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Synthesis and Characterization of Biologically Active Organosilicon and Organotin Complexes of Phenylglycyl Hydrazones

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Abstract

A few organosilicon and organotin complexes of phenylglycyl hydrazones were synthesized and characterized by elemental analyses, conductivity measurements, infrared and proton magnetic resonance spectral data. The complexes were found to be non-electrolytes in DMF solution and exhibit a 1:1 (metal:ligand) stoichiometry. Also, the complexes are biologically active as indicated by antibacterial testing.

Introduction

In view of the biological and pharmacological importance [1–4] of phenylglycine hydrazones, a few complexes of dimethyldichlorosilane (DMDCS) and diphenyltindichloride (DPTDC) with phenylglycine hydrazones were synthesized. The complexes were characterized by elemental analyses, conductivity measurements, infrared (IR) and proton magnetic resonance (PMR) data. Antibacterial tests established structure–activity relationships.

Experimental

Preparation of Phenylglycinehydrazones

Reagent grade chemicals were used. Phenylglycyl hydrazone hydrazones were prepared in three steps:

(1) Preparation of phenylglycine ester (PGE), $C_{10}H_{13}O_2N$

Equimolar quantities of aniline, chloroethyl acetate and sodium acetate were mixed with absolute alcohol. The mixture was refluxed on an oil bath for six hours at 225–230 °C. The product was cooled and mixed with 300 ml of water. The solid PGE was extracted with ether, and dried in vacuo over $CaCL_2$. Excessive chloroethyl acetate was removed by vacuum distillation. A 80% product yield was obtained.

(2) Preparation of phenylglycylhydrazide (PGH), $C_8H_{11}ON_3$

One mole of PGE and five moles of 90% hydrazine hydrate were mixed with 200 ml of absolute alcohol. The mixture was heated to reflux on a water bath for eight hours. Alcohol and excess hydrazine hydrate were removed by rotary evaporation. The remaining portion was cooled to get PGH (90% yield).

(3) Preparation of N-salicylidene phenylglycine-hydrazone, $C_{15}H_{15}O_2N_3$

PGE was combined with salicylaldehyde and absolute alcohol in equimolar quantities. This mixture was refluxed for one hour. The product was recrystallized from absolute alcohol. Product purity was maintained by repeating the cooling, filtration process three times. The final product yield was 90%.

The ligands prepared are shown in Scheme 1.

Preparation of Complexes

Reagant grade DMDCS was used; no purification was required. DPTDC was prepared in the laboratory as described. 52.7 g of dry benzene and 4.1 g of sodium metal were placed in a reaction flask. The mixture was refluxed. 6.1 g of tin tetrachloride, (BDH), in 13.3 g of chlorobenzene was slowly added through a dropping funnel into the reaction vessel and heated to reflux for two hours. Following this procedure, a precipitate was present in the mixture which was suction filtered. The remaining filtrate was cooled; this cooling resulted in additional precipitate being formed. All precipitates were collected and further purified by techniques described above. The product was colorless tetraphenyltin

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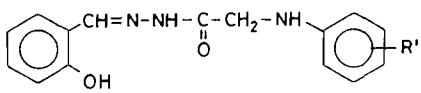


Ligand	R'	Name	Melting point (°C)
A	H	*N*-Salicylidene phenylglycine hydrazone	280–281
B	*o*-Cl	*N*-Salicylidene-*o*-chlorophenylglycyl hydrazone	89–90
C	*p*-Cl	*N*-Salicylidene-*p*-chlorophenylglycyl hydrazone	206–207
D	*o*-CH_3	*N*-Salicylidene-*o*-methylphenylglycyl hydrazone	208–210
E	*p*-CH_3	*N*-Salicylidene-*p*-methylphenylglycyl hydrazone	182–184
F	*o*-OCH_3	*N*-Salicylidene-*o*-methoxyphenylglycyl hydrazone	81–83
G	*p*-OCH_3	*N*-Salicylidene-*p*-methoxyphenylglycyl hydrazone	160–162

Scheme 1.

crystals (m.p. 230–232 °C; yield 75%). Equimolar ratios of tetraphenyltin and tin tetrachloride were refluxed on an oil bath (220 °C) for ten hours. The mixture was vacuum distilled; purification procedures were similar to those used previously. The product was diphenyltindichloride (m.p. 46–47 °C; yield 80%).

