Syntheses, Crystal Structures, and Antitumor Activities of Dinuclear Platinum(II) Complexes, Di-μ-sulfoacetato-bis[(diamine)platinum(II)] Trihydrate

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A series of new dinuclear platinum(II) complexes have been prepared from the reaction of $[PtL_2(OH)_2]$ with sulfoacetic acid: $[PtL_2(slac)]_2 \cdot 3H_2O$, where slac=sulfoacetate dianion; L_2=1,2-diaminocyclohexane (**1a**—**1c**) or 1,2-diaminoethane (**2**) and L=isopropylamine (**3**) or ammine (**4**). They have di-μ-carboxylato bridged dinuclear zwitterionic structures in crystals. Among them, complexes (**1a**—**1c**) show significant antitumor activities against mice ieukemia L1210.

Since the discovery of broad-spectrum activities of *cis*-dichlorodiammineplatinum(II) (trade name *cis-platin*), a large number of platinum complexes have been synthesized as antitumor agents. Among them there are promising compounds such as (1,2-diaminocyclohexane)platinum(II) derivatives.[1] Many of these compounds are, however, mononuclear complexes; few oligonuclear platinum complexes have shown antitumor activity.[2]

In recent years, the formation of hydroxo-bridged di-,[3] or tri-nuclear[4] complexes has been reported in the hydrolysis reaction of *cis-platin*. Other platinum oligomers, such as "platinum blue",[5] have also received much attention. These studies emphasized a structural diversity of oligonuclear species in the platinum chemistry; antitumor activities have not been reported concerning these oligomers, except a few examples.

We describe here the syntheses, crystal structures, and antitumor activities of a series of new dinuclear platinum complexes, di-μ-sulfoacetato-bis[(diamine)-platinum(II)] trihydrate, $[Pt(diamine)(slac)]_2 \cdot 3H_2O$. Preliminary accounts of the synthesis and structural work have appeared.[6,7]

Experimental

The Three Isomers of Di-μ-sulfoacetato-bis[(1,2-diaminocyclohexane)platinum(II)], Compounds 1a—c. The compounds were synthesized by modified methods from those described in a previous publication.[8] Dinitrato[(1*R*,2*R*)-1,2-diaminocyclohexane]platinum(II), [Pt(*RR*-dach)$(NO_3)_2$] (4.30 g, 10 mmol), was dissolved in water (100 cm^3) with heating. The solution was passed through a column packed with an anion-exchange resin (Diaion SA10AOH); and additional amount of water was then passed through the column. To the combined eluate, 1.40 g of sulfoacetic acid (10 mmol) was dissolved. The reaction mixture was evaporated to ca. 30 ml

Table 1. Crystallographic Data for $[Pt(diamine)(slac)]_2 \cdot 3H_2O$

Compound	[Pt(*RR*-dach)(slac)]$_2 \cdot 3H_2O$(**1a**)	[Pt(en)(slac)]$_2 \cdot 3H_2O$(**2**)	[Pt(ipr)$_2$(slac)]$_2 \cdot 3H_2O$(**3**)
T/K	298	298	298
Formula	$Pt_2S_2O_{13}N_4C_{16}H_{38}$	$Pt_2S_2O_{13}N_4C_8H_{18}$	$Pt_2S_2O_{12}N_4C_{16}H_{22}$
Fw	948.80	832.55	916.67
Crystal system	Orthorhombic	Triclinic	Orthorhombic
Space group	$P2_12_12_1$	$P\bar{1}$	*Pbcn*
Lattice parameters/Å	a=19.186(4)	a=10.392(2)	a=18.21(3)
	b=14.577(2)	b=12.363(2)	b=17.790(4)
	c=9.876(1)	c=9.521(2)	c=19.281(2)
		α=105.56(1)°	
		β=113.08(1)°	
		γ=92.351(1)°	
V/Å^3	2762(1)	1069.1(3)	6246(1)
Z	4	2	8
D_x/g cm^{-3}	2.28	2.589	1.95
D_m/g cm^{-3}	2.25	2.59	1.96
Range of transmittance (for Absorption correction)		0.75—1.00	0.50—2.24
F(000)	1816	772	3440
μ/cm^{-1}(Mo $K\alpha$)	108.59	134.59	92.23
$(\Delta\sigma)_{max}$	0.63	0.00	0.69
$(\Delta\rho)_{max}$/eÅ^{-3}	0.88	5.47	2.92
No. Ref. Measured	3261	6590	7800
No. Ref. Observation	2455	3161	1905
R	0.033	0.042	0.078
R_w	0.031	0.045	0.081

