkness at room temperature[10].

In H_2O_2 radical scavenging activity, 0.6 mL of 40mM H_2O_2 dissolved in PBS (pH 7.4) was combined with 0.4 mL of an 80% MeOH solution, which included samples or BHT at varying concentrations (5 µg/mL - 25 µg/mL). At room temperature, the solution was incubated for ten minutes. BHT (5 µg/mL - 25 µg/mL) was used as standard in this study[11].

Evaluation of anti-inflammatory activity

The experimental setup comprised samples at different concentrations (5 µg/mL - 25 µg/mL) with 200 µL of fresh albumin protein. Subsequently, 2.8 mL of PBS (pH 6.4) was mixed to the solution mixture

to reach a total quantity of 5 mL. The resulting mixture was heated for five minutes up to 70 degrees Celsius after being incubated for fifteen minutes at 37 degrees Celsius. A UV-Visible spectrophotometer was used to detect the absorbance at 660nm after the reaction mixture had cooled. Diclofenac sodium was used as standard[12].

Evaluation of anti-diabetic activity

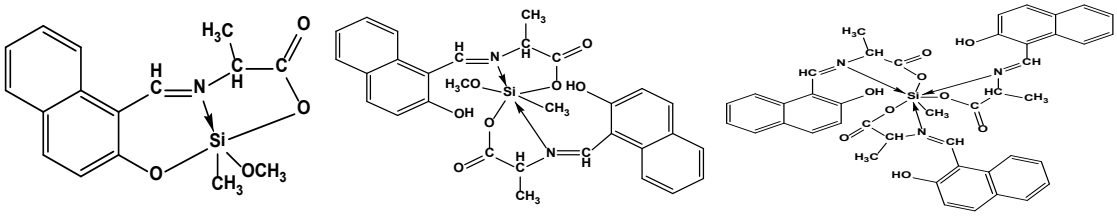
The standard medication acarbose and varying amounts of the samples (5 µg/mL–25 µg/mL) were introduced into a mixture containing 200 µL of α-amylase solution, along with 100 µL of 2mM PBS (pH 6.9). Followed by incubation for twenty minutes[13]. Afterward, 100 µL of a 1% starch solution was introduced into the sample solution. Following five-minute incubation at 37°C, 500 µL of DNSA reagent was mixed into the mixture, which was then subjected to boiling in a water bath for five minutes. The absorbance was measured at 540nm.

RESULT DISCUSSION

Reactions of trimethoxymethylsilane with ligand were conducted in 1:1, 1:2, and 1:3 molar ratios in benzene. The reaction resulted in the release of methanol due to acidic hydrogen(s) from ligand (1) and the methoxy group(s) from methyl silicon alkoxides, yielding (1a, 1b, 1c) (Fig. 1). All the newly synthesized methyl silicon (IV) Schiff base complexes are colored solids, soluble in most of the common organic solvents. The results of elemental analysis data were tabulated in Table 1.

$$CH_3Si(X)_3 + LH_2\ /2LH_2\ /3LH_2 \xrightarrow[1:1,\ 1:2,\ 1:3]{\text{Benzene}} CH_3SiX\ (L)/CH_3SiX(LH)_2\ /CH_3Si(LH)_3 + 2XH\ /3XH$$

(Where X = OCH_3)



(1a) (1b) (1c)

Fig. 1. Proposed structures of methyl silicon (IV) Schiff base complexes (1a-1c)

Table 1: Elemental analysis, color, and melting points of ligand and methyl silicon (IV) Schiff base complexes

Ligand and complexes	Color	m.p. (°C)	Calculated (found)%				Mol. Wt.gmol^{-1}
		C	H	N	Si		
$C_{14}H_{13}NO_3$ (1)	Ethnic brown	82	69.12(68.82)	5.39(5.01)	5.76(5.15)	-	243.255
$C_{16}H_{17}NO_4Si$ (1a)	Peanut Butter	84	60.93(60.25)	5.43(5.13)	4.44(4.02)	8.90(8.45)	315.396
$C_{30}H_{30}N_2O_7Si$ (1b)	Machaccino	88	64.51(64.14)	5.41(5.05)	5.01(4.81)	5.02(4.75)	558.655
$C_{43}H_{39}N_3O_9Si$ (1c)	Sunderbans	92	67.08(66.84)	5.10(4.91)	5.46(5.03)	3.66(3.15)	769.871

^{1}H NMR spectra

In the case of ligand, the signal assigned to phenolic –OH proton is observed at a δ value of 12.17ppm, which disappears in the spectra of the silicon complexes 1a[14]. A sharp singlet proton signal of the -CH=N group is observed at δ 10.82ppm, which appears at δ10.83-10.98ppm in the spectra of complexes due to the coordination of the azomethine nitrogen to the metal atom[15]. The results of ^{1}H-NMR spectral data were tabulated in Table 2.

