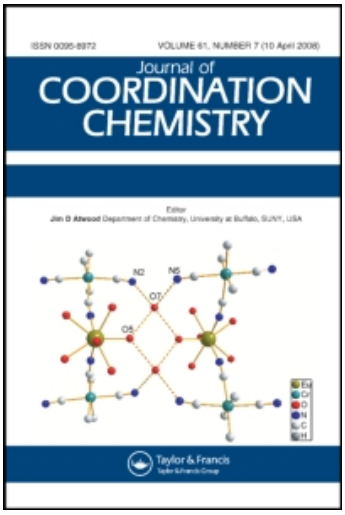

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

SYNTHESIS AND CHARACTERIZATION OF A SERIES OF LIPOPHILIC CISPLATIN ANALOGS WITH PIPERIDINE AS NONLEAVING AMINE LIGAND

S. Rounaq Ali Khan[a]; Abdul R. Khokhar[a]
[a] Department of Clinical Investigation, Box 52, The University of Texas, Houston, Texas, USA

To cite this Article Khan, S. Rounaq Ali and Khokhar, Abdul R.(2000) 'SYNTHESIS AND CHARACTERIZATION OF A SERIES OF LIPOPHILIC CISPLATIN ANALOGS WITH PIPERIDINE AS NONLEAVING AMINE LIGAND', Journal of Coordination Chemistry, 52: 2, 119 — 127
To link to this Article: DOI: 10.1080/00958970008022580
URL: http://dx.doi.org/10.1080/00958970008022580

J. Coord. Chem., 2000, Vol. 52, pp. 119–127
Reprints available directly from the publisher
Photocopying permitted by license only

SYNTHESIS AND CHARACTERIZATION OF A SERIES OF LIPOPHILIC CISPLATIN ANALOGS WITH PIPERIDINE AS NONLEAVING AMINE LIGAND

S. ROUNAQ ALI KHAN and ABDUL R. KHOKHAR*

Department of Clinical Investigation, Box 52, The University of Texas, M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030 (USA)

(Received 5 November 1999; In final form 15 February 2000)

A series of lipophilic platinum(II) complexes of the type *cis*-$[Pt(PIP)_2L_2]$ where PIP = piperidine and L = acetate, propionate, butanoate, pentanoate, hexanoate, heptanoate, octanoate, nonanoate, decanoate, undecanoate, laurate, tridecanoate, myristate, pentadecanoate, palmitate, heptadecanoate, stearate, nonadecanoate and eicosanoate has been synthesized and characterized by elemental analysis, and by infrared, ^{13}C and ^{195}Pt nuclear magnetic resonance spectroscopic techniques. The complexes have been prepared as potential antitumor agents for liposome entrapment.

Keywords: Platinum(II); Piperidine; Carboxylates; Lipophilic complexes

INTRODUCTION

Interest in platinum coordination chemistry has been greatly stimulated by the finding that *cis*-dichlorodiammineplatinum(II) (cisplatin) is a potent anticancer agent [1]. The usefulness of cisplatin is, however compromised by its propensity to cause several severe dose-limiting toxicities including nephrotoxicity, ototoxicity, neurotoxicity, nausea, vomiting and myelosuppression [2–4]. In an attempt to overcome these limitations, much effort has been devoted to develop new cisplatin analogs which are less toxic and non-cross resistant to cisplatin.

*Corresponding author. Tel.: 713 792 2837, Fax: 713 792 6759.

Consequently new platinum drugs with equal or greater antitumor activity but less toxicity have been developed by modifying the pharmacokinetics of cisplatin by replacing the labile chloro ligands with other leaving groups and extending the stable amine ligands to a series of cyclic or acyclic amines [5, 6]. Another approach to modify the therapeutic index of cisplatin analogs is by the use of drug carriers, among which liposomes are particularly attractive because they are essentially nontoxic, biodegradable lipid vesicles that can alter the distribution and bioavailability of the drug [7, 8]. This has been demonstrated in both preclinical and clinical studies using water-soluble and amphipathic antitumor drugs [9]. In fact, studies have shown that entrapping cytotoxic antitumor agents in liposomes can sometimes preserve antitumor activity and reduce toxicity [10, 11].