Complexes were prepared by mixing equimolar quantities of ligand with either DMDCS or DPTDC in dry benzene. The mixture was stirred vigorously for one hour. The solid was filtered, washed repeatedly with dry benzene and dried *in vacuo* over P_2O_5.

Physico-Chemical Measurements

Elemental analyses were carried out by a procedure previously described [5]. Chlorine was estimated as silver chloride; nitrogen was determined by Duma's method. Coordinated tin was estimated as its oxide and carbon using microanalytical methods.

Conductivities were measured using an Elico-CM-82 conductivity bridge (cell constant of 0.829 cm^{-1}). All conductivity measurements were done at room temperature. Samples were dissolved in dimethylformamide (DMF) at a concentration of 10^{-3} M. The infrared spectra in KBr matrix were obtained using a Carl-Zeiss UR-10 infrared spectrometer. The PMR spectra were obtained using deuterated dimethylsulfoxide (DMSO-d_6) as a solvent. Tetramethylsilane (TMS) was the internal standard. The cup-plate method [6] was used for antibacterial tests. Nutrient agar was used as the medium. The microorganisms tested were *E. coli, B. subtilis, S. aureus* and *P. vulgaris.*

Results and Discussion

Analytical Data

The dark yellow colored complexes are crystalline and insoluble in most of the organic solvents with the exception of polar solvents such as DMF and DMSO. Elemental analysis exhibit 1:1 (metal:ligand) stoichiometry (Tables I and II). This stoichiometry combined with the conductivity data suggest non-electrolytic behavior.

Infrared Data

The IR spectra exhibit two bands around 3200–3230 cm^{-1} and 1640–1650 cm^{-1} which are respectively assigned to γ(N–H) and γ(C=O) vibrations [7, 8]. A weak band in the region 2790–2810 cm^{-1} is attributed to the intramolecular hydrogen bonded OH group. The azomethine γ(C=N) stretch and phenolic γ(C–O) modes are seen respectively around 1600–1610 cm^{-1} and 1355–1360 cm^{-1}. In the complexes of DMDCS and DPTDC, only the bands due to γ(C=O) and γ(C=N) are shifted to higher regions. This suggests participation of ketonic group and azomethine nitrogen during coordination [9].

In view of the published results [10–13], the bands in the regions 830–835 cm^{-1}, 620–630 cm^{-1}, 695–720 cm^{-1} and 585–605 cm^{-1} are assigned to γ(Si–O), γ(Si–C), γ(Si–N) and γ(Si–Cl) respectively. Similarly, the regions 595–610 cm^{-1}, 565–575 cm^{-1}; 395–410 cm^{-1} and 345–350 cm^{-1} are respectively assigned [14–19] to γ(Sn–O), γ(Sn–C), γ(Sn–N) and γ(Sn–Cl) vibrations.

Proton Magnetic Resonance Data

In the spectra of ligands, signals observed at δ 11.0, 8.63 and 8.0–8.05 are attributed respectively to the protons of intramolecularly hydrogen bonded OH group, azomethine group and NH group. Phenyl protons of hydrazone ligands are seen around δ 6.8 to 7.86. A signal at δ 3.30 is due to CH_2 protons of phenylglycine residue.

In the spectra of complexes of DMDCS (**I–VII**), proton signal due to azomethine group is shifted to δ 9.0. The NH group proton is shifted to δ 8.40. These observations confirm the coordination of azomethine to the metal ion. A sharp doublet around δ 1.2–1.5, absent in the ligands, is assigned to methyl protons of DMDCS. In the spectra of complexes of DPTDC (**VIII–XIV**), the same changes in signal positions are observed. The exception being the region δ 7.5–7.56 which is assigned [22, 23] to phenyl protons of

TABLE I. Analytical and Physical Data of Complexes of Phenylglycyl Hydrazones with Dimethyldichlorosilane