Table 2: ^{1}H-NMR spectra of ligand and methyl silicon (IV) Schiff base complexes

Ligand and Complexes	-HC=N	-CH_3	-CH_3Si	Phenoic –OH	aromatic proton	DMSO
$C_{14}H_{13}NO_3$ (1)	10.82(s)	1.62(d)	-	12.17 (s)	7.19-8.86(d,t,m)	2.50(m)
$C_{16}H_{17}NO_4Si$ (1a)	10.83(s)	1.63(d)	1.01(s)	-	6.23-8.35(d,t,m)	2.50(m)
$C_{30}H_{30}N_2O_7Si$ (1b)	10.85(s)	1.62(d)	1.13(s)	12.09(s)	6.24-8.34(d,t,m)	2.50(m)
$C_{43}H_{39}N_3O_9Si$ (1c)	10.98(s)	1.62(d)	1.10(s)	12.11(s)	6.21-8.35(d,t,m)	2.50(m)

^{13}C-NMR spectra

The signals due to the carbon atom attached to the carboxylic acid group in the ligand appear at δ192.93ppm[16]. A signal of the azomethine

group appears at δ163.88ppm. However, these occur at δ163.30 ± 0.5ppm in the spectra of methyl silicon (IV) Schiff base complexes[17,18]. The significant shift in the resonance of the carbon atom bonded to nitrogen suggests that the azomethine nitrogen has participated in coordination[19]. The results of ^{13}C-NMR spectral data were tabulated in Table 3.

Table 3: ^{13}C-NMR spectra of ligand and methyl silicon (IV) Schiff base complexes

Ligand and Complexes	-HC=N	-COOH	-C=O	-COO-	-OCH_3	-C-OH	Aromatic carbon	DMSO
$C_{14}H_{13}NO_3$ (1)	163.88	192.93	-	-	-	-	112.24-138.27	39.50
$C_{16}H_{17}NO_4Si$ (1a)	163.21	-	175.15	170.80	52.85	-	112.17-138.26	39.50
$C_{30}H_{30}N_2O_7Si$ (1b)	163.25	-	175.02	170.74	52.84	159.59	112.21-138.28	39.50
$C_{43}H_{39}N_3O_9Si$ (1c)	163.35	-	175.11	170.79	-	159.65	112.25-137.25	39.50

Infrared spectra

In the ligand, the peak observed at 1592.32 cm^{-1}, attributed to the υ C=N[20], is found to be shifted to higher wave numbers in the complexes, suggesting coordination of the azomethine nitrogen with the silicon ion[21]. The observed broadband at 3430.84 cm^{-1} and 3369.74-2865.93 cm^{-1} was attributed to the υ(OH)[22] and δCOOH groups[23]. These stretching frequencies support the formation of the ligand. The complexes show two sharp bands observed at 1622.24-1646.81 cm^{-1} which are assigned to the υ_{asy}(COO) and 1310.94-1382.06 cm^{-1}, which are assigned to the υ_{sym}(COO) stretching modes[24]. The amino acid carboxyl group coordinates in a monodentate manner, as indicated by the variation in frequency (Δν) between the two types of stretching modes. The results of IR spectral data were tabulated in Table 4.

Table 4: IR spectra of ligand and methyl silicon (IV) Schiff base complexes

Ligand and complexes	υ Ar-CH	υ(OH)	υ C=Oδ	υ (C=N)	δ_{asy}(COO)	δ_{sym}(COO)	δ_{asy}(Si-O)	δ_{sym}(Si-O)	δ(Si←N)
$C_{14}H_{13}NO_3$ (1)	3094.88	3430.84	1723.25	1592.32	1622.24	1382.06	-	-	-
$C_{16}H_{17}NO_4Si$ (1a)	3077.83	-	-	1594.53	1646.81	1368.23	838.96	653.66	531.21
$C_{30}H_{30}N_2O_7Si$ (1b)	3075.75	3433.15	1720.10	1594.54	1633.27	1315.17	841.11	652.13	532.19
$C_{43}H_{39}N_3O_9Si$ (1c)	3074.87	3432.48	1730.41	1594.52	1624.25	1310.94	840.01	650.27	533.01

Pharmacological activities

Evaluation of Antioxidant activity

As the concentrations of the ligand and methyl silicon (IV) Schiff base complexes increased, so did their chelation activity. The results of the activity indicated that the methyl silicon (IV) complexes from **1b** and **1c** exhibited a less metal chelating effect compared to ascorbic acid. The IC_{50} values for the various samples were arranged in the following sequence: ascorbic acid (15.64 ± 0.02)>**(1c)** (18.18 ± 0.01)>**(1b)** (18.20 ± 0.01)>**(1a)** (18.24 ± 0.01)>**(1)** (24.07 ± 0.05) (Table 5).