Table 2. Positional Parameters and B(eq) for **2**

Atom	x	y	z	B(eq)	Atom	x	y	z	B(eq)
Pt(1)	0.06213(07)	0.13347(06)	0.02400(08)	1.81(2)	C(1)	−0.1765(16)	0.1927(13)	−0.2252(18)	1.7(5)
Pt(2)	0.05529(07)	0.37809(05)	0.01573(08)	1.72(2)	C(2)	−0.3101(19)	0.1476(14)	−0.3774(21)	2.5(6)
S(1)	−0.2802(05)	0.0350(04)	−0.5207(05)	2.4(1)	C(3)	−0.0453(17)	0.2953(13)	0.2273(18)	1.8(5)
S(2)	−0.2474(05)	0.3870(05)	0.3274(06)	3.1(2)	C(4)	−0.0959(19)	0.3203(14)	0.3585(24)	2.8(6)
O(1)	−0.1371(12)	0.1237(10)	−0.1467(14)	2.9(5)	C(5)	0.2612(24)	0.0133(20)	−0.0638(27)	5(1)
O(2)	−0.1195(11)	0.2918(09)	−0.1923(13)	2.2(4)	C(6)	0.3460(22)	0.0922(22)	0.0931(30)	5(1)
O(3)	−0.0005(13)	0.2053(10)	0.2011(14)	2.8(5)	C(7)	0.3163(19)	0.4330(15)	−0.0013(23)	3.1(7)
O(4)	−0.0468(12)	0.3712(10)	0.1630(13)	2.5(4)	C(8)	0.3276(20)	0.5177(17)	0.1472(24)	3.8(7)
O(5)	−0.4151(13)	−0.0022(11)	−0.6598(14)	3.9(5)	H(1)	−0.3389	0.2078	−0.4222	3.1
O(6)	−0.2353(14)	−0.0526(10)	−0.4465(15)	3.7(5)	H(2)	−0.3833	0.1193	−0.3539	3.1
O(7)	−0.1689(13)	0.0836(11)	−0.5520(15)	3.8(5)	H(3)	−0.0197	0.3691	0.4542	4.3
O(8)	−0.2863(13)	0.3843(11)	0.4583(15)	3.5(5)	H(4)	−0.1155	0.2506	0.3761	4.3
O(9)	−0.1969(16)	0.5042(13)	0.3411(19)	5.3(7)	H(5)	0.2432	−0.0591	−0.0532	6.8
O(10)	−0.3524(14)	0.3190(16)	0.1735(17)	6.8(7)	H(6)	0.3126	0.0090	−0.1278	6.8
O(11)	−0.1042(13)	0.8157(10)	0.3597(15)	3.2(5)	H(7)	0.3868	0.1575	0.0822	7.4
O(12)	0.4239(14)	0.3471(12)	0.3847(16)	4.3(6)	H(8)	0.4188	0.0562	0.1508	7.4
O(13)	0.3450(15)	0.3220(12)	0.6042(19)	5.2(6)	H(9)	0.3541	0.3680	0.0221	4.3
N(1)	0.1258(15)	0.0477(12)	−0.1442(17)	2.7(5)	H(10)	0.3669	0.4653	−0.0485	4.3
N(2)	0.2567(14)	0.1273(12)	0.1848(15)	2.4(5)	H(11)	0.2995	0.5855	0.1255	4.7
N(3)	0.1620(15)	0.3980(12)	−0.1172(17)	2.6(5)	H(12)	0.4232	0.5337	0.2256	4.7
N(4)	0.2318(14)	0.4693(12)	0.2101(16)	2.5(5)					

