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Notes

Five-Coordinate Platinum Olefin Complexes: Synthesis, ^{1}H NMR Investigations, and Crystal Structure of a Platinum η^2-Ethylene Crown Ether Complex

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Introduction

The synthesis of derivatives of the tumor-inhibiting metal complex cisplatin (INN), *cis*-diamminedichloroplatinum(II), is presently aimed at achieving an improved water-solubility, a slower decomposition rate of the substance to toxic byproducts through shielding of the platinum using bulky groups as done in carboplatin,[1] and an improved membrane permeability through an increased lipophilia of the ligands. High lipophilic and kinetically inert Pt(IV) compounds are good candidates for oral application.[2]

We used crown ethers, which, owing to their structure and their good solubility properties both in lipophilic and in hydrophilic media, meet the above mentioned requirements and are therefore suitable constituents for new complexes. Several platinum crown ether complexes are known in the literature,[3,4] but in these adducts the platinum fragment is only linked through hydrogen bonds to the macrocycle. We previously reported on a four-coordinate crown ether complex in which the platinum is involved in *covalent* bonding to the crown,[5] which shows reasonable antitumor activity. Here we describe the synthesis, magnetic properties, and X-ray structure analysis of the first example of a *five*-coordinate platinum *crown ether* complex with ethylene as the fifth ligand. The structural properties of this compound are in good agreement with those generally made for the rising number of five-coordinate platinum complexes with olefins and other sterically hindered ligands.[6]

Experimental Section

Table 1. Crystal Data for **3a**

formula	$C_{22}H_{30}N_2O_5Cl_2Pt_1$	λ(Mo Kα), Å	0.710 73
system	triclinic	Z	2
space group	$P\bar{1}$ (No. 2)	T, °C	22
cell dimens[a]		$F(000)$	656
a, Å	8.450(2)	μ, mm^{-1}	6.16
b, Å	11.044(3)	ϱ_{calc}, g cm^{-3}	1.85
c, Å	13.972(3)	R^b	2.9
α, deg	73.22(2)	$R_w{}^c$	3.3
β, deg	75.47(2)		
γ, deg	79.98(2)		
V, Å^3	1201.2		

[a] From 27 reflections, $4.3 < 2\theta < 29.4°$. [b] $R = \sum||F_o| - |F_c||/\sum|F_o|$. [c] $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$.

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients (Å$^2 \times 10^3$) for **3a**

atom	x	y	z	U(eq)[a]
Pt	1400(1)	1452(1)	2301(1)	30(1)
Cl(1)	3981(2)	1668(2)	2479(1)	44(1)
Cl(2)	−1190(2)	1267(2)	2129(2)	56(1)
N(1)	2539(6)	958(4)	813(3)	31(2)
N(2)	1431(6)	3296(4)	1079(3)	31(2)
C(1)	2804(8)	−257(5)	745(5)	37(2)
C(2)	3165(8)	−491(6)	−217(5)	46(3)
C(3)	3108(8)	476(5)	−1081(5)	41(3)
C(4)	2762(7)	1722(5)	−995(4)	33(2)
C(5)	2615(7)	1934(5)	−33(4)	29(2)
C(6)	2667(9)	−1299(5)	1694(5)	54(3)
C(7)	921(7)	4421(5)	1284(5)	35(2)
C(8)	1412(8)	5539(5)	574(5)	39(2)
C(9)	2531(8)	5481(5)	−316(5)	40(2)
C(10)	3097(7)	4296(5)	−527(4)	33(3)
C(11)	2389(7)	3221(5)	146(4)	31(2)
C(12)	−241(8)	4435(6)	2291(5)	46(3)
O(1)	2417(5)	2727(3)	−1759(3)	40(2)
O(2)	2547(6)	2476(5)	−4352(3)	55(2)
O(3)	6098(6)	2582(4)	−4555(4)	56(2)
O(4)	6069(5)	4398(4)	−3478(3)	47(2)
O(5)	4318(5)	4117(3)	−1338(3)	40(2)
C(13)	3157(8)	2696(6)	−2811(4)	39(2)
C(14)	1961(8)	2284(7)	−3283(5)	48(3)
C(15)	3876(9)	1567(7)	−4649(5)	56(3)
C(16)	5381(9)	2227(8)	−5246(6)	64(4)
C(17)	6935(9)	3689(7)	−4991(5)	56(3)
C(18)	7477(8)	4043(7)	−4194(6)	56(3)
C(19)	6531(8)	4867(6)	−2738(5)	46(3)
C(20)	5037(8)	5246(5)	−2005(5)	40(2)
C(21)	1101(9)	102(6)	3713(5)	57(3)
C(22)	458(9)	1356(6)	3849(5)	48(3)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

The ^{1}H NMR spectra were recorded on a Bruker WH 200 NMR spectrometer in chloroform-d_1 at room temperature and are referenced to external tetramethylsilane. Elemental analyses were performed in our own laboratories. All reactions were carried out under dry argon in the dark to avoid reduction of the platinum. Bidistilled water was used as solvent; the solid products within the ethylene complexes were air stable.

