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Synthesis and Characterization of Tolbutamide Palladium Complex by Thermal, Spectral and X-Ray Studies

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This paper deals with the synthesis and characterization of a tolbutamide(I)-palladium complex. Tolbutamide is an oral hypoglycemic agent. The conductometric titrations were conducted using monovariation method which shows the ligand:metal ratio as 2:1. Molar conductance value indicate that complex as non-ionic in nature. Analytical results agree to the molecular formula $(C_{12}H_{17}N_2O_3S)_2Pd{\cdot}2H_2O$. Structure of the complex was assigned as octahedral in which ligand molecules joining the central palladium atom and one water molecule each attached vertically with the palladium. Infrared spectral studies confirm coordination of sulfonyl oxygen on side and enolic oxygen attached from other side with the palladium ion. IR and ^1H NMR studies supports structure (II) purposed on the basis of analytical data. Magnetic susceptibility data suggested that complex is diamagnetic. Thermal studies supports the presence of ligand moities and coordinated water. X-ray diffraction data also support the structures of the complex.

Key Words: Synthesis, Characterization, Palladium-Tolbutamide complex.

INTRODUCTION

In recent years, much attention is given to the use of sulphonylureas because of their high complexing nature with essential metals. Sulphonylureas are effective for non-insulin dependent *Diabetes mellitus*[1-3]. These compounds are completely absorbed on oral administration. They are metabolized by lever and are excreted predominantly through urine.

Complexation of sulphonylureas with lighter transition metals have been studied in detail by several workers[4-11]. A perusal of available literature shows that systemic study on complexation of palladium with sulphonylureas is relatively scanty. The study of chemistry and chemical reaction of coordination compound help in establishing structure-activities relationship. It has been reported that in biological activity metal complex is more potent and less toxic as compared to the free ligand[12-17]. In view of the above and in continuation of our work, it is interesting to have an insight into the synthesis of palladium complex with tolbutamide and to diagnose various structural aspects of the isolated complex.

Herein, the synthesis and characterization of palladium complex with tolbutamide have been described[18-20].

EXPERIMENTAL

Pure tolbutamide m.p. 129 ºC (Lit. 128.5-129.5) 0.005 M and palladium dichloride 0.01 M (AnalaR grade) were prepared in purified 80 % ethanol. 20 mL of tolbutamide was diluted to 200 mL and titrated conductometrically against palladium trioxide at 27 ± 1 ºC. Results were plotted in the form of a graph which indicate ligand-metal ratio as 2:1.

Formation 2:1 (L_2:M) ratio was also confirmed by Job's method of continuous variation as modified by Turner and Anderson, using Δ conductance as index property. From these values the stability constant (log k) and free energy change (-ΔF) were also calculated[21,22] (Tables 1 and 2, Fig. 1).

Synthesis of complex: The chemicals used in this synthesis were all of analytical grade. A weighed quantity of tolbutamide (2 mol) was dissolved in minimum quantity of 80 % ethanol. The palladium solution was prepared by dissolving it separately in the same solvent. Ligand solution was added slowly with stirring into the solution of metallic salt at room temperature maintaining the pH between 6 to 6.5 by adding dilute NaOH solution. On refluxing the mixture for 3 h and on cooling, the complex separated out, which was filtered off, washed well with ethanol and finally dried in vacuum and weighed.

TABLE-1
TOLBUTAMIDE WITH PALLADIUM CHLORIDE (JOB'S METHOD); Tolbutamide: 0.005 M, Pd Cl_2: 0.005 M, Solvent: 80 % ethanol, Temperature: 27 ± 1 ºC