Sample number	Molecular formula of complex	Found (Calculated) (%)			Molar conductivity (ohm^{-1} cm^2 mol^{-1})	Melting point (°C)
		Cl	N	C		
I	$C_{17}H_{21}N_3O_2SiCl_2$	18.08 (17.63)	11.85 (10.58)	51.45 (51.38)	49.08	205–7
II	$C_{17}H_{20}N_3O_2SiCl_3$	16.72 (24.62)	11.90 (9.71)	47.38 (47.17)	47.83	225–6
III	$C_{17}H_{20}N_3O_2SiCl_3$	16.54 (24.62)	11.08 (9.71)	47.40 (47.17)	40.26	230–2
IV	$C_{18}H_{23}N_3O_2SiCl_2$	17.38 (16.63)	11.60 (9.98)	52.70 (51.25)	35.58	185–8
V	$C_{18}H_{23}N_3O_2SiCl_2$	17.30 (16.63)	11.59 (9.98)	52.20 (51.25)	39.60	178–80
VI	$C_{18}H_{23}N_3O_3SiCl_2$	16.28 (16.02)	10.78 (9.61)	48.00 (49.43)	48.79	300–01
VII	$C_{18}H_{23}N_3O_3SiCl_2$	16.15 (16.02)	10.70 (9.61)	48.85 (49.43)	20.86	290–1

TABLE II. Analytical and Physical Data of Phenylglycyl Hydrazone Complexes with Diphenyltindichloride

Sample number	Molecular formula of complex	Found (calculated) (%)			Molar Conductivity (ohm^{-1} cm^2 mol^{-1})	Melting point (°C)
		Cl	N	Sn		
VIII	$C_{27}H_{25}N_3O_2SnCl_2$	12.05 (11.44)	6.998 (6.87)	19.50 (19.41)	52.70	250–1
IX	$C_{27}H_{24}N_3O_2SnCL_3$	16.28 (16.46)	6.427 (6.49)	18.40 (18.34)	48.60	278–80
X	$C_{27}H_{24}N_3O_2SnCl_3$	15.89 (16.46)	6.378 (6.49)	18.30 (18.34)	45.78	290–2
XI	$C_{28}H_{27}H_3O_2SnCl_2$	11.50 (11.19)	6.589 (6.71)	19.19 (18.97)	43.48	198–200
XII	$C_{28}H_{27}N_3O_2SnCl_2$	11.36 (11.19)	6.608 (6.71)	19.08 (18.97)	42.78	270–2
XIII	$C_{28}H_{27}N_3O_3SnCl_2$	10.98 (10.91)	6.423 (6.55)	18.50 (18.49)	54.60	275–6
XIV	$C_{28}H_{27}N_3O_3SnCl_2$	11.23 (10.91)	6.354 (6.55)	18.52 (18.49)	55.85	268–70

TABLE III. Antibacterial Tests for Ligands and Complexes

Sample number	Inhibition zone (mm)											
	P. vulgaris			*S. aureus*			*E. coli*			*B. subtilis*		
	a	b	c	a	b	c	a	b	c	a	b	c
1	13	–	18	11	±17	22	15	26	19	17	±18	30
2	±20	±21	21	18	±19	21	15	±15	22	±16	17	20
3	28	±24	±25	23	22	±23	24	18	±28	18	±18	26
4	±15	20	±17	±12	18	20	±15	–	19	±17	±17	22
5	23	22	24	25	19	±27	20	20	±25	±25	±19	±29
6	20	±25	20	14	±20	22	±18	20	23	±14	17	19
7	20	±26	±23	15	24	±25	±23	±25	26	18	20	±30
Phenol	29	29	29	±18	±18	±18	±25	±25	±25	18	18	18

[a]Indicates ligands A through G. [b]Indicates complexes I through VII. [c]Indicates complexes VIII through XIV. ± Indicates partial inhibition.

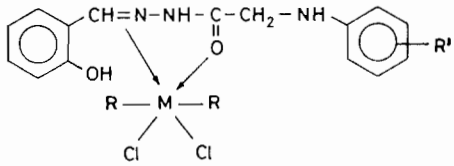
of DPTDC. In all the complexes (**I–XIV**), the unchanged signal due to *o*-hydroxy proton indicates non-reactivity of *o*-hydroxy group during coordination.

Antibacterial Tests

These data are presented in Table III. Phenol tests are included for comparison. It is observed that substituted phenylglycyl analogues have a greater zone of inhibition compared to phenylglycyl hydrazone. The para substituted compounds have better activity than the ortho isomers. The chlorosubstituted compounds are good bacteriostats. However, none of the compounds have shown better results than the standard phenol.

Silicon and tin complexes of phenylglycyl hydrazones are better bactericides than the simple ligands. The tin complexes are superior. It is repeatedly noted that the para isomers have better inhibitory action than ortho substituted compounds.

Our data suggest the following structure (**I**) for the complexes under study.



where R = CH_3 or C_6H_5 and M = Si or Sn.

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