The DPPH scavenging activity of ligand and methyl silicon (IV) Schiff base complexes was assessed against the standard antioxidant, BHT, which has an IC_{50} value of 8.56 ± 0.02 µg/mL. Samples **1c** and **1b** exhibited strong antioxidant activity closest to the BHT. The IC_{50} values for the various samples were arranged in the following sequence: BHT (8.56 ± 0.02)>**(1c)** (17.75 ± 0.02)>**(1b)** (17.91 ± 0.02)>**(1a)** (18.17 ± 0.01)>**(1)** (19.87 ± 0.01) (Table 5).

The results of the activity indicated that the methyl silicon (IV) Schiff base complexes from **1b** and **1c** exhibited a less H_2O_2 scavenging compared to BHT. The IC_{50} values for the various samples were arranged in the following sequence: BHT (10.46 ± 0.02)>**(1c)** (19.66 ± 0.02)>**(1b)** (19.72 ± 0.01)>**(1a)** (20.06 ± 0.01)>**(1)** (23.57 ± 0.01) (Table 5).

Evaluation of Anti-inflammatory activity

In comparison to other samples, sample **1c** exhibited higher potency. However, against diclofenac sodium (IC_{50} = 7.26 ± 0.04 µg/mL), ligand and all complexes showed lesser activity. The sequence of samples in inhibiting protein denaturation, accompanied by their IC_{50} values, was as follows: standard (7.26 ± 0.04)>**(1c)** (14.95 ± 0.06)>**(1b)** (15.10 ± 0.01)>**(1a)** (15.22 ± 0.01)>**(1)** (16.76 ± 0.02) (Table 5).

Evaluation of Anti-diabetic activity

The sample demonstrated notable α-amylase inhibitory activity, though to a lower degree compared to the acarbose. Results obtained

from performing the activity revealed that ligand **(1)** exhibited less anti-diabetic activity. Methyl silicon (IV) Schiff base complexes **1a, 1b,** and **1c** exhibited more inhibition, closer to the reference Acarbose. The IC_{50} values for the various samples were arranged in the following sequence: standard (7.17 ± 0.02)>**(1c)** (13.75 ± 0.01)>**(1b)** (13.93 ± 0.01)>**(1a)** (13.98 ± 0.02)>**(1)** (15.68 ± 0.01) (Table 5).

Table 5: Pharmacological activities of ligand and methyl silicon (IV) Schiff base complexes in terms of IC_{50} (μg/mL ± SD

Ligand, complexes and standard	Metal Chelating	Antioxidant DPPH radical	H_2O_2 radical	Anti-inflammatory Protein denauration	Anti-diabetic α-amylase inhibitory
$C_{14}H_{13}NO_3$ (1)	24.07±0.05	19.87±0.01	23.57±0.01	16.76±0.02	15.68±0.01
$C_{16}H_{17}NO_4Si$ (1a)	18.24±0.01	18.17±0.01	20.06±0.01	15.22±0.01	13.98±0.02
$C_{30}H_{30}N_2O_7Si$ (1b)	18.20±0.01	17.91±0.02	19.72±0.01	15.10±0.01	13.93±0.01
$C_{43}H_{39}N_3O_9Si$ (1c)	18.18±0.01	17.75±0.02	19.66±0.02	14.95±0.06	13.75±0.01
BHT	-	8.56±0.02	10.46±0.02	-	-
Ascorbic acid	15.64±0.02	-	-	-	-
Diclofenac sodium	-	-	-	7.26±0.04	-
Acarbose	-	-	-	-	7.17±0.02

CONCLUSION

Methyl silicon (IV) Schiff base complexes were successfully synthesized and characterized by the spectroscopic investigations. It was established that the ligand acts as bidentate and coordinated through imine nitrogen and carboxylate oxygen to the silicon atoms. Trigonal bipyramidal, octahedral, and pentagonal bipyramidal geometries have been proposed for methyl silicon (IV) complexes with the help of different spectral studies like IR, ^1H, and ^{13}C NMR. Interestingly in our present pharmacological investigations, it was concluded that the methyl silicon (IV) Schiff base complexes **(1a-1c)** showed better pharmacological activity than the ligand (LH_2) **(1)**. The pharmacological activity increases with the number of electron-donating groups, as well as the coordinating environment of silicon.

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Conflict of interest

The author declare that we have no conflict of interest.