Mole metal ligand ratio	Conductance × 10^{-4} Mhos			Conductance × 10^{-4} Mhos	Corrected Δ conductance × 10^{-4} Mhos
	M:S C_1	S:L C_2	M:L C_3	$C_1+C_2-C_3$	
0:12	0.06	4.56	4.55	0.07	0.00
1:11	0.46	4.29	4.57	0.18	0.10
2:10	0.77	4.02	4.49	0.30	0.22
3:9	1.18	3.75	4.48	0.45	0.35
4:8	1.48	3.45	4.40	0.53	0.44
5:7	1.72	3.14	4.40	0.46	0.36
6:6	2.00	2.79	4.40	0.39	0.29
7:5	2.35	2.33	4.34	0.34	0.26
8:4	2.66	1.96	4.33	0.29	0.20
9:3	2.97	1.56	4.33	0.20	0.12
10:2	3.33	1.10	4.27	0.16	0.08
11:1	3.64	0.71	4.25	0.10	0.04
12:0	3.95	0.34	4.24	0.05	0.00

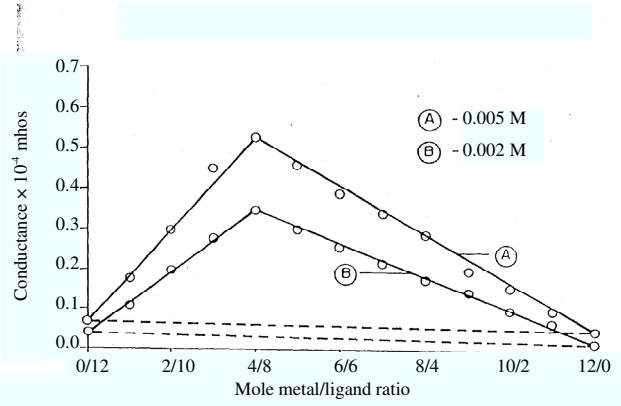
M = Metal solution, L = Ligand solution, S = Solvent.

TABLE-2
TOLBUTAMIDE WITH PALLADIUM CHLORIDE (JOB'S METHOD); Tolbutamide: 0.002 M, $PdCl_2$: 0.002 M, Solvent: 80 % ethanol, Temperature: 27 ± 1 ºC

Mole metal ligand ratio	Conductance × 10^{-4} Mhos			Conductance × 10^{-4} Mhos	Corrected Δ conductance × 10^{-4} Mhos
	C_1	C_2	C_3	$C_1+C_2-C_3$	
0:12	0.04	3.40	3.40	0.04	0.00
1:11	0.32	3.18	3.39	0.11	0.06
2:10	0.57	2.96	3.33	0.20	0.15
3:9	0.87	2.74	3.33	0.28	0.23
4:8	1.10	2.52	3.27	0.35	0.30
5:7	1.25	2.28	3.23	0.30	0.25
6:6	1.48	2.00	3.22	0.26	0.22
7:5	1.73	1.68	3.19	0.22	0.18
8:4	1.97	0.48	2.27	0.18	0.14
9:3	2.14	0.28	2.27	0.15	0.10
10:2	2.18	0.20	2.28	0.10	0.05
11:1	2.48	0.12	2.52	0.08	0.02
12:0	2.58	0.04	2.60	0.02	0.00

M = Metal solution, L = Ligand solution, S = Solvent.

Estimation of palladium in complex: The elemental analyses of the isolated complex was carried out using the reported methods[23-25] (Table-3). To the metal solution add 1 % solution of dimethyl glyoxime in 95 % ethanol at room temperature. Allow the solution to stand for 1 h and then filter the



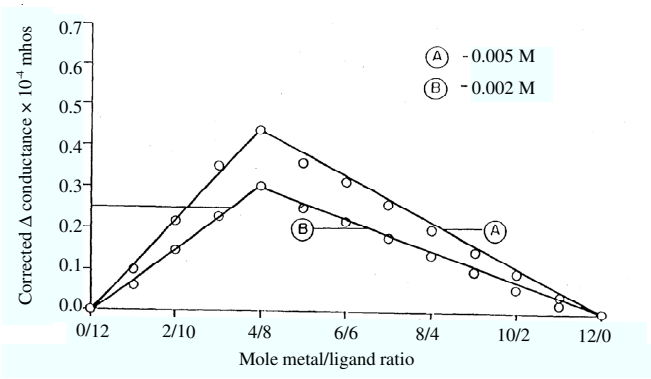


Fig. 1.