Lipophilic antitumor drugs have several potential advantages such as improved encapsulation efficiency and stability over water-soluble antitumor drugs for liposomal formulation [12]. Therefore, over the past few years we have undertaken the design and synthesis of highly lipid-soluble platinum complexes for liposomal entrapment [13]. Such complexes have shown high entrapment efficiency and good antitumor activity [14]. A liposomal preparation of one of these drugs L-NDDP (*cis*-bis(neodecanoate)(*trans*-1*R*,2*R*,diaminocyclohexane)platinum(II)), is currently undergoing clinical trials [15, 16].

We have successfully designed and synthesized a series of highly lipid soluble platinum(II) complexes using piperidine as the carrier ligand and carboxylate groups as leaving group. Each complex has been characterized by elemental analysis, infrared (IR) spectroscopy, ^{13}C, and ^{195}Pt nuclear magnetic resonance (NMR) spectroscopy.

EXPERIMENTAL

Chemicals

Piperidine was purchased from Aldrich Chemical Co., Milwaukee, WI. K_2PtCl_4 was purchased from Johnson Matthey, Seabrook, NH. Acetic acid, propionic acid, butanoic acid, pentanoic acid, hexanoic acid, heptanoic acid, octanoic acid, nonanoic acid, decanoic acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, palmitic acid, heptadecanoic acid, stearic acid, nonadecanoic acid, and eicosanoic acid were purchased from Aldrich Chemical Co. (Milwaukee, WI). Silver nitrate was obtained from Fisher Scientific Co., Houston, TX. All chemicals obtained from commercial sources were used as supplied.

Physical Measurements

Elemental analysis of the complexes was performed by Robertson Laboratory Inc., Madison, NJ. Infrared (IR) spectra in the range of 600–4000 cm^{-1} were recorded in KBr pellets and far-infrared spectra in the range of 150–600 cm^{-1} were recorded in polyethylene pellets on a Perkin-Elmer 2000 spectrophotometer. ^{195}Pt nuclear magnetic resonance (NMR) spectra were recorded using a Bruker 200/AF spectrometer with a 10-mm tunable probe. Chemical shifts were collected in methanol solution at room temperature and were measured relative to an external standard of 1 M Na_2PtCl_6 in D_2O at 0.00 ppm. ^{13}C-NMR spectra were recorded in CD_3OD solution, with the carbon-13 chemical shifts referenced to the CD_3OD peak at 49.0 ppm.

Preparation of Sodium Salts

Sodium acetate: 5 N NaOH (1.15 mL, 5.80 mmol) was added dropwise to acetic acid (0.348 g, 5.80 mmol) in 25 mL of ethanol. The reaction mixture was stirred for 30 min and evaporated to dryness under reduced pressure at room temperature. A colorless sticky material formed. It was dissolved in 20 mL of methanol and evaporated to dryness. To the evaporated material was added 10 ml of ether. This was evaporated to dryness, collected, and dried under vacuum. (Yield: 95%).

The sodium salts of propionic, butanoic, pentanoic, hexanoic, heptanoic, octanoic, nonanoic, decanoic, undecanoic, lauric, tridecanoic, myristic, pentadecanoic, palmitic, heptadecanoic, stearic, nonadecanoic, and eicosanoic acids were prepared in a manner similar to that mentioned above.