Zeise's salt (**2**) was prepared according to the method described by

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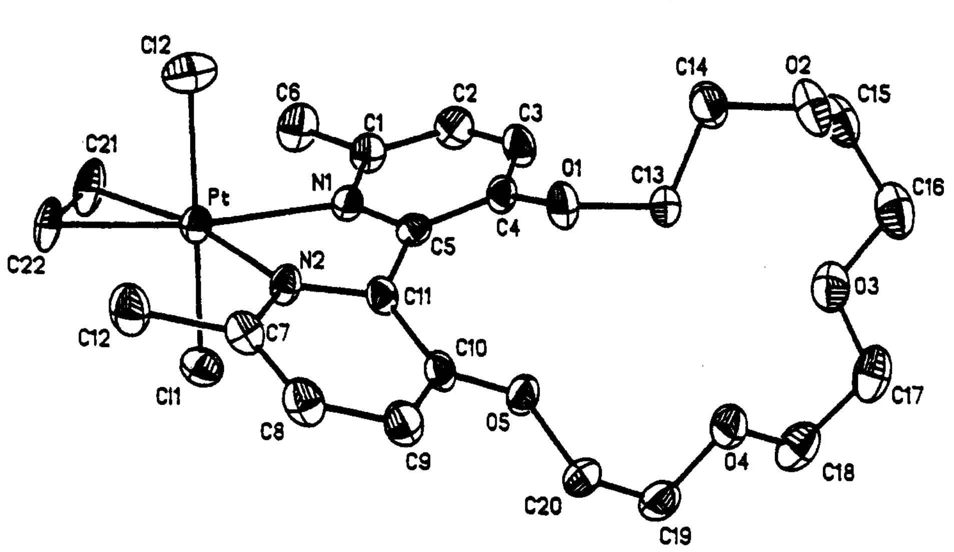
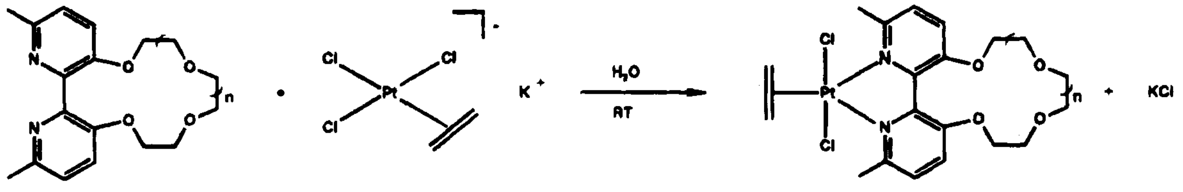


Figure 1. Molecular structure and atom-labeling scheme for 3a.

Scheme 1



n = 2 1a

n = 3 1b

2

n = 2 3a

n = 3 3b

Cramer *et al.*[8] from potassium tetrachloroplatinate, ethylene gas, and tin(II) chloride, crowns **1a,b** were synthesized according to the methods developed by Rebek.[9]

Preparation of the Platinum 6,6′-Dimethylbipyridyl Crowns (3a,b) (Scheme 1). General method: 1 mmol of the crown (**1a,b**) was dissolved in 20 mL of water and added under stirring at room temperature to a solution of 1 mmol (0.388 g) of Zeise's salt ($K[PtCl_3(C_2H_4)]* H_2O$) in 10 mL of water. A pale yellow solid precipitated immediately. Stirring was continued for 1 h and then the product was filtered off, washed with water, and dried under high vacuum. **3a.** Yield: 72.3% (mp: 161 °C). Anal. Calcd: C, 39.53; H, 4.52; N, 4.19; Cl, 10.61; Pt, 29.18. Found: C, 39.57; H, 4.62; N, 4.17; Cl, 10.76; Pt, 29.29. **3b.** Yield: 67.8% (mp: 65 °C). Anal. Calcd: C, 40.46; H, 4.81; N, 3.93; Cl, 9.95; Pt, 27.38. Found: C, 40.20; H, 4.82; N, 3.96; Cl, 10.19; Pt, 27.63.

X-ray Structure Determination. The structure was determined on a Syntex R3-diffractometer at room temperature using Mo Kα radiation (λ 0.710 73 Å) and a graphite monochromator. The crystal structure was solved by the SHELXTL PLUS program[10] and Patterson and Fourier methods. The positions of the H atoms were calculated by the option HFIX, except for ethylene H atoms. Also, they could not be located in the difference map. Crystallographic data for **3a** are collected in Table 1, atomic coordinates, bond lengths and angles are given in Tables 2 and 3.

Results and Discussion

^{1}H NMR. The NMR data of the complexes **3a,b** is summarized in Table 4. The sharp singlet of the ethylene protons, flanked by two ^{195}Pt satellites (J_{Pt-H} = 70 Hz), appears at 3.69 ppm. It is shifted upfield by 2 ppm relative to the signal of free ethylene. This value is in good agreement with those reported for other five-coordinate ethylene platinum complexes with sterically hindered chelating ligands.[6,7] The ethylene resonance remains unchanged even after prolonged heating of the complexes in CH_2Cl_2, which indicates a high stability of these substances. This stability can be explained by the fact that the aromatic methyl groups keep the platinum in the trigonal bipyramidal configuration, in which the steric hindrance to the chloride ligands is at a minimum.