TABLE-3
PHYSICO-CHEMICAL AND ANALYTICAL DATA OF TOLBUTAMIDE-PALLADIUM COMPLEX

Composition of complex	$(C_{12}H_{17}N_2O_3S)_2Pd{\cdot}2H_2O$
Ligand metal ratio	2:1
Colour	Dark green
% Yield	64
Melting point (ºC)	134
% of metal observed (required)	15.71 (16.51)
% of carbon observed (required)	43.72 (44.69)
% of hydrogen observed (required)	5.48 (5.27)
% of nitrogen observed (required)	8.87 (8.68)
% of sulphur observed (required)	11.02 (9.93)
Stability constant (log K)	11.54 L/mol
Free energy charge (-ΔF)	-15.84 K Cal/mol

product through a weighed sintered crucible. Test the filtrate with a little of the reagent to make sure that the precipatation is complete. Washed the orange yellow precipitate of palladium dimethyl glyoximate thoroughly, first with cold water and then with hot water. Dry at 110 ºC to a constant weight, weighed as $(C_4H_7O_2N_2)_2Pd$.

RESULTS AND DISCUSSION

From stoichiometery and analytical data the composition of the complex comes out to be $(C_{12}H_{17}N_2O_3S)_2Pd{\cdot}2H_2O$, which favours 2:1 (L:M) ratio. The tentative structure assigned to the complex on the basis of analytical data is further supported by differential scanning calorimetry, (DSC), XRD and spectral data[31-36].

The infrared spectrum of the ligand as well as of the complex was recorded on B.OMEM-FTIR (USA). The infrared spectra of the ligand and the isolated complex were scanned within the rage 4000-400 cm^{-1}. The assignments of the infrared spectral bands are given in Table-4.

A strong band in the region of 3334 cm^{-1} indicating the presence of co-coordinated water which was further confirmed by thermal studies.

The proposed structure for the isolated complex is also supported by infrared absorption bands[43-47] obtained are mentioned in Table-4.

The ^{1}H-NMR sepctra of the ligand and isolated complex was reported on a Bruker AM-200 spectrometer δ-6. DMSO was used as a solvent. The other features of NMR spectrum were the aromatic proton resonances located and the presence of unresolved multiplet is suggestive of excessive deshielding

TABLE-4
SPECIFIC INFRARED ASSIGNMENTS OF TOLBUTAMIDE AND ITS PALLADIUM COMPLEX

IR Frequencies (cm^{-1})	Assignments
662 ± 5	Metal oxygen bond
715	Aromatic ring vibration
980	S=O frequency (LJB/359)
1060	C–O of chelate ring
1158 ± 5	SO_2 N frequency
1385	Six membered enolic ring structure modified in complex
1662 ± 5	C-O stretching frequency (KN/184)
2350	C=N stretching frequency
3333	Coordinated water
715 ± 5	Ar–S linkage (LJB/355)
815 ± 5	1,4-Disubstituted benzene ring frequency

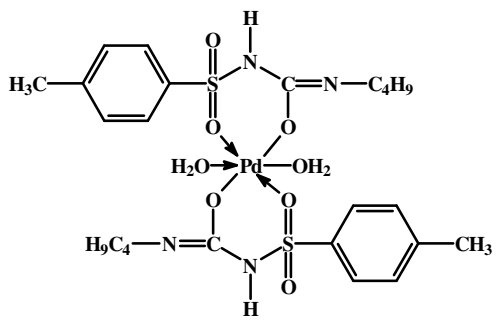
of aromatic protons.The NMR signal of enolic OH group is observed in the ligand while absent in the complex indicates the involvement of enolic OH group in complexation[37-42]. The important frequencies are recorded in the Table-5.

