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Syntheses and Antitumor Activities of 1*R*,2*R*-Cyclohexanediamine Pt(II) Complexes Containing Dicarboxylates

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New 1*R*,2*R*-cyclohexanediamine(=1*R*,2*R*-dach) Pt(II) complexes containing dicarboxylate ions, *i.e.*, ketomalonate, malate, saccharate, glutarate, diphenate, and α,β -diphenylsuccinate were synthesized and tested against leukemia L1210 *in vivo*. All of the dicarboxylato Pt(II) complexes showed relatively high antitumor activities with T/C% values of more than 200 at optimal doses. In particular, mucato and α,β -diphenylsuccinato Pt(II) complexes exhibited excellent antitumor activities with T/C% values of 348 and 369, respectively, with 3 cured mice out of six.

The dicarboxylato Pt(II) complexes were determined by elemental analyses to contain dicarboxylates : Pt : 1*R*,2*R*-dach in a ratio of 1 : 1 : 1. The molecular secondary ion mass spectra of saccharato and glutarate Pt(II) complexes indicate that these complexes exist in a binuclear form together with a mononuclear form in aqueous solution.

Keywords—dicarboxylato Pt(II) complex; 1*R*,2*R*-cyclohexanediamine Pt(II) complex; mass spectrum; binuclear complex; antitumor activity

cis-Diamminedichloroplatinum(II) (cisplatin) has been used clinically as an antitumor agent effective against testicular, ovarian, and bladder cancers, although it causes severe renal toxicity, nausea and vomiting.¹⁾ Recently, much effort has been devoted to developing more antitumor-active Pt complexes with less toxicity. New antitumor Pt complexes, diammine(1,1-cyclobutanedicarboxylato)platinum(II)²⁾ and *cis*-dichloro-*trans*-dihydroxobis(isopropylamine)platinum(IV),³⁾ are now under clinical trial.

We have reported that Pt(II) complexes containing 1*R*,2*R*-cyclohexanediamine (=1*R*,2*R*-dach) showed the highest antitumor activity against leukemia L1210 and P 388 among Pt(II) complexes containing 1*S*,2*S*- or 1*R*,2*S*-dach as a carrier ligand.^{4,5)} We have introduced D-glucuronate and D-gluconate as leaving groups into dach Pt(II) complexes in order to increase the water-solubility, since antitumor dach Pt(II) complexes containing chloride, oxalate, or malonate ions are difficult to dissolve in water. These water-soluble Pt(II) complexes showed remarkable antitumor activity against leukemia L1210 *in vivo*, but they are relatively unstable in water.^{4,6,7)}

Thus, we have designed more water-stable Pt(II) complexes by introducing dicarboxylates as leaving groups. The dicarboxylates adopted were ketomalonate, malate, saccharate and glutarate anions. Such compounds were expected to show moderate water-solubility. Diphenate and α,β -diphenylsuccinate anions were also used as leaving groups, and were expected to provide lipo-solubility.

In this paper, syntheses and antitumor activities of the dicarboxylato Pt(II) complexes of

1*R*,2*R*-dach are described and the structures of these compounds are discussed on the basis of the infrared IR and molecular secondary ion mass (SIMS) spectral data.

Experimental

Syntheses of Pt(II) Complexes

Ketomalonato- or Saccharato(1*R*,2*R*-dach)platinum(II); [Pt(ketomal)(1*R*,2*R*-dach)] or [Pt(sac)(1*R*,2*R*-dach)]—Pt(NO₃)₂(1*R*,2*R*-dach) (1.0 g) was dissolved in 10 ml of H₂O by heating, then an equimolar amount of ketomalic acid monohydrate (0.31 g) or potassium hydrogen saccharate (0.57 g) dissolved in 10 ml of H₂O was added. The resultant solution was filtered and the pH of the filtrate was adjusted to 5 with a 5% NaOH solution. After several days at room temperature, white precipitates deposited were collected by filtration, and washed with H₂O and EtOH.

Mucato(1*R*,2*R*-dach)platinum(II); [Pt(muc)(1*R*,2*R*-dach)]—Pt(NO₃)₂(1*R*,2*R*-dach) (1.0 g) was dissolved in 10 ml of H₂O by heating, then an equimolar amount of mucic acid (0.49 g) dissolved in 10 ml of H₂O with a minimum amount of a 5% NaOH solution was added. The pH of the resultant solution was adjusted to 5 with a 5% NaOH solution. After 4 d of standing at room temperature, white precipitates gradually deposited and they were collected by filtration and washed with H₂O and EtOH.