Table 3. Selected Bond Distances (Å) and Angles (deg) with Esd's in Parentheses for **3a**

	Distances		
Pt−Cl(1)	2.316(2)	Pt−Cl(1)	2.310(2)
Pt−N(1)	2.240(5)	Pt−N(2)	2.248(4)
Pt−C(21)	2.089(6)	Pt−C(22)	2.087(6)
C(21)−C(22)	1.444(10)		
	Angles		
Cl(1)−Pt−Cl(2)	179.1(1)	Cl(1)−Pt(1)−C(22)	90.3(2)
Cl(1)−Pt−N(1)	89.7(1)	Cl(2)−Pt(1)−C(22)	89.4(2)
Cl(2)−Pt−N(1)	90.9(1)	N(1)−Pt−C(22)	163.7(2)
Cl(1)−Pt−N(2)	90.2(1)	N(2)−Pt−C(22)	122.7(2)
Cl(2)−Pt−N(2)	89.4(1)	C(21)−Pt−C(22)	40.5(3)
N(1)−Pt−N(2)	73.6(2)	C(5)−C(4)−O(1)	117.8(5)
Cl(1)−Pt−C(21)	88.8(2)	N(1)−C(5)−C(11)	115.3(5)
Cl(2)−Pt−C(21)	91.4(2)	C(11)−C(10)−O(5)	117.8(5)
N(1)−Pt−C(21)	123.3(2)	N(2)−C(11)−C(5)	113.9(4)
N(2)−Pt−C(21)	163.1(2)	Pt−C(21)−C(22)	69.7(3)
		Pt−C(22)−C(21)	69.8(4)

When platinum is bound, the aromatic signals of the ethylene complexes are shifted downfield by only 0.2−0.3 ppm relative to the signals of the aromatic protons of the uncomplexed macrocycles. This contrasts with the earlier reported four-coordinate complexes,[5] in which the chemical shifts of these resonances were about 1 ppm and can be explained by a greater electron density at the platinum and therefore by smaller electron-withdrawing effects of the platinum on the bipyridyl ring.

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Table 4. ^1H NMR Data[a]

	chem shift, ppm				
compd	arom protons	Ar−O−CH_2	R−CH_2−O	Ar−CH_3	C_2H_4
3a	7.42 (2H), 7.34 (2H)	4.12 (4H) m	3.64−3.87 (12H) m	3.1 (6H) s	3.69[b] (4H) s
3b	7.43 (2H), 7.36 (2H)	4.19 (4H) m	3.63−3.83 (16H) m	3.1 (6H) s	3.69[b] (4H) s

[a] Key: m = multiplet, s = singlet, Ar = aryl, and R = aliphatic group. [b] This signal shows Pt satellites, J_{Pt-H} = 70 Hz.

Description of the Structure. The crystal structure of **3a** (Figure 1) shows that the platinum is placed in the center of a trigonal bipyramid, in which the two chlorine atoms occupy the axial positions (Cl(1)−Pt−Cl(2) 179.1(1)°). The nitrogen atoms of the bipyridyl ring and the ethylene molecule are in equatorial positions (N(1)−Pt−N(2) 73.6(2)°). Both ethylene carbon atoms lie directly in the Pt−N−N plane (the distances from C(21) and C(22) out of this plane are 0.04 and 0.002 Å). The Pt−N bond distances (Pt−N(1) 2.240(5) Å, Pt−N(2) 2.248(4) Å) are slightly longer than in the comparable square planar complex,[5] and this is in agreement with other platinum complexes containing ethylene. The bending back of the ethylene protons could not be determined, because the positions of these protons could not be located in the Fourier map by this method.

The two aromatic rings are not coplanar as also reported for the *four*-coordinate platinum crown ether complex.[5] They are twisted by about 32.5°, which is caused by steric repulsions in the crown ether, especially between O(1) and O(5). So in this case binding of a transition metal to the bipyridyl unit almost brings both aromatic rings into plane with regard to the ligands **1a,b**, but not totally.

All $-OCH_2CH_2O-$ units in the crown ether moiety approximately adopt the energetically favorable gauche conformation, except for the $-O(1)C(13)H_2C(14)H_2O(2)-$ group, which is fully staggered. By contrast, the structure of the four-coordinate complex[5] exhibits an all-gauche conformation of the $-OCH_2CH_2O-$ units, resulting in a highly symmetrical crown ether part.

The complexes **3a,b** are quite soluble in chloroform, but not so in water. In order to increase the water solubility, syntheses of larger crown ether rings are under way. Interestingly, antitumor activity of other five-coordinate platinum complexes could be detected by De Renzi *et al.*[11]

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Supplementary Material Available: A listing of crystallographic data, thermal parameters, bond lengths and angles (23 pages). Ordering information is given on any current masthead page.

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