Table 3. Positional Parameters and B(eq) for **3**

Atom	x	y	z	B(eq)	Atom	x	y	z	B(eq)
Pt(1)	0.1827(1)	0.15906(7)	0.54245(6)	2.92(7)	N(3)	0.379(2)	0.174(2)	0.445(1)	4(2)
Pt(2)	0.3382(1)	0.21216(8)	0.53382(6)	3.45(7)	N(4)	0.388(2)	0.133(2)	0.588(1)	5(2)
S(1)	0.177(1)	0.4423(6)	0.4920(6)	5.5(7)	C(1)	0.212(2)	0.295(2)	0.467(2)	2.2(6)
S(2)	0.257(1)	0.282(1)	0.7873(6)	7.2(9)	C(2)	0.195(2)	0.368(2)	0.429(1)	2.6(7)
O(1)	0.171(2)	0.251(1)	0.482(1)	4(1)	C(3)	0.240(3)	0.262(2)	0.648(2)	2.4(7)
O(2)	0.188(2)	0.225(2)	0.627(1)	6(2)	C(4)	0.220(2)	0.316(2)	0.709(1)	2.9(7)
O(3)	0.283(2)	0.296(1)	0.479(1)	4(1)	C(5)	0.115(5)	0.059(4)	0.441(3)	10(2)
O(4)	0.304(2)	0.257(2)	0.624(1)	5(1)	C(6)	0.120(4)	0.008(3)	0.365(3)	10(2)
O(5)	0.118(3)	0.420(2)	0.532(2)	10(3)	C(7)	0.054(5)	0.099(4)	0.438(4)	13(2)
O(6)	0.245(3)	0.454(2)	0.526(2)	12(3)	C(8)	0.117(3)	0.040(2)	0.638(2)	4.0(9)
O(7)	0.161(2)	0.507(2)	0.448(2)	9(2)	C(9)	0.131(3)	−0.035(3)	0.669(2)	6(1)
O(8)	0.240(2)	0.333(2)	0.838(1)	7(2)	C(10)	0.094(3)	0.092(2)	0.691(2)	6(1)
O(9)	0.227(4)	0.212(2)	0.800(2)	14(4)	C(11)	0.460(4)	0.193(4)	0.426(3)	11(2)
O(10)	0.326(4)	0.264(4)	0.781(2)	20(6)	C(12)	0.459(4)	0.276(4)	0.417(3)	12(2)
O(11)	0.678(2)	0.020(1)	0.196(2)	9(2)	C(13)	0.479(3)	0.162(3)	0.353(3)	8(1)
O(12)	0.301(2)	0.095(2)	0.713(1)	5(1)	C(14)	0.468(4)	0.145(4)	0.608(3)	10(2)
N(1)	0.182(2)	0.100(2)	0.455(1)	5(2)	C(15)	0.478(4)	0.211(4)	0.646(3)	12(2)
N(2)	0.188(2)	0.068(2)	0.605(1)	3(1)	C(16)	0.483(4)	0.071(3)	0.653(3)	11(2)

at ca. 60 °C under reduced pressures to give the precipitate of the product, [Pt(*RR*-dach)(slac)]$_2\cdot 3H_2O$ (**1a**). Yield: 3.2 g (3.4 mmol, 67%). A crystal suitable for X-ray crystal analysis was obtained by recrystallization from water as a pale-yellow plate. In a similar manner, two other isomers of di-μ-sulfoacetato-bis[(1,2-diaminocyclohexane)platinum(II)] were synthesized. Found: **1a**: C, 20.05; H, 3.93; N, 5.99; S, 6.76%; **1b**: C, 20.04; H, 4.02; N, 5.97; S, 6.57%; **1c**: C, 20.42; H, 3.94; N, 5.84; S, 6.76%. Calcd for $C_{16}H_{38}N_4O_{13}S_2Pt_2$: C, 20.25, H, 4.04; N, 5.91; S, 6.76%.

Di-μ-sulfoacetato-bis[(1,2-diaminoethane)platinum(II)] [Pt(en)(slac)]$_2\cdot 3H_2O$, Compound 2: In a similar way, the title complex was prepared from a 12.0 g (31.6 mmol) portion of dinitrato(1,2-diaminoethane)platinum(II) and 4.5 g (32.1 mmol) of sulfoacetic acid. Yield: 9.0 g (10.7 mmol, 68%). Found: C, 11.13; H, 2.95; N, 6.52; S, 7.28%. Calcd for $C_8H_{26}N_4O_{13}S_2Pt_2$: C, 11.43; H, 3.12; N, 6.67; S, 7.63%. The sample for X-ray crystallography was recrystallized from water as a yellow needle.