Malato- or Glutarato(1*R*,2*R*-dach)platinum(II); [Pt(mala)(1*R*,2*R*-dach)] or [Pt(glut)(1*R*,2*R*-dach)]—Pt(NO₃)₂(1*R*,2*R*-dach)(1.0 g) was dissolved in 10 ml of H₂O by heating, then 2 eq of malic acid (0.62 g) or glutaric acid (0.61 g) dissolved in 15 ml of H₂O was added. The resultant solution was adjusted to pH 5 with a 5% NaOH solution, and after 2 weeks at room temperature, white precipitates gradually deposited and were collected by filtration. They were washed with H₂O and EtOH.

Diphenato- or α,β -Diphenylsuccinato(1*R*,2*R*-dach)platinum(II); [Pt(diphen)(1*R*,2*R*-dach)] or [Pt(diphsuc)(1*R*,2*R*-dach)]—One gram of Pt(NO₃)₂(1*R*,2*R*-dach) was dissolved in 10 ml of H₂O by heating. An equimolar amount of diphenic acid (0.56 g) or diphenylsuccinic acid (0.62 g) was dissolved in 100 ml of H₂O by the addition of a 5% NaOH solution under pH 7. These solutions were mixed and the pH of the resultant solution was adjusted to ca. 7. After standing overnight at room temperature, white precipitates were collected by filtration.

All Pt(II) complexes thus synthesized were dried under reduced pressure at 60 °C. The results of elemental analyses are shown in Table I together with the yields.

Measurements

The solubilities of the dicarboxylato Pt(II) complexes in H₂O were measured by suspending them in 5 ml of H₂O with constant agitation at 37 °C. After incubation for 2 d, the suspensions were filtered and the Pt contents of the filtrates were determined with a Shimadzu AA-607G flameless atomic absorption spectrometer.

MS spectrometry—SIMS spectrometry was performed using a double focusing Hitachi M-80 B mass spectrometer fitted with a high-field magnet (M-8089), SIMS source and M-0101 data system. Operating conditions were; primary ion, Xe⁺; accelerating voltage, 8 kV (primary) and 3 kV (secondary); source temperature, 35 °C. Samples were dissolved in H₂O in the concentration range of 0.9–3.4 mg/ml. Each sample solution (0.5–1 μ l) was loaded on a silver target. About 1 μ l of matrix material was added to the sample on the target. Calibration was achieved by using glycerol-derived oligomers. Linked-field scanning was performed in the B/E mode with a Hitachi linked-scan unit (M-8084).

TABLE I. Elemental Analyses of 1*R*,2*R*-Cyclohexanediamine Pt(II) Complexes Containing Dicarboxylates

Complexes	Found (%)			Calcd (%)			Yield (%)
	C	H	N	C	H	N	
Pt(ketomalonato)(dach)·4H ₂ O	21.93	4.32	5.92	21.73	4.46	5.63	30
Pt(<i>dl</i> -malto)(dach)·3H ₂ O	24.12	4.76	5.61	24.24	4.88	5.65	50
Pt(<i>d</i> -malato)(dach)·3H ₂ O	24.09	4.77	5.40	24.24	4.88	5.65	60
Pt(<i>l</i> -malato)(dach)·2.5H ₂ O	24.52	4.76	5.94	24.70	4.77	5.77	50
Pt(glutarato)(dach)·2H ₂ O	27.76	4.69	6.04	27.78	5.09	5.89	21
Pt(saccharato)(dach)·H ₂ O	26.95	4.60	5.15	26.92	4.52	5.23	67
Pt(mucato)(dach)·3H ₂ O	25.10	4.81	5.03	25.22	4.94	4.90	58
Pt(diphenato)(dach)·3H ₂ O	39.88	4.36	4.94	39.80	4.68	4.64	30
Pt(α,β -diphenylsuccinato)(dach)·3H ₂ O	41.96	4.81	4.72	41.84	5.11	4.43	48

dach = 1*R*,2*R*-cyclohexanediamine.

Evaluation of Antitumor Activity

Antitumor activities of the Pt(II) complexes were tested according to the protocols for routine screening at the National Cancer Institute (Bethesda, Md.). L1210 cells (10^5) were transplanted intraperitoneally into CDF₁ mice (each group consisted of 6 mice) on day 0, and the samples were given intraperitoneally on days 1, 5, and 9. From the mean survival times (d) of treated (T) and control (C) mice, T/C% values were calculated. Samples with T/C% values that exceeded 125 were evaluated as antitumor-active. A dose at which the T/C% value was less than 85% was designated as a toxic dose.

