

MONONUCLEAR PLATINUM(II) CHLORIDE COMPLEXES WITH *N*-[(TRIORGANYLSILYL)ALKYL]ETHYLENEDIAMINES

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Summary

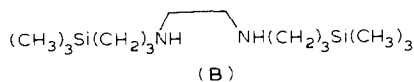
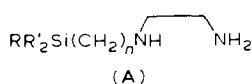
(Triorganylsilylalkyl)ethylenediamines $RR'_2Si(CH_2)_nNHCH_2CH_2NH_2$ ($R = CH_3, 4-CH_3C_6H_5, C_6H_5$; $R' = CH_3, C_6H_5$; $n = 1-3$) and $[(CH_3)_3Si(CH_2)_3NHCH_2]_2$ and the siloxane derivatives $[NH_2(CH_2)_2NH(CH_2)_3Si(CH_3)_2]_2O$ and $NH_2(CH_2)_2N(CH_2Si(CH_3)_2)O$ were allowed to react with K_2PtCl_4 or K_2PtI_4 to produce the corresponding *cis*-diaminodichloroplatinum(II) compounds in yields ranging from 63 to 97%. The complexes were characterized by C,H analyses, ^{13}C NMR and IR spectroscopy.

Introduction

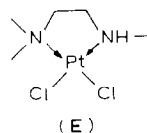
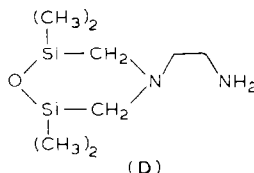
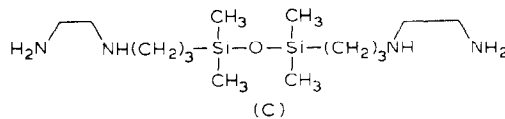
The effectiveness of *cis*-diamminedichloroplatinum(II) (Cisplatin) as a chemotherapeutic agent for the treatment of a variety of cancers with [1] or without [2,3] radiation therapy has led to attempts to synthesize "second generation" platinum complexes with therapeutic activity similar to or better than Cisplatin but with much lower toxicity. Both types of groups bonded to platinum in Cisplatin have been exchanged for other ligands; for instance, ammonia for organic amines and diamines, and chloride for carboxylates. Several of these second generation compounds (Carboplatin, Iproplatin) are in clinical trials [4]. The availability of *N*-[(tri-alkylsilyl)alkyl]ethylenediamines (**A**, **B**) and related siloxanes (**C**, **D**) [5] prompted us to investigate the reaction of tetrachloroplatinate(II) with these diamines and

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prepare a series of *N*-[(trialkylsilyl)alkyl]ethylenediaminedichloroplatinum(II) (**E**) complexes.



R	R'	n
CH ₃	CH ₃	1
CH ₃	CH ₃	3
CH ₃	C ₆ H ₅	1
CH ₃	C ₆ H ₅	3
4-CH ₃ C ₆ H ₅	CH ₃	1
C ₆ H ₅	CH ₃	1
C ₆ H ₅	CH ₃	3
C ₆ H ₅	C ₆ H ₅	1



Experimental

N-[(Triorganylsilyl)alkyl]ethylenediamines were prepared as described earlier [5]. Potassium tetrachloroplatinate(II) (Alfa) was used as received. The ¹³C NMR spectra were obtained with dimethyl sulfoxide-*d*₆ (Aldrich, 99.9 atom % D) solutions of the complexes on a JEOL PFT-100 spectrometer. DMSO-*d*₆ served as an internal lock. Chemical shifts are reported in ppm downfield from TMS. A sweep width of 6 kHz was used and 5000 to 15000 transients were collected in 8 k data points. Infrared spectra of the complexes were recorded on a Sargent-Welch 3-200 (600-4000 cm⁻¹, KBr) or a Perkin-Elmer 580B (200-600 cm⁻¹, Nujol mulls on polyethylene) IR spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

N-[(Triorganylsilyl)alkyl]ethylenediamine]dichloroplatinum(II) (**2-8**). K₂PtCl₄ (415 mg, 1.0 mmol) was dissolved in water (20 ml), and filtered. The ethylenediamine (1.1 mmol) in water (10 ml) was added to the stirred filtrate. The mixture was stirred for 24 h. The yellow precipitate was filtered, washed in sequence with water, acetone, and ether and dried in vacuo. The complexes were recrystallized from *N,N*-dimethylformamide (DMF). Yields and ¹³C chemical shifts are listed in Table 1.