Di-μ-sulfoacetato-bis[bis(isopropylamine)platinum(II)] [Pt(ipr)$_2$(slac)]$_2\cdot 3H_2O$, Compouns 3: This complex was similarly prepared as a pale yellow powder. Found: C, 19.89; H, 4.72; N, 5.83; S, 6.53%. Calcd for $C_{16}H_{46}N_4O_{13}S_2Pt_2$; C, 20.08; H, 4.85; N, 5.86; S, 6.70%. A crystal for X-ray crystallographic analysis was obtained as a orange-yellow plate by leaving the aqueous solution in a desiccator (desiccant: $CaCl_2$) for 2 months.

Di-μ-sulfoacetato-bis[diammineplatinum(II)][Pt(NH$_3$)$_2$-(slac)]$_2\cdot 3H_2O$, Compound 4: A white crystalline solid containing a small amount of green material was obtained. A green impurity could not be removed by recrystallization. Found: C, 5.87; H, 2.77; N, 7.10; S, 7.56%. Calcd for $C_4H_{22}N_4O_{13}S_2Pt_2$: C, 6.09; H, 2.81; N, 7.11; S, 8.13%.

Solubility Test. Solubility (mg cm^{-3}) in H_2O at 26 °C: **1a**:

5; **1b**: 5; **1c**: 50; **2**: 18.

X-Ray Diffraction Measurements and Structure Determination. Among a series of new complexes, three compounds, [Pt(*RR*-dach)(slac)]$_2$·3H$_2$O (**1a**), [Pt(en)(slac)]$_2$·3H$_2$O (**2**), and [Pt(ipr)$_2$(slac)]$_2$·3H$_2$O (**3**), were applied to X-ray crystal structure analysis.

The X-ray diffraction intensities were collected on a Rigaku AFC-5R goniometer with graphite-monochromatized Mo $K\alpha$ (λ=0.71069 Å) radiation (40 kV, 120 mA). Details of the X-ray structure analysis on [Pt(*RR*-dach)(slac)]$_2$·3H$_2$O were described in a previous report.[7] Crystallographic data are summarized in Table 1 and positional parameters and B(eq) for **2** or **3** are given in Table 2 or 3, respectively. The complete F_o-F_c data are deposited as document No. 9114 at the Office of the Editor of Bull. Chem. Soc. Jpn.

Antitumor Assay in vivo. A preliminary animal test against mice leukemia L1210 was carried out at The Cancer Chemotherapy Center, J. C. R., through the courtesy of Dr. Tazuko TASHIRO. There, 10^5 cells/mouse were transplanted i.p. into CDF$_1$ mice (6 mice/group), and the samples administered i.p. on days 1,5, and 9. From the mean survival times of treated (T) and control (C) mice, the T/C values were calculated as indicators of activity. Compounds **3** and **4** were not suitable for the animal test because of their instability in saline solution. Thus, comounds **1a**—**c** and **2** were subjected to the primary screening.

Results and Discussion

Syntheses. A series of complexes were synthesized by a neutralization reaction of dihydroxoplatinum(II) complexes with the equivalent mole of sulfoacetic acid (Scheme 1). Compounds **1a**—**c** and **2** were recrystallized from hot water. However, an attempt to recrystallize **3** from a hot aqueous solution led to an immediate decomposition, precipitating a black solid. The

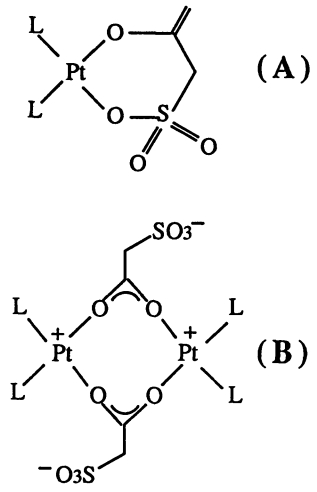

Fig. 1. Possible species of Pt(diamine)(slac); (A) Monomer, (B): Dimer.