Results and Discussion

Judging from the elemental analyses shown in Table I, these dicarboxylato Pt(II) complexes were composed of the dicarboxylates, 1*R*,2*R*-cyclohexanediamine (= 1*R*,2*R*-dach), and Pt(II) in a ratio of 1 : 1 : 1. Based upon the infrared spectral data shown in Table II, the dicarboxylates and dach coordinated through the carboxyl and amino groups, respectively. For example, the IR spectrum of Pt(sac)(1*R*,2*R*-dach) exhibited absorption peaks at 3200 and 3100 cm^{-1} due to the asymmetric and symmetric stretching frequencies of the amino groups, being shifted toward higher frequencies compared with those of the hydrogen chloride salt of 1*R*,2*R*-dach. Two strong peaks at 1610 and 1340 cm^{-1} were assigned to asymmetric and symmetric stretching frequencies of the carboxyl groups, respectively, being shifted toward the lower frequency side due to the coordination to the central metal ions, compared with those of saccharic acid.

Other dicarboxylato Pt(II) complexes showed IR spectral behavior similar to that of Pt(sac)(1*R*,2*R*-dach), exhibiting coordination of the carboxyl and amino groups.

Solubility of the Dicarboxylato Pt(II) Complexes in Water

Expecting water-solubility, we had chosen saccharic and mucic acids, which have four hydroxyl groups, as leaving groups, but in fact the solubilities of the complexes in H₂O were rather poor (3.38 and 2.58 mg/ml at 37 °C, respectively, as shown in Table III).

However, the glutarate Pt(II) complex has a solubility of 2.91 mg/ml in H₂O, indicating that the water-solubility is not proportional to the numbers of hydroxyl groups.

The diphenato and α,β -diphenylsuccinato (mixture of *meso* and racemic forms) Pt(II) complexes were hardly soluble in either H₂O or organic solvents such as chloroform benzene, and ethanol.

TABLE II. Vibrational Frequencies of Dicarboxylato Pt(II) Complexes of 1*R*,2*R*-Cyclohexanediamine (cm^{-1})

Complexes	ν_{OH}	ν_{NH}	ν_{CH}	$\nu_{\text{C=O}}$	$\nu_{\text{C-O}}$
Pt(ketomalonato)(dach)	3400 (s, br)	3200 (s) 3100 (s)	2920 (m) 2850 (w)	1610 (s)	1350 (s)
Pt(malato)(dach)	3400 (s, br)	3200 (s, br)	2920 (m) 2850 (w)	1600 (s)	1370 (s)
Pt(glutarato)(dach)	3400 (s, br)	3200 (s) 3100 (s)	2920 (m) 2850 (w)	1600 (s)	1350 (s)
Pt(saccharato)(dach)	3400 (s, br)	3200 (s) 3100 (s)	2920 (m) 2850 (w)	1610 (s)	1340 (s)
Pt(mucato)(dach)	3400 (s, br)	3200 (s) 3100 (s)	2920 (m) 2850 (w)	1610 (s)	1340 (s)
Pt(diphenato)(dach)	3400 (s, br)	3200 (s) 3100 (s)	2920 (m) 2850 (w)	1600 (s)	1350 (s)
Pt(α,β -diphenylsuccinato)(dach)	3400 (s, br)	3250 (s)	2920 (m) 2850 (w)	1600 (s)	1340 (s)

Abbreviations: s, m, w, and br mean strong, medium, weak, and broad.

TABLE III. Solubilities of Dicarboxylato Pt(II) Complexes in H₂O (37 °C)

Complexes	Solubility (mg/ml)
Pt(ketomalonato)(dach)	2.7
Pt(<i>l</i> -malato)(dach)	0.9
Pt(glutarato)(dach)	2.9
Pt(saccharato)(dach)	3.4
Pt(mucato)(dach)	2.6
Pt(diphenato)(dach)	0.1
Pt(α,β -diphenylsuccinato)(dach)	0.2

TABLE IV. Antitumor Activities of Dicarboxylato Pt(II) Complexes of 1*R*,2*R*-Cyclohexanediamine against Leukemia L1210