REFERENCES

1. Kelode, S. R., *J. Chem. Pharm. Res.*, **2013**, *5*(8), 74-77.
2. Wang, P. H.; Keck, G. J.; Lien, E. J.; Lai, M. M. C., *J. Med. Chem.*, **1990**, *33*, 608.
3. Abdel-Rahman, L. H.; El-Khatib, R. M.; Nassr, L. A. E.; Abu-Dief, A. M., *J. Mol. Struct.*, **2013**, *1040*, 9-18, http://dx.doi.org/10.1016/j.molstruc.2013.02.023.
4. Singh, K.; Puri, P.; Dharampal., *Turk. J. Chem.*, **2010**, *34*, 499-507, https://doi.org/10.3906/kim-0912-354.
5. Jain, M.; Singh, R., *Bioinorg. Chem. Appl.*, **2006**, *2006*, 1-10, https://doi.org/10.1155/BCA/2006/13743.
6. Kumari, A.; Singh, I.; Tandon., *J. P. Organomet. Chem.*, **2004**, *9*, 127-132, https://doi.org/10.1002/aoc.590090206.
7. Franz, A. K.; Wilson, S. O., *J. Med. Chem.*, **2013**, *56*, 388-405, http://dx.doi.org/10.1021/jm3010114.
8. Singh, M. K.; Bhaumik, S.; Lal, R. A., *J. Indian Chem. Soc.*, **2007**, *87*, 418-426, https://dx.doi.org/10.5281/zenodo.5819486.
9. Karakoti, H.; Mahawer, S. K.; Tewari, M.; Kumar, R.; Prakash, O.; Oliveira, M. S. D.; Rawat, D. S., *Antioxidants.*, **2022**, *11*, 1911, https://dx.doi.org/10.3390/antiox11101911.
10. Bhatt, S.; Tewari, G.; Pande, C.; Prakash O.; Tripathi, S., *J. Essent. Bear. Plants.*, **2019**, *22*(1), 214-230, https://dx.doi.org/10.1080/0972060X.2019.1599736.
11. Joshi, M.; Himani; Kumar, R.; Prakash, O.; Pant, A. K.; Rawat, D. S., *J. Med. Herb.*, **2021**, *12*, 35-46.

12. Kanyal, J.; Prakash, O.; Kumar, R.; Rawat, D. S.; Srivastava, R. M.; Singh R. P.; Pant, A. K., *J. Essent. Bear. Plants*., **2021**, *24*(4), 808-825, https://dx.doi.org/10.1080/0972060X.2021.1958701.
13. Aneesa, N. N.; Anitha, R.; Varghese, S., *J. Pharm. Bio Allied Sci*., **2019**, *11*, 142, https://dx.doi.org/10.4103/jpbs.JPBS_128_18.
14. Singh, M. S.; Singh, P. K., *Syn. React. Inorg. Met. Org. Chem*., **2003**, *33*(2), 271-280, https://dx.doi.org/10.1081/SIM-120017786.
15. Raju, M. D., *J. Curr. Chem. Pharm. Sci*., **2011**, *1*(1), 9-14.
16. Wady, A. F.; Hussein, M. B.; Mohammed, M. M. Sch., *Int. J. Chem. Mater. Sci*., **2021**, *4*(5), 46-53, http://dx.doi.org/10.36348/sijcms.2021.v04i05.001.
17. Devi, J.; Devi, S.; Kumar, A. Monatsh., *Chem*. **2016**, https://doi.org/10.1007/s00706-016-1720-z.
18. Bhanuka, S.; Khaturia, S.; Chahar, M.; Singh, H. L., *Asian J. Chem*., **2020**, *32*(11), 2821-2828, https://doi.org/10.14233/ajchem.2020.22850.
19. Singh, H. L.; Singh, J. B.; Bhanuka, S. J. Assoc. Arab Univ. Basic Appl. Sci., **2017**, *23*(1), 1-9, https://dx.doi.org/10.1016/j.jaubas.2016.05.003.
20. Aliyu, H. N.; Ado, I. Bayero *J. Pure Appl. Sci*., **2010**, *3*(1), 245-249.
21. Singh, K.; Dharampal. *J. Serb. Chem. Soc*., **2010**, *75*(7), 917-927, https://dx.doi.org/10.2298/JSC081216063S.
22. Shoaib, K.; Rehman, W.; Mohammad, B.; Ali, S., *J. Proteomics. Bioinform*., **2013**, *6*(7), 153-157, https://dx.doi.org/10.4172/jpb.1000274.
23. Kakanejadifard, A.; Esna-ashari, F.; Hashemi, P.; Zabardasti, A., *Spectrochim. Acta-A: Mol. Biomol. Spectrosc*., **2013**, *106*, 80-85, https://dx.doi.org/10.1016/j.saa.2012.12.044.
24. Devi, J.; Batra, N.; Kumari, S., *Int. J. Res. Chem. Environ*., **2011**, *1*(2), 50-56.