Synthesis of Platinum Complexes

Preparation of cis-[Pt(PIP)$_2$(acetate)$_2$] · H_2O (Complex 1)

K_2PtCl_4 (20.76 g, 50 mmol) was dissolved in 250 mL of deionized water and filtered. KI (83.0 g, 0.5 mol) in 100 mL of water was added, and the reaction mixture was stirred for 10 min. Piperidine (8.5 g, 100 mmol) was added drop-wise while stirring to get a yellow precipitate, *cis*-[Pt(PIP)$_2$I$_2$]. The stirring was continued for a further 30 min, and the precipitate was collected by filtration. This compound was dissolved in dimethylformamide and filtered. To the filtrate, excess cold water was added to get a bright yellow precipitate, *cis*-[Pt(PIP)$_2$I$_2$], which was washed with water, ethanol, and acetone and dried under vacuum (yield, 95%). *cis*-[Pt(PIP)$_2$I$_2$] (12.38 g,

20 mmol) was suspended in an aqueous solution of silver nitrate (6.72 g, 39.8 mmol) in 250 mL of water. The reaction mixture was stirred for 24 h at room temperature in the dark. The AgI precipitate was filtered off, and a solution of NaCl was added drop-wise to the filtrate with constant stirring until a yellow precipitate of *cis*-$[Pt(PIP)_2Cl_2]$ formed. The precipitate was filtered and recrystallized from dimethylformamide. The yellow crystals obtained were washed with water and acetone and dried under vacuum

TABLE I Elemental analysis of platinum(II) complexes

Complex No.	*Complex name*	*Observed (calculated)*		
		%C	*%H*	*%N*
1.	*cis*-$[Pt(PIP)_2(acetate)_2] \cdot H_2O$	33.48 (33.53)	5.89 (5.98)	5.47 (5.58)
2.	*cis*-$[Pt(PIP)_2(propionate)_2] \cdot 2H_2O$	36.19 (36.29)	6.38 (6.42)	5.22 (5.29)
3.	*cis*-$[Pt(PIP)_2(butanoate)_2]$	39.82 (40.07)	6.55 (6.67)	5.16 (5.19)
4.	*cis*-$[Pt(PIP)_2(pentanoate)_2]$	42.05 (42.32)	6.97 (7.05)	4.87 (4.93)
5.	*cis*-$[Pt(PIP)_2(hexanoate)_2]$	44.24 (44.36)	7.47 (7.39)	4.82 (4.70)
6.	*cis*-$[Pt(PIP)_2(heptanoate)_2]$	45.99 (46.22)	7.78 (7.70)	4.54 (4.49)
7.	*cis*-$[Pt(PIP)_2(octanoate)_2]$	47.83 (47.92)	7.89 (7.98)	4.23 (4.30)
8.	*cis*-$[Pt(PIP)_2(nonanoate)_2]$	49.63 (49.48)	8.02 (8.10)	3.98 (4.05)
9.	*cis*-$[Pt(PIP)_2(decanoate)_2]$	51.01 (50.91)	8.45 (8.48)	3.92 (3.96)
10.	*cis*-$[Pt(PIP)_2(undecanoate)_2]$	52.15 (52.24)	8.93 (8.70)	3.73 (3.80)
11.	*cis*-$[Pt(PIP)_2(laurate)_2]$	53.18 (53.47)	9.03 (8.91)	3.83 (3.66)
12.	*cis*-$[Pt(PIP)_2(tridecanoate)_2]$	54.55 (54.61)	9.20 (9.10)	3.59 (3.53)
13.	*cis*-$[Pt(PIP)_2(myristate)_2]$	55.39 (55.67)	9.18 (9.27)	3.53 (3.41)
14.	*cis*-$[Pt(PIP)_2(pentadecanoate)_2]$	56.79 (56.67)	9.38 (9.44)	3.17 (3.30)
15.	*cis*-$[Pt(PIP)_2(palmitate)_2]$	57.80 (57.60)	9.67 (9.60)	3.42 (3.20)
16.	*cis*-$[Pt(PIP)_2(heptadecanoate)_2] \cdot H_2O$	57.18 (57.32)	9.85 (9.77)	3.09 (3.04)
17.	*cis*-$[Pt(PIP)_2(stearate)_2]$	59.37 (59.29)	9.78 (9.88)	2.92 (3.00)
18.	*cis*-$[Pt(PIP)_2(nonadecanoate)_2]$	60.18 (60.06)	10.12 (10.01)	2.85 (2.91)
19.	*cis*-$[Pt(PIP)_2(eicosanoate)_2]$	60.97 (60.79)	10.25 (10.31)	2.67 (2.83)

PIP = piperidine.