Complexes	100	50	Dose (mg/kg)			
			25	12.5	6.25	3.12
			T/C %			
Pt(ketomalonato)(dach)	0	0	229 (2)			
Pt(<i>dl</i> -malato)(dach)		177 (1)	236 (1)	250 (1)		
Pt(<i>d</i> -malato)(dach)		78 ^a	293 (1)	210		
Pt(<i>l</i> -malato)(dach)		193 (1)	273 (1)	214		
Pt(glutarato)(dach)		238 (1)	176	172		
Pt(saccharato)(dach)	134 ^a	231 (2)	302 (1)	210 (1)	134	118
Pt(mucato)(dach)	112 ^a	348 (3)	247	240	148	132
Pt(diphenato)(dach)		238 (1)	208 (2)	133		
Pt(α,β -diphenylsuccinato)(dach)		176	369 (3)	145		
Pt(1,1-cyclobutanedicarboxylato)(dach)			235	177	125	

Underlined figures indicate significant antitumor activity (T/C % ≥ 125). ^a Indicates toxicity. 10⁵ cells/mouse were transplanted i.p. into CDF₁ mice (6 mice/group), and the test samples were administered i.p. on days 1, 5 and 9.

Antitumor Activity

The antitumor activities of the dicarboxylato Pt(II) complexes of 1*R*,2*R*-dach were tested against leukemia L1210, and the results are shown in Table IV, together with those of 1,1-cyclobutanedicarboxylato(1*R*,2*R*-cyclohexanediamine)platinum(II). All of the Pt(II) complexes exhibited relatively high antitumor activities as compared with cisplatin, with T/C % values of more than 200 at the optimal doses. The optical isomers of malic acids as leaving groups did not show much difference as far as antitumor activities were concerned, but Pt(*d*-malato)(1*R*,2*R*-dach) showed toxicity at the dose of 50 mg/kg, while *l*-malato Pt(II) did not. However, mucato and saccharato are diastereomers and their Pt(II) complexes showed different antitumor activities with T/C % values of 348 and 302 at the optimal doses, respectively.

Among the dicarboxylato Pt(II) complexes examined, α,β -diphenylsuccinato Pt(II) complex showed the highest antitumor activity against L1210 with a T/C % value of 369, and gave three cured mice out of six.

MS Spectra by Molecular SIMS Method

The dicarboxylato Pt(II) complexes were suspended in H₂O and continuously stirred overnight at room temperature. The suspensions were filtered, portions of the filtrates were mixed well with glycerol, and the mixtures were introduced to a MS spectrometer as samples. Among 7 dicarboxylato Pt(II) complexes examined, only 3 complexes, *i.e.*, saccharato,

Fig. 1. Structure of $[\text{Pt}(\text{ox})(1R,2R\text{-dach})]$ Determined by X-Ray Anomalous Scattering Techniques

TABLE V. MS Spectral Data for Dicarboxylato Pt(II) Complexes of 1R,2R-Cyclohexanediamine

Complexes	m/z values and relative ion abundances (%)		
	$[\text{PtLC}_1\text{C}_2]^+$	$[\text{Pt}_2\text{LC}_3\text{C}_1]^+$	$[\text{Pt}_2\text{L}_2\text{C}_1\text{C}_2]^+$
$\text{Pt}(\text{ox})(1R,2R\text{-dach})$	401 (24)	707 (0.6)	797 (0.4)
	399 (79)	706 (0.7)	796 (0.5)
	398 (100)	705 (0.8)	795 (0.5)
	397 (82)	704 (0.7)	794 (0.4)
		703 (0.4)	793 (0.2)
$\text{Pt}(\textit{l}\text{-mala})(1R,2R\text{-dach})$	443 (130)	751 (7)	
	442 (100)	750 (14)	
	441 (120)	749 (17)	
		748 (11)	
$\text{Pt}(\text{sac})(1R,2R\text{-dach})$	519 (67)	827 (28)	1037 (30)
	518 (100)	826 (31)	1036 (31)
	517 (80)	825 (45)	1035 (60)
		824 (31)	1034 (43)
		823 (12)	1033 (18)
$\text{Pt}(\text{glut})(1R,2R\text{-dach})$	441 (94)	749 (13)	881 (9)
	440 (100)	748 (13)	880 (11)
	439 (100)	747 (12)	879 (11)
		746 (4)	878 (8)
		745 (3)	877 (5)

L denotes dicarboxylate anions. C_1 represents neutral 1R,2R-dach ($\text{C}_6\text{H}_{14}\text{N}_2$). C_2 denotes protonated 1R,2R-dach ($\text{C}_6\text{H}_{15}\text{N}_2$). C_3 denotes deprotonated 1R,2R-dach ($\text{C}_6\text{H}_{13}\text{N}_2$). Numbers in parentheses indicate ion abundances in per cent, taking mononuclear ions containing ^{195}Pt as a standard.

glutarato, and malato Pt(II) exhibited MS spectra. The other complexes did not show the spectra due to their low solubilities in H_2O .