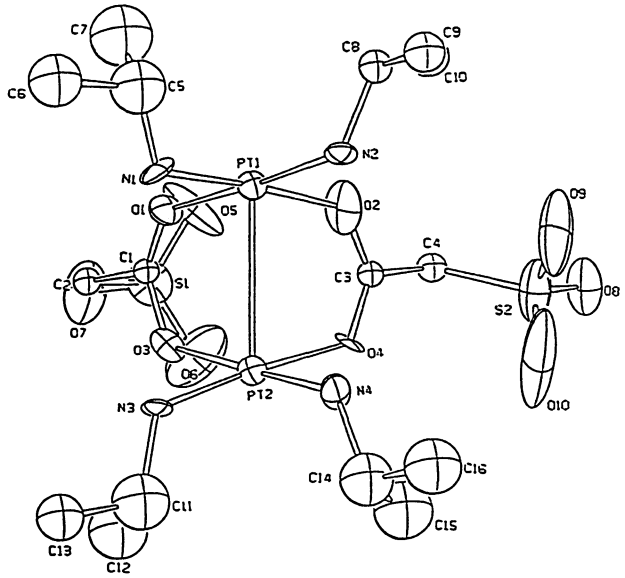

Fig. 3. Molecular structure of **3**.

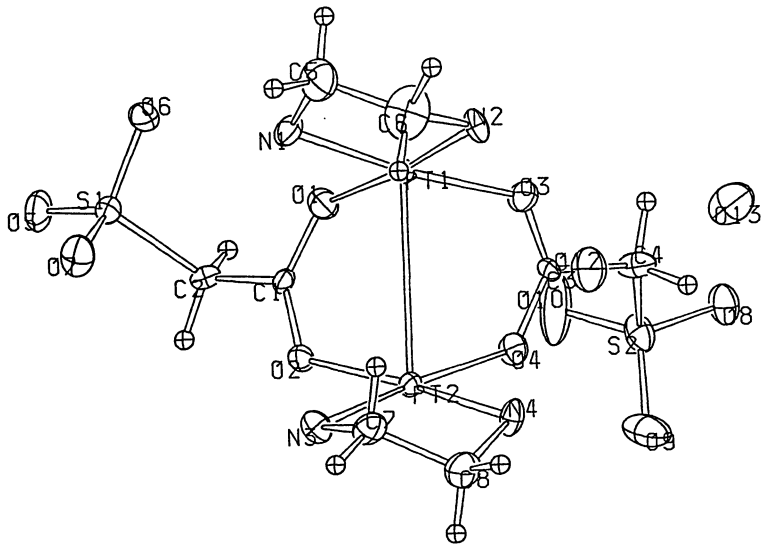

Fig. 2. Molecular structure of **2**.

$$cis\text{-}[PtL_2(NO_3)_2] \xrightarrow[\text{exchange}]{\text{anion}} \{cis\text{-}[PtL_2(OH)_2]\}$$

$$\xrightarrow[\text{acid}]{\text{sulfoacetic}} [PtL_2(slac)_2]_2 \cdot 3H_2O$$

Scheme 1. Synthetic procedure to dinuclear sulfoacetatoplatinum(II).

crystalline product **3** was, therefore, prepared by long standing of a dilute solution at room temperature in a desiccator (see Experimental). An attempt to recrystallize **4** was also unsuccessful: the colorless solution soon turned to green, presumably forming an oligomeric species.

At the beginning we planned to make mononuclear chelate compounds (Fig. 1(A)). Subsequent X-ray crystal analyses, on the contrary, revealed their dinuclear structures (Fig. 1(B)).

Molecular Structures of 1a, 2, and 3. The molecular structure of **1a** was reported in a previous paper.[7]

The molecular structures of **2** and **3** are shown in Figs. 2 and 3, respectively. The bond lengths and angles are listed in Tables 4 and 5.

As a whole, the molecular structures of **1a**, and **3** resemble each other. They are dinuclear complexes having di-μ-bridged carboxylate ligands. Because of a weak coordination of the sulfonate ligand, a mononuclear structure with six-membered chelation of the sulfoacetate ligand (Fig. 1(A)) might be less stable than the dinuclear structur (Fig. 1(B)).

The local positive charge on Pt atoms(+1) and the negative charge of SO_3 groups(−1), in a formal sense, give a zwitterionic character to the dinuclear complexes. Although the geometric requirement imposed by the bridging carboxyl group causes a relatively short Pt–Pt distances (ca. 3.0 Å), they are slightly too long to be regarded as being metal–metal bonds. The two coordination planes around Pt in a dimeric structure are not parallel to each other. The steric repulsion between the amine ligands may cause such a tilt. The Pt–Pt distances and the dihedral angles(°) between the coordination planes are summarized in Table 6 together with other dinuclear platinum(II) which have been reported so far.[9,10] As a general trend, the steric bulk of amine

Table 4. Selected Bond Lengths (Å) and Angles (°) of **2** with esd's in Parentheses