(yield, 75%). To a suspension of *cis*-$[Pt(PIP)_2Cl_2]$ (2.32 g, 5 mmol) in 100 mL of water, an aqueous solution of Ag_2SO_4 (1.49 g, 4.8 mmol) was added. The reaction mixture was then stirred continuously in the dark for 24 h at room temperature. The yellow precipitate of AgCl was filtered off and the filtrate was evaporated to dryness under reduced pressure at 35°C. The pale yellow solid *cis*-$[Pt(PIP)_2(OSO_3)(H_2O)]$, was then dried under vacuum (yield, 80%). Sodium acetate (0.82 g, 10 mmol) was dissolved in 200 mL of methanol and *cis*-$[Pt(PIP)_2(OSO_3)(H_2O)]$ (2.39 g, 5 mmol) was added to it as a solid. The reaction mixture was stirred at room temperature for 5 days and filtered through celite. The filtrate was evaporated to dryness, redissolved in methanol, again filtered through Millipore GV fine filter paper (pore size 0.22 μM), and evaporated to dryness. A solid was obtained which was recrystallized from acetone. The final compound *cis*-$[Pt(PIP)_2(acetate)_2]$ was dried under vacuum (color, off-white; yield, 70%).

Complexes **2–19** (Tab. I) were prepared in a similar manner. They are all off-white in color and the yield is 60–65%.

RESULTS AND DISCUSSION

The steps involved in the synthesis of platinum complexes are shown in Scheme 1. *cis*-$[Pt(PIP)_2Cl_2]$ was prepared according to Dhara's method [17]. This method was adopted because it is rapid, easy and gives much higher yield than when K_2PtCl_4 is treated directly with piperidine. K_2PtCl_4 was reacted with an excess of KI to give K_2PtI_4 in solution. K_2PtI_4 was then reacted with two equivalent of piperidine to precipitate *cis*-$[Pt(PIP)_2I_2]$. The reaction of *cis*-$[Pt(PIP)_2I_2]$ with $AgNO_3$ led to the formation of *cis*-$[Pt(PIP)_2(H_2O)_2](NO_3)_2$ [17], in solution, which was further converted to their corresponding dichloride *cis*-$[Pt(PIP)_2Cl_2]$ [18] by treating it with an excess of NaCl. *cis*-$[Pt(PIP)_2(OSO_3)(H_2O)]$ [18] was prepared by the reaction of *cis*-$[Pt(PIP)_2Cl_2]$ with Ag_2SO_4. Complexes of the type *cis*-$[Pt(PIP)_2L_2]$ (L = acetate, propionate, butanoate, pentanoate, hexanoate, heptanoate, octanoate, nonanoate, decanoate, undecanoate, laureate, tridecanoate, myristate, pentadecanoate, palmitate, heptadecanoate, stearate, nonadecanoate, and eicosanoate) were prepared by the interaction of *cis*-$[Pt(PIP)_2(OSO_3)(H_2O)]$ with the sodium salts of the corresponding carboxylic acid. All the reactions were carried out in methanol because sodium salts of carboxylic acids and the final products are soluble in methanol, while the insoluble Na_2SO_4 precipitates as a very fine powder that can be easily separated by filtration. Since the sodium sulfate precipitates as a