[*N,N'*-Bis(1-trimethylsilylprop-3-yl)ethylenediamine]dichloroplatinum(II) (**9**). **9** was obtained (65%) as described above. Anal. Found: C, 30.07; H, 6.61. C₁₄H₃₆Cl₂N₂Si₂Pt calcd.: C, 30.32; H, 6.54%. ¹³C NMR: -1.5 (CH₃Si); 13.2 (CH₂Si); 21.2 (CCH₂C); 51.0 (CCCH₂N); 54.6 (CH₂N) ppm.

{Bis[dimethyl(4-aza-6-amino-1-hexyl)silyl]oxide}bis[dichloroplatinum(II)] (**10**). **10** was obtained (69%) as described above. Anal. Found: C, 19.64; H, 4.60. C₁₄H₃₈Cl₄N₄OSi₂Pt₂ calcd.: C, 19.40; H, 4.42%. ¹³C NMR: 0.4 (CH₃Si); 14.9 (CH₂Si); 20.5 (CCH₂C); 55.2 (CNH); 46.6 (CH₂CH₂) ppm.

N-[(Trimethylsilyl)methylethylenediamine]dichloroplatinum(II) (**1**). K₂PtCl₄ (415 mg, 1.0 mmol) was dissolved in water (20 ml) and filtered. KI (664 mg, 4.0 mmol)

TABLE 1
 YIELDS AND ^{13}C CHEMICAL SHIFTS FOR n -[(TRIORGANYLSILYL)ALKYL]ETHYLENEDIAMINEDICHLOROPLATINUM(II) COMPLEXES
 $[\text{RR}'_2\text{Si}(\text{CH}_2)_n\text{NHCH}_2\text{CH}_2\text{NH}_2]\text{PtCl}_2$ ^a

No.	R	R'	n	Yield (%)	^{13}C NMR shifts (ppm)								
					MeSi	CH_2Si	CCH_2C	CH_2NH	NHCH_2	CH_2NH_2	PhSi		
1	CH_3	CH_3	1	75	-1.1	44.6	-	-	-	59.0	46.6	-	-
2	C_6H_5	CH_3	1	97	-2.7	43.7	-	-	-	58.9	46.6	133.7	129.4
3	C_7H_7 ^b	CH_3	1	95	-2.6	43.8	-	-	-	58.9	46.6	138.7	133.6
4	CH_3	C_6H_5	1	63	-4.6	41.7	-	-	-	59.0	46.6	134.3	129.7
5	C_6H_5	C_6H_5	1	70	-	^c	-	-	-	58.1	45.2	135.9	130.2
6	CH_3	CH_3	3	96	-1.5	13.2	21.2	55.2	55.2	55.2	46.7	-	-
7	C_6H_5	CH_3	3	92	-3.0	12.2	21.1	55.2	55.2	55.2	46.6	133.4	129.0
8	CH_3	C_6H_5	3	89	-4.8	10.5	21.1	55.3	55.2	55.2	46.6	134.1	129.3

^a Elemental analyses calcd./found are within the error limits: $\text{C} \pm 0.03\%$ and $\text{H} \pm 0.2\%$. ^b $\text{C}_7\text{H}_7 = 4\text{-CH}_3\text{C}_5\text{H}_5$; ^c ^{13}C shift for CH_3 , 21.1 ppm. ^e Obscured by solvent resonances.

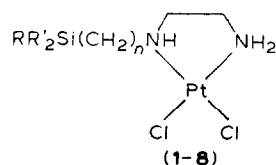
was added and the mixture stirred for 10 min. The diamine ligand (1.1 mmol), dissolved in water (5 ml), was added and the mixture stirred for 5 h. The (diamino)diodoplatinum(II) that precipitated was filtered and washed with water. The iodo complex was suspended in water (15 ml). After addition of AgNO_3 (340 mg, 2.0 mmol), the mixture was stirred for 10 h. AgI was filtered, the filtrate mixed with 0.1 M aqueous HCl until no more AgCl precipitated and the AgCl filtered. Addition of excess KCl precipitated *N*-[(trimethylsilylmethyl)ethylenediamine]dichloroplatinum(II). The product was filtered, washed with water and diethyl ether, dried in vacuo, and recrystallized from DMF. Yield and ^{13}C and proton NMR chemical shifts are listed in Table 1.