Bond length (Å)					
Pt1–Pt2	3.049(1)	Pt1–O1	2.04(1)	Pt1–O3	2.04(1)
Pt2–O2	2.06(1)	Pt2–O4	2.08(1)	S1–O5	1.45(1)
S1–O6	1.44(1)	S1–O7	1.45(1)	S1–C2	1.80(2)
S2–O8	1.46(1)	S2–O9	1.47(2)	S2–O10	1.43(1)
S2–C4	1.77(2)	O1–C1	1.26(2)	O2–C1	1.24(2)
O3–C3	1.22(2)	O4–C3	1.25(2)	C1–C2	1.50(2)
C3–C4	1.50(2)				
Bond angle (°)					
Pt2–Pt1–O1	77.3(3)		Pt2–Pt1–O3	77.4(3)	
Pt2–Pt1–N1	108.5(4)		Pt2–Pt1–N2	107.8(4)	
O1–Pt1–O3	90.5(5)		O1–Pt1–N1	91.6(5)	
O1–Pt1–N2	174.7(5)		O3–Pt1–N1	174.1(5)	
O3–Pt1–N2	92.2(5)		Pt1–Pt2–O2	78.6(3)	
Pt1–Pt2–O4	78.2(3)		Pt1–Pt2–N3	105.5(4)	
Pt1–Pt2–N4	104.4(4)		O2–Pt2–O4	93.8(4)	
O2–Pt2–N3	89.7(5)		O2–Pt2–N4	175.4(5)	
O4–Pt2–N3	175.4(5)		O4–Pt2–N4	90.2(5)	
O5–S1–O6	112.9(8)		O5–S1–O7	113.4(8)	
O6–S1–O7	111.0(8)		O5–S1–C2	105.2(8)	
O6–S1–C2	107.0(7)		O7–S1–C2	106.7(8)	
O8–S2–O9	111.6(8)		O8–S2–O10	112.6(9)	
O9–S2–O10	117(1)		O8–S2–C4	105.6(8)	
O9–S2–C4	104.1(8)		O10–S2–C4	105(1)	
Pt1–O1–C1	126(1)		Pt2–O2–C1	125(1)	
Pt1–O3–C3	129(1)		Pt2–O4–C3	125(1)	
O1–C1–O2	128(1)		O1–C1–C2	115(1)	
O2–C1–C2	117(1)		S1–C2–C1	110(1)	
O3–C3–O4	127(1)		O3–C3–C4	116(1)	
O4–C3–C4	116(1)		S2–C4–C3	117(1)	