TABLE-5

Tolbutamide	**Tolbutamide-Palladium complex**
^{1}H NMR (200 MHz, $CDCl_3$): 10.08 (bs, 1H, -SO_2NH), 7.76 (d, 2H, *J* = 8 Hz); 7.21 (d, 2H, *J* = 8 Hz) 5.98 (t, 1H - NH - CH_2, *J* = 6 Hz); 2.95 (q, 2H, *J* = 6 Hz), 2.33 (S, 3H); 1.37-1.06 (m, 4H), 0.76 (t, 3H, *J* = 6 Hz); δ 10.8 (due to OH proton)	^{1}H NMR (200 MHz DMSO-d_6): 10.04 (6s, H-SO_2 NH); 7.70 (d, 2H-NH-CH_2); 7.18 (d, 2H, *J* = 8 Hz) 6.07 9s, H-NH-CH_2); 2.95 (m, 2H), 2.32 (S, 3H), 1.36-1.05 (m, 4H); 0.76 (t, 3H, *J* = 6 Hz)

X-ray diffractometer model Rigaku D-max/B, with 12 KW rotating anode X-ray generator was used for scanning the ligand, metal salt and respective complex. Radiation used was CuK_α (1w = 1.5418 Å). The samples were scanned in the range 10-70 ºC. Powder data was indexed using computer software. X-ray diffraction studies also confirm the complexation and formation of new bands. The number of peaks in the complex is 26 (Table-6), which indicated that the complex formed is a well knit one. Moreover the X-ray pattern of neither tolbutamide nor palladium trioxide is seen in the diffractogram of the complex. The diffractogram of the complex is characterized by an almost complete lack of periodicity suggesting its amorphons nature.

Keeping in view all these observations and results, the following structure of tolbutamide-palladium complex can be proposed for the isolated complex.



Tolbutamide-Palladium Complex

TABLE-6
X-RAY DIFFRACTION DATA OF TOLBUTAMIDE-PALLADIUM COMPLEX

Peak	2θ	D-space	I (CPS)	FWHM
1	8.714	10.1400	799	0.190
2	12.076	7.3229	549	3.620
3	12.970	6.8202	499	0.590
4	14.310	6.1845	448	0.590
5	15.470	5.7232	312	0.140
6	17.290	5.1247	365	0.550
7	19.470	4.5555	363	0.450
8	19.290	4.4536	452	0.020
9	20.816	4.2638	615	0.334
10	23.020	3.8604	355	0.478
11	24.650	3.6087	219	0.360
12	26.240	3.3935	296	1.411
13	28.090	3.1741	220	0.250
14	28.680	3.1101	292	0.290
15	30.360	2.9417	161	0.020
16	31.670	2.8230	153	0.740
17	32.930	2.7178	182	0.340
18	35.050	2.5581	151	0.310
19	35.430	2.5315	166	0.470
20	36.740	2.4442	132	0.130
21	38.620	2.3294	158	0.293
22	40.000	2.2522	147	0.290
23	42.350	2.1325	111	0.830
24	43.660	2.0715	109	0.650
25	45.850	1.9775	101	0.430
26	46.520	1.9502	107	0.330

The tentative structure of the complex is further supported from the values of ^{1}H NMR as well as from the IR frequencies. Magnetic susceptibility studies indicate that the tolbutamide palladium complexes have octahedral geometry, where 2 water molecules as ligands joining the metal atom with a frequency 3333 cm^{-1}. Moreover a peak at 815 cm^{-1} may be due to rocking vibrations of coordinated water. ν(C=N) 1482 and 2530 indicate the enolization through nitrogen nitrogen. NMR signal at δ 10.8 in the ligand while absent in the complex indicate the involvement of enolic OH group in complexation. Moreover the enolization of N1 hydrogen is not possible because it is simultaneously attracted from the groups SO_2 from ones side and C=O on the other side.

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