Pt(oxalato)(1R,2R-dach)

As a standard sample, $\text{Pt}(\text{ox})(1R,2R\text{-dach})$ (ox = oxalate) was taken since it is stable in an aqueous solution. Its absolute structure was determined by X-ray diffraction analyses to be square planar and monomeric, as shown in Fig. 1.⁸⁾ $\text{Pt}(\text{ox})(1R,2R\text{-dach})$ exhibited MS spectrum with 4 peaks at m/z values of 401, 399, 398, and 397; such a pattern is expected for a complex containing naturally abundant Pt isotopes, i.e., ^{198}Pt (7.2%), ^{196}Pt (25.2%), ^{195}Pt (33.8%) and ^{194}Pt (32.9%). These peaks were assigned to the molecular ion of $[\text{Pt}(\text{ox})(1R,2R\text{-dachH})]^+$ (dachH denotes protonated dach). The peaks due to the less abundant Pt isotopes, i.e., ^{190}Pt (0.01%) and ^{191}Pt (0.8%), were not observed in the spectrum.

In addition, the oxalato complex showed two groups of peaks around m/z values of 705 and 795 with very low intensities, each of which consists of 5 peaks. Their patterns were characteristic of binuclear Pt complexes. Since the solubility of the complex in H_2O was limited, the peaks due to the less abundant Pt isotopes, i.e., ^{190}Pt , ^{191}Pt , and ^{198}Pt were not observed. These peaks may be assigned to binuclear complexes, where an oxalate ion bridges two Pt ions through the carboxyl groups. The mass number of $[\text{Pt}_2(\text{ox})_2(1R,2R\text{-dach})]$

$(1R,2R\text{-dachH})^+$ is 795 and that of $[^{195}\text{Pt}_2(\text{ox})(1R,2R\text{-dach})(1R,2R\text{-dach-H})]^+$ (dach-H denotes deprotonated dach) is 705. These binuclear Pt complexes may be formed by recombinations of fragments, judging from their extremely low intensities.

The MS spectral data of oxalato Pt(II) complex are summarized in Table V, together with those of other dicarboxylato Pt(II) complexes; relative peak intensities are expressed in per cent taking the corresponding mononuclear species containing ^{195}Pt as a standard.

Pt(sac)(1*R*,2*R*-dach)

In contrast to the oxalato Pt(II) complex, Pt(sac)(1*R*,2*R*-dach) gave a somewhat different MS spectrum as shown in Fig. 2. Three peaks were observed at m/z values of 517, 518, and 519, which may be assignable to mononuclear $[\text{Pt}(\text{sac})(1R,2R\text{-dach})(1R,2R\text{-dachH})]^+$ containing ^{194}Pt , ^{195}Pt , and ^{196}Pt isotopes, respectively. In the higher mass region, two groups of peaks each consisting of five peaks were also observed around m/z values of 1035 and 825 with high relative intensities, and these may be assignable to binuclear Pt complexes. The peaks at m/z values of 1033, 1034, 1035, 1036, 1037 correspond to $[\text{Pt}_2(\text{sac})_2(1R,2R\text{-dach})(1R,2R\text{-dachH})]^+$ and the peaks at m/z values of 823, 824, 825, 826, and 827 are assignable to $[\text{Pt}_2(\text{sac})(1R,2R\text{-dach})(1R,2R\text{-dach-H})]^+$, which may be formed by cleavage of a saccharate ion from the former complex. In both binuclear complexes, saccharate ions bridge two different Pt ions.

Fragmentation of a binuclear complex, *i.e.*, $[\text{Pt}_2(\text{sac})_2(1R,2R\text{-dach})(1R,2R\text{-dachH})]^+$, may occur as shown in Fig. 3, where a saccharate anion was cleaved first with resultant

Fig. 2. MS Spectrum of Pt(sac)(1*R*,2*R*-dach) Complex Obtained by the Molecular SIMS Method

Figures with *a*) indicate peaks due to background glucerol. Underlined figures denote the most intense peaks due to the dachcharato Pt(II) complex.