$K_2PtCl_4 + 8KI \longrightarrow K_2PtI_4 + 4KI + 4KCl$

$K_2PtI_4 + 2(PIP) \longrightarrow cis\text{-}[Pt(PIP)_2I_2] + 2KI$

$cis\text{-}[Pt(PIP)_2I_2] + 2AgNO_3 \longrightarrow cis\text{-}[Pt(PIP)_2(H_2O)_2](NO_3)_2 + 2AgI$

$cis\text{-}[Pt(PIP)_2(H_2O)_2](NO_3)_2 + 2NaCl \longrightarrow cis\text{-}[Pt(PIP)_2Cl_2] + 2HNO_3 + 2H_2O$

$cis\text{-}[Pt(PIP)_2Cl_2] + Ag_2SO_4 \longrightarrow cis\text{-}[Pt(PIP)_2(OSO_3)(H_2O)] + 2AgCl$

$cis\text{-}[Pt(PIP)_2(OSO_3)(H_2O)] + 2NaL \longrightarrow cis\text{-}[Pt(PIP)_2L_2] + Na_2SO_4$

where L = acetate, propionate, butanoate, pentanoate, hexanoate, heptanoate, octanoate, nonanoate, decanoate, undecanoate, laurate, tridecanoate, myristate, pentadecanoate, palmitate, heptadecanoate, stearate, nonadecanoate, or eicosanoate groups.

SCHEME 1

very fine powder, filtration through celite alone is not sufficient. We used Millipore GV fine filter paper (pore size 0.22 μM) for second filtration to get a clear filtrate. Evaporation of the filtrate gave a light yellow solid, which was recrystallized form acetone at 40°C to get white crystalline compound.

Characterization of the Platinum Complexes

The complexes were characterized by elemental analysis, IR, ^{13}C-NMR and ^{195}Pt-NMR spectroscopic techniques. Elemental analysis (Tab. I) confirms the stoichiometry of two carboxylate ligands per platinum atom. Complexes of the type *cis*-[Pt(PIP)$_2L_2$] have the general structure shown in Figure 1 [19, 20].

Various other data such as IR, ^{13}C NMR and ^{195}Pt NMR (Tab. II) also support this structure. All complexes exhibited N—H stretching bands between 3165 and 3130 cm^{-1} due to the coordinated N—H of PIP. The carbonyl regions for the carboxylate complexes displayed a band characteristic of carboxylate ligands bound to the platinum in a unidentate fashion. The ν_{as}(C—O) bands appeared in the range of 1630 to 1590 cm^{-1}, while the ν_s(C—O) bands appeared in the range of 1370 to 1390 cm^{-1} [21].

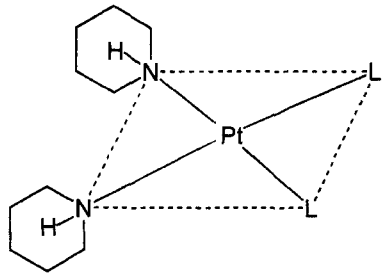

FIGURE 1 Chemical structure of *cis*-[Pt(PIP)$_2L_2$] (where PIP = piperidine and L = acetate, propionate, butanoate, pentanoate, hexanoate, heptanoate, octanoate, nonanoate, decanoate, undecanoate, laurate, tridecanoate, myristate, pentadecanoate, palmitate, heptadecanoate, stearate, nonadecanoate and eicosanoate).