Table 5. Bond Lengths (Å) and Angles (°) of **3** with esd's in Parentheses

Bond length (Å)					
Pt1–Pt2	2.990(5)	Pt1–O1	2.01(2)	Pt1–O2	2.00(2)
Pt1–N1	1.99(3)	Pt1–N2	2.03(3)	Pt2–O3	2.09(3)
Pt2–O4	2.01(2)	Pt2–N3	1.99(2)	Pt2–N4	1.98(3)
S1–O5	1.37(4)	S1–O6	1.41(4)	S1–O7	1.46(3)
S1–C2	1.82(3)	S2–O8	1.36(3)	S2–O9	1.39(5)
S2–O10	1.29(6)	S2–C4	1.77(3)	O1–C1	1.13(4)
O2–C3	1.23(5)	O3–C1	1.30(4)	O4–C3	1.26(5)
N1–C5	1.44(7)	N2–C8	1.51(5)	N3–C11	1.55(8)
N4–C14	1.52(7)	C1–C2	1.53(4)	C3–C4	1.56(4)
C5–C6	1.71(8)	C5–C7	1.33(9)	C8–C9	1.48(5)
C8–C10	1.45(5)	C11–C12	1.49(7)	C11–C13	1.55(7)
C14–C15	1.39(7)	C14–C16	1.59(7)		
Bond angle (°)					
Pt2–Pt1–O1	79.2(9)		Pt2–Pt1–O2	79(1)	
Pt2–Pt1–N1	97(1)		Pt2–Pt1–N2	104.2(9)	
O1–Pt1–O2	90(1)		O1–Pt1–N1	87(1)	
O1–Pt1–N2	176(1)		O2–Pt1–N1	176(1)	
O2–Pt1–N2	89(1)		N1–Pt1–N2	94(1)	
Pt1–Pt2–O3	78.1(8)		Pt1–Pt2–O4	77.5(8)	
Pt1–Pt2–N3	107.2(9)		Pt1–Pt2–N4	100(1)	
O3–Pt2–O4	90(1)		O3–Pt2–N3	89(1)	
O3–Pt2–N4	178(1)		O4–Pt2–N3	175(1)	
O4–Pt2–N4	88(1)		N3–Pt2–N4	92(1)	
O5–S1–O6	118(3)		O5–S1–O7	114(3)	
O5–S1–C2	107(2)		O6–S1–C2	105(2)	
O7–S1–C2	103(2)		O8–S2–O9	113(3)	
O8–S2–O10	117(4)		O8–S2–C4	107(2)	
O9–S2–O10	101(4)		O9–S2–C4	108(3)	
O10–S2–C4	112(3)		Pt1–O1–C1	130(3)	
Pt1–O2–C3	129(3)		Pt2–O3–C1	124(3)	
Pt2–O4–C3	129(2)		Pt1–N1–C5	116(3)	
Pt1–N2–C8	118(2)		Pt2–N3–C11	119(3)	
Pt2–N4–C14	118(4)		O1–C1–O3	128(4)	
O1–C1–C2	126(4)		O3–C1–C2	106(4)	
S1–C2–C1	109(2)		O2–C3–O4	123(3)	
O2–C3–C4	114(4)		O4–C3–C4	123(4)	
S2–C4–C3	109(2)		N1–C5–C6	113(6)	
N1–C5–C7	116(6)		C6–C5–C7	107(6)	
N2–C8–C9	109(4)		N2–C8–C10	110(4)	
C9–C8–C10	110(3)		N3–C11–C12	104(6)	
N3–C11–C13	111(5)		C12–C11–C13	104(6)	
N4–C14–C15	111(7)		N4–C14–C16	101(5)	
C15–C14–C16	113(5)				

Table 6. Comparison of Geometric Properties of Oligonuclear Platinum Diammine Complexes

Compound	**1a**	**2**	**3**	**5***	**6***	**7***
Oxid. state[a]	2.0	2.0	2.0	2.25	2.0	2.0
Distance[b]	3.044(1)	3.049(1)	2.990(5)	2.775(1)	2.877(1)	2.992(1)
γ[c]	42.9	43.2	34.1	27.4	30.0	39.6
ω[d]	1.1	13.1	3.0	22.8	20.3	24.9

a) Formal oxidation state of platinum. b) Pt–Pt distance (Å), the shortest one is listed. c) Dihedral angle (°) between the coordination planes. d) Average torsion angle (°) along Pt–Pt vector.
***5**: $[Pt_2(NH_3)_4(C_5H_4NO)_2]_2(NO_3)_5 \cdot H_2O$, Ref. 5. **6**: $[Pt_2(NH_3)_4(C_5H_4NO)_2]_2(NO_3)_4$, Ref. 9. **7**: $[Pt_2(en)_2(C_5H_4NO)_2]_2(NO_3)_4$, Ref. 10.

Table 7. Antitumor Activities against Mice Leukemia L1210

Compound		T/C(%)[a–c] Dose (mg kg^{-1}) 50	25	12.5	6.25
[Pt(*RR*-dach)(slac)]$_2 \cdot 3H_2O$	**1a**	Toxic	128P	269P(3)	230P(1)
[Pt(*SS*-dach)(slac)]$_2 \cdot 3H_2O$	**1b**	287P(2)	301P(3)	141P	
[Pt(*cis*-dach)(slac)]$_2 \cdot 3H_2O$	**1c**	^{T}191P(1)	335P(3)	383P(5)	
[Pt(en)(slac)]$_2 \cdot 3H_2O$	**2**	^{T}119	113	113	

a) T/C value over 125 was evaluated as anticancer active and indicated with P. b) The number in parentheses indicate 30 days survivors out of 6 mice. c) The weight decrease over 4 g on day 5 was judged as toxic and indicated with a superscript^T.

ligands has a good correlation with the Pt–Pt distances and dihedral angles.

Antitumor Activities. The results of animal tests against mice leukemia L1210 are listed in Table 7. Complex **2** had no detectable antitumor activity. The dach complexes **1a**—**c**, however, have shown the significant antitumor activity in this primary screening. It should thus be emphasized that the dinuclear complex has potential in the drug design of an antineoplastic platinum(II) agent.

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