Fig. 3. Proposed Fragmentation of $\text{Pt}(\text{sac})(1R,2R\text{-dach})$ Complex and the Positions of Bond Breakages

formation of $[\text{Pt}_2(\text{sac})(1R,2R\text{-dach})(1R,2R\text{-dach-H})]^+$. The latter ion was decomposed into the mononuclear $[\text{Pt}(\text{sac})(1R,2R\text{-dachH})]^+$ with further dissociation of a sac ion. However, there is a possibility that the binuclear complex dissociates into $[\text{Pt}_2(\text{sac})(1R,2R\text{-dach})_2]$ and $[\text{Pt}(\text{sac})(1R,2R\text{-dach})]$ in a dilute aqueous solution, and these complexes are expected to show MS spectra similar to that illustrated in Fig. 2. In reality, both processes may contribute to the observed MS spectrum.

At this stage we can not distinguish whether the solid saccharato $\text{Pt}(\text{II})$ complex exists as a binuclear form or a mixture of mono- and binuclear forms, since in both cases similar spectra will be obtained. However, considering its low solubility in H_2O and the very slow formation of its precipitates in the process of synthesis, we speculate that saccharato $\text{Pt}(\text{II})$ complex exists as a binuclear form.

$\text{Pt}(\text{glut})(1R,2R\text{-dach})$

Glutarato $\text{Pt}(\text{II})$ complex exhibited a MS spectrum similar to that of saccharato $\text{Pt}(\text{II})$ complex, except that the peak intensities around m/z values of 879 and 747 (originated from the binuclear glutarato $\text{Pt}(\text{II})$ complexes) were lower than those of saccharato complex. Moreover, the peak intensities of $[\text{Pt}_2(\text{glut})(1R,2R\text{-dach})(1R,2R\text{-dach-H})]^+$ were less than those of $[\text{Pt}_2(\text{glut})_2(1R,2R\text{-dach})(1R,2R\text{-dachH})]^+$, indicating a lower abundance of the former complex in an aqueous solution. The most intense peaks were observed at m/z values of 439, 440, and 441, which were assigned to the mononuclear $[\text{Pt}(\text{glut})(1R,2R\text{-dachH})]^+$ ions.

$\text{Pt}(l\text{-mala})(1R,2R\text{-dach})$

In the case of the *l*-malato $\text{Pt}(\text{II})$ complex, its MS spectrum lacked the expected peaks at m/z values around 883, which may be assignable to binuclear species, *i.e.*, $[\text{Pt}_2(l\text{-mala})_2(1R,2R\text{-dach})(1R,2R\text{-dachH})]^+$, but only exhibited four peaks around m/z values of 749, which may originate from $[\text{Pt}_2(l\text{-mala})(1R,2R\text{-dach})(1R,2R\text{-dach-H})]^+$. The mononuclear species showed three peaks at m/z values of 441, 442, and 443, whose intensities were not proportional to the natural abundances of Pt isotopes; this may be due to over-lapping background peaks.

These SIMS spectral data give very important information as to the species existing in aqueous solutions. In the case of saccharato $\text{Pt}(\text{II})$ complex, the binuclear species is relatively abundant in an aqueous solution (comparable to the mononuclear species). From the MS spectral data we could not confirm whether the saccharato $\text{Pt}(\text{II})$ complex exists as a

mononuclear or binuclear species in the solid state, but in an aqueous solution it may coexist in three states, *i.e.*, $[\text{Pt}_2(\text{sac})_2(1R,2R\text{-dach})_2]$, $[\text{Pt}_2(\text{sac})(1R,2R\text{-dach})_2]$, and $[\text{Pt}(\text{sac})(1R,2R\text{-dach})]$, of which the last species is the most stable. The *l*-malato Pt(II) complex did not exist in the form of $[\text{Pt}_2(l\text{-mala})_2(1R,2R\text{-dach})_2]$, which may be unstable in an aqueous solution and may dissociate mainly into $[\text{Pt}(l\text{-mala})(1R,2R\text{-dach})]$ and partly into $[\text{Pt}_2(l\text{-mala})(1R,2R\text{-dach})_2]$. These SIMS spectral data offer valuable information as to the species of the dicarboxylato Pt(II) complexes existing in aqueous solutions, and may help to identify the antitumor-active Pt(II) species.

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