TABLE II IR, ^{13}C-NMR, and ^{195}Pt-NMR data for platinum(II) complexes

	IR[a], cm^{-1}			^{13}C[b] (> C=O), *ppm*			^{195}Pt[c]
Complex No.	$\nu(N—H)$	$\nu_{as}(C—O)$	$\nu_s(C—O)$	*Ligand*	*Complex*	ΔC	*NMR, ppm*
1.	3160	1590	1370	175.4	182.3	6.9	−1758
2.	3130	1640	1380	180.7	182.5	1.8	−1740
3.	3165	1620	1390	180.7	182.5	1.8	−1754
4.	3165	1610	1380	180.6	182.6	2.0	−1752
5.	3140	1630	1380	180.7	182.6	1.9	−1743
6.	3160	1600	1385	180.5	182.7	2.2	−1688
7.	3150	1610	1390	180.6	182.7	2.1	−1691
8.	3160	1620	1370	180.6	182.6	2.0	−1696
9.	3135	1610	1380	180.6	182.6	2.0	−1692
10.	3135	1600	1385	180.6	182.6	2.0	−1745
11.	3140	1605	1390	180.6	182.7	2.1	−1743
12.	3145	1610	1380	180.7	182.6	1.9	−1736
13.	3130	1600	1370	180.5	182.6	2.1	−1737
14.	3160	1600	1370	180.6	182.7	2.1	−1750
15.	3160	1610	1390	180.5	182.7	2.2	−1729
16.	3165	1620	1385	180.7	182.7	2.0	−1693
17.	3150	1630	1375	180.5	182.6	2.1	−1696
18.	3160	1620	1380	180.5	182.8	2.3	−1693
19.	3165	1615	1385	179.8	182.8	3.0	−1698

a = recorded in KBr pellets.
b = ^{13}C-NMR spectra recorded in CD_3OD.
c = ^{195}Pt-NMR spectra recorded in methanol.
$\Delta C = \delta$[complex] − δ[ligand].

The Pt—N and Pt—O stretching frequencies in all the complexes appeared around 520 and 420 cm^{-1}, respectively.

The proton-decoupled ^{13}C-NMR spectroscopic data for the carboxylate ligands showed a single peak in the carbonyl range, 182.3–182.8 ppm (Tab. II) which was close to the values for carboxylate carbons reported for other platinum carboxylate complexes [13]. This suggests that the two

carboxylate carbons are magnetically equivalent in these complexes. The ^{13}C-NMR shifts of the free acids and platinum complexes are shown in Table II. The values of the complexation shifts ($\Delta C = \delta$[complex] − [ligand]) for all complexes were between 1.8−3.0, except for complex 1, where this value is 6.9.

Finally, ^{195}Pt NMR spectra of the platinum complexes (Tab. II) further support the structure of these complexes. The ^{195}Pt NMR resonance of these complexes in methanol showed a signal in the range of −1688 to −1758 ppm. Such chemical shifts values are characteristic for square planar platinum(II) complexes having two nitrogen and two oxygen donors [13, 22].

In summary, we have synthesized and characterized a series of new lipophilic carboxylate platinum(II) complexes with piperidine, which are fairly soluble in methanol, chloroform, *t*-butanol and other common organic solvents.

Acknowledgements

This work was supported by American Cancer Society Grant DHP No. 148 to Abdul R. Khokhar.