Bis(3,3,5,5-tetramethyl-1-aza-3,5-disila-4-oxacyclohex-1-ylethylamine)dichloroplatinum(II) (**11**). **11** was prepared (70%) according to the procedure and with molar quantities of reagents given above for complex **1**. Anal. Found: C, 20.01; H, 4.70. $\text{C}_8\text{H}_{22}\text{Cl}_2\text{N}_2\text{OSi}_2$ calcd.: C, 19.83; H, 4.58%. ^{13}C NMR: 2.5, 1.3 (CH_3Si); 45.2 (SiCH_2N); 54.1 (CH_2NH_2); 67.5 (NCH_2) ppm.

Results and discussion

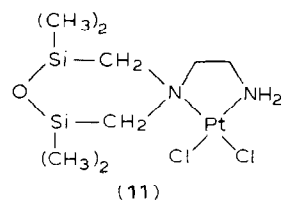
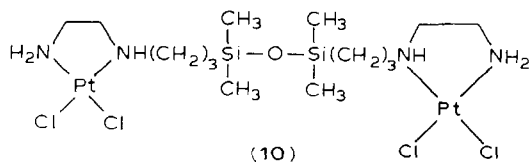
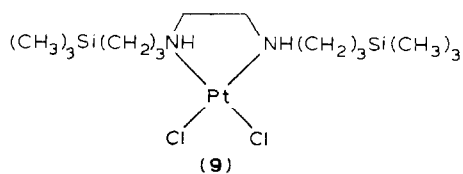
The *N*-(triorganylsilylalkyl)ethylenediamines, *N,N'*-bis(1-trimethylsilyl-3-propyl)ethylenediamines, bis[dimethyl(4-aza-6-amino-1-hexyl)silyl] oxide and (3,3,5,5-tetramethyl-1-aza-3,5-disila-4-oxa-1-cyclohexyl)ethylamine easily formed the dichloroplatinum(II) complexes **1–8**, **9**, **10**, and **11**, in which the chemotherapeutically active *cis*-(HN) $_2\text{PtCl}_2$ moiety is associated with bulky triorganylsilylalkyl groups. Complexes **2–10** were obtained as yellow precipitates in yields ranging from 63–97%. (Table 1) when aqueous solutions of the diamine were mixed with aqueous solutions of equimolar amounts of K_2PtCl_4 [6]. One recrystallization from DMF produced analytically pure complexes. Complexes **1** and **11** were prepared by the alternate method [7] using K_2PtI_4 and converting the aminediiodoplatinum(II) to the dichloro compound.

^{13}C data for the platinum complexes are listed in Table 1. All resonances are close to those found for the free ligands [5]. The CH_3Si groups in the complexes are deshielded by not more than 1.7 ppm. The effect of the Cl_2Pt group on the ^{13}C resonances is strongest for the carbons connecting the two nitrogen atoms. The resonances of these ethylene carbons are shifted downfield by 2 to 6 ppm relative to the resonances of the free ligands.



R, R': CH_3 , C_6H_5 , or $4\text{-CH}_3\text{C}_6\text{H}_4$

$n = 1, 3$



The IR spectra of **1–11** are in agreement with the postulated structures. Most complexes (exceptions: **9**, one band; **10**, 2 bands) have three bands (3110–3250 cm^{-1}) in the $\nu(\text{N–H})$ region [8] at wavenumbers lower than those characteristic of the free ligands. The $\delta(\text{NH}_2)$ mode gave a strong band between 1560 and 1580 cm^{-1} . The strong absorption at 1105 cm^{-1} can be assigned to the $\text{C}_6\text{H}_5\text{Si}$ group. A band at 1060 cm^{-1} corresponds to a skeletal mode of the diamine-Pt group involving the C–N stretch [8]. The intense, sharp band at 570 cm^{-1} is probably caused by the Pt–N stretch [9]. The two Pt–Cl stretching vibrations expected for square-planar *cis*-dichloroplatinum complexes [10] are observed in the region 297–338 cm^{-1} .

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