References

[1] B. Rosenberg, L. Vancamp, J. E. Troska and V. H. Mansour, *Nature* (*London*) **222**, 385 (1969).
[2] (a) P. L. Loehrer, S. D. Williams Sr. and L. H. Einhorn, *J. Natl. Cancer Inst.* **80**, 1373 (1988); (b) P. J. Loehrer and L. H. Einhom, *Ann. Intern. Med*, **100**, 704 (1984).
[3] I. H. Krakoff, In: M. Nicolini (Ed.), *Platinum and Other Metal Coordination Compounds in Cancer Chemotherapy* (Martinus Nijhoff Publishing, Boston, MA, 1988), p. 351.
[4] L. R. Kelland, S. J. Clarke and M. J. McKeage, Advances in Platinum Cancer Chemotherapy: *Platinum Met. Rev.* **12**, 101 (1991).
[5] Z. Guo and P. J. Sadler, In: *Metals in Medicine, Angew. Chem. Int. Ed.* **38**, 1512 (1999).
[6] (a) W. A. J. DeWaal, F. J. M. J. Meassen and J. C. Kraak, *J. Pharm. Biomed. Anal.* **8**, 1 (1990); (b) P. Umapathy, *Coord. Chem. Rev.* **95**, 129 (1989).
[7] J. N. Weinstein and L. D. Leserman, *Pharmacol. Ther.* **24**, 207 (1994).
[8] E. Mayhew and D. Papahadjopoulos, In: M. J. Ostro (Ed.), "*Therapeutic applications of liposomes. In Liposomes*" (Marcel Dekker, New York, 1983), p. 289.
[9] D. D. Lasic, *Liposomes: from physics to applications* (Elsevier Science Publishers, New York, 1993).
[10] (a) G. Lopez-Berestein, V. Fainstein, R. Hoffer, K. Mehta, N. P. Sullivan, M. Keating, M. G. Rosenblum, R. Mehta, M. Luna, E. M. Hersh, J. Reuben, R. J. Juliano and G. P. Bodey, *J. Infect. Dis.* **151**, 704 (1985); (b) G. Poste, R. Kirch and P. Bugelski, In: P. S. Sunkara (Ed.), "*Novel Approaches to Cancer Chemotherapy*" (Academic Press, Orlando, 1984).
[11] G. Kokotos, V. Theodorou, V. Constantinuo-Kokotou, W. A. Gibbons and C. Roussakis, *Bioorganic and Medicinal Chemistry Letters* **8**, 1525 (1998).
[12] C. G. Knight, In: C. G. Knight (Ed.), "*Hydrophobic pro-drugs in liposomes, Liposomes: from physical structure to therapeutic applications*" (Elsevier/North Holland Biomedical Press, 1981), p. 381.

[13] (a) A. R. Khokhar, S. Al-Baker, T. Brown and R. Perez-Soler, *J. Med. Chem.* **34**, 321 (1991); (b) S. Al-Baker, R. Perez-Soler and A. R. Khokhar, *J. Coord. Chem.* **29**, 1 (1993).
[14] (a) R. Perez-Soler, A. R. Khokhar and G. Lopez-Berestein, *Cancer Res.* **47**, 6462 (1997); (b) A. R. Khokhar, S. Al-Baker and R. Perez-Soler, *Anticancer Drug Des.* **3**, 177 (1998); (c) A. R. Khokhar, S. Al-Baker, I. H. Krakoff and R. Perez-Solar, *Cancer Chemother. Pharmacol.* **23**, 219 (1989).
[15] R. Perez-Soler, G. Lopez-Berestein, J. Lautersztain, S. Al-Baker, K. Francis, D. Macias-Kiger, M. N. Raber and A. R. Khokhar, *Cancer Res.* **50**, 4252 (1991).
[16] R. Perez-Soler, A. R. Khokhar, J. Lautersztain, S. Al-Baker, K. Francis, D. Macias-Kiger and G. Lopez-Berestein, *J. Liposome Res.* **1**, 437 (1990).
[17] S. C. Dhara, *Ind. J. Chem.* **8**, 193 (1970).
[18] S. Rounaq Ali Khan, Ilse Guzman-Jimenez, K. H. Whitmire and A. R. Khokhar, Paper submitted to *Polyhedron.*
[19] A. R. Khokhar and Q. Xu, *J. Coord. Chem.* **22**, 53 (1990).
[20] S. Al-Baker, R. Perez-Soler and A. R. Khokhar, *J. Inorg. Biochem.* **47**, 99 (1992).
[21] K. Nakamoto, "*Infrared and Raman Spectra of Inorganic and Coordination Compounds*", 3rd edn. (John Wiley & Sons, New York, 1978), p. 232.
[22] (a) J. H. Price, A. N. Williamson, R. F. Schramm and B. B. Wayland, *Inorg Chem.* **11**, 1280 (1972); (b) P. Bitha, G. O. Morton, T. S. Dunne, E. F. Delos Santos, Y. Lin, S. R. Boone, R. Haltiwanger and C. G. Pierpont, *Inorg. Chem.* **29**, 645 (1990).