Linkage Isomerism Dependent on Solvent and Temperature. Synthesis and Structural Properties of Diamineplatinum(II) Complexes of Allyl- and Diallylmalonate Ligands

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The linkage isomerism between (O,O′)- and (O,alkene)-chelates has been investigated for the complexes A_2PtL_2 (A_2 = 2,2-dimethyl-1,3-propanediamine (DMPDA), *trans*-(±)-1,2-diaminocyclohexane (DACH); L_2 = allylmalonate (AM), diallylmalonate (DAM)). The crystal structures of (DMPDA)Pt(AM)·$2H_2O$ (tetragonal $P4_2/m$, a = 13.614(3) Å, b = 13.614(3) Å, c = 8.451(4) Å, V = 1566.3(9) Å^3, Z = 4, R = 0.0472) and (DMPDA)Pt(DAM)·$2H_2O$ (monoclinic $P2_1/n$, a = 11.021(3) Å, b = 8.996(2) Å, c = 18.765(7) Å, β = 106.92(3) °, V = 1780.0(9) Å^3, Z = 4, R = 0.0531) have been solved. Each platinum atom adopts a typical square planar arrangement with two nitrogen atoms in cis positions. However, surprisingly, the AM anionic ligand is coordinated to the platinum atom via (O,O′)-chelation mode through its two carboxylate groups with the alkene group uncoordinated in the solid state, breaking the hard/soft rule. The tetradentate DAM ligand is chelated to the platinum atom through one carboxylate and one alkene group resulting in (O,alkene)-chelation mode with another uncoordinated carboxylate and alkene group. Multinuclear (^{1}H, ^{13}C, and ^{195}Pt) NMR studies clearly disclose that the linkage isomerism depends on the solvents employed. Both allyl- and diallylmalonate ligands are chelated exclusively to the platinum(II) atom via (O,O′)-mode in dimethylformamide or Me_2SO solution whereas only (O,alkene)-chelation mode is observed in an aqueous solution. At room temperature, the complexes both of the AM and DAM ligands exist in methanol as a mixture of (O,O′)- and (O,alkene)-modes. Furthermore, interconversion between the two isomers occurs reversibly depending on temperature: the (O,alkene)-chelate is predominant at low temperatures while the (O,O′)-chelate is favorable at elevated temperatures.

Introduction

Although the coordination mode of multidentate ligands toward various metal ions may be vaguely predicted via the "hard/soft" rule, the coordination selectivity is sensitive to various factors such as the properties of central metals and coligands, solution pH and temperature, the solvent properties, etc.[1−7] Among the various properties of metal complexes containing multidentate ligands, linkage isomerism is an expanding field that offers the possibility for rational control of important biological molecules.[1,8] The results of these initial studies have been extended to such diverse areas as quantum mechanical calculations, molecular switches, isomeric catalysts, design of therapeutic agents, imaging agents in the body, and separation of diastereomers. An example of apparent electronic control of linkage isomerism comes from potential bidentates bearing one strong and one weak donor atom. In some cases, the steric factor may play an important role in determining the relative stability of linkage isomers. For the series of A_2PtL_2 (A_2 = diamine, L_2 = anionic leaving group), the chelation modes of the anionic ligands were found to be strongly dependent on the antitumor activity and pharmacokinetic stability.[9−13] According to our previous work, a unique isomerism between (O,S)- and (S,S′)-chelates was observed for (DACH)Pt(DTEYM).[14,15] Such a variety of chelation modes stimulated our interest in understanding the coordination chemistry of platinum complexes.

In this context, a series of malonates containing alkene group were used as fascinating multidentate ligands for antitumor platinum complexes in our laboratory.[16] In the present work, so as to expand platinum(II) coordination chemistry, coordination modes of allyl- and diallylmalonate ligands were scrutinized

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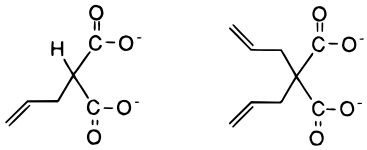
both in the solid state and in solution. The ligands may coordinate to a platinum atom via one of the three distinct modes of (O,O′)-, (O,alkene)-, or (alkene,alkene′)-chelation. No research on diamineplatinum(II) complexes of allyl- or diallylmalonate anionic ligands has been reported yet. Current study reports the synthesis and structural properties of these complexes along with their linkage isomerism.



AM DAM

Experimental Section

Materials and Instrumentation. Potassium tetrachloroplatinate(II) (Kojima), 2,2-dimethyl-1,3-propanediamine (DMPDA) (Aldrich), and *trans*-(±)-1,2-diaminocyclohexane (DACH) (Aldrich) were used as received. Esters of the allylmalonate (AM) and diallylmalonate (DAM) ligands (Aldrich) were also used without further purification. The esters were hydrolyzed with 1.5 equiv of $Ba(OH)_2 \cdot 8H_2O$ in 95% methanol to obtain the corresponding barium salts, which were reacted with *cis*-diamineplatinum(II) sulfate prepared by the literature method.[17,18]

Elemental analyses were performed by the Advanced Analysis Center at KIST. The infrared spectra in the 5000−400 cm^{-1} region were measured as KBr pellets on a Perkin-Elmer 16F PC model FT-IR spectrometer. ^1H, ^{13}C, and ^{195}Pt NMR spectra were recorded on a Varian Gemini-300 NMR spectrometer operating at 300.00 MHz (^1H), 75.48 MHz (^{13}C), and 64.39 MHz (^{195}Pt), respectively, in pulse mode with Fourier transform. Variable temperature ^1H NMR spectra were measured on a Varian Unity *Plus* 600 MHz NMR spectrometer. The chemical shifts were relative to $SiMe_4$ (^1H and ^{13}C) and Na_2PtCl_6 (^{195}Pt) as an internal and external standard for the indicated nuclei, respectively.

Synthesis of (DMPDA)Pt(AM). To a solution of $(DMPDA)PtSO_4 \cdot H_2O$ (0.41 g, 1.0 mmol) in water (50 mL) was added $Ba(AM) \cdot 2H_2O$ (0.32 g, 1.0 mmol) in water (50 mL), and the resulting solution was then stirred for 3 h at room temperature. After barium sulfate was filtered off, the filtrate was evaporated to dryness. The crude white solid was recrystallized from a solvent pair of water and acetone (1:1) to obtain colorless crystals suitable for X-ray crystallography (78.1% yield). Mp 196 °C (dec). Anal. Calcd for $C_{11}H_{20}N_2O_4Pt \cdot 2H_2O$: C, 27.8; H, 5.09; N, 5.89. Found: C, 27.7; H, 5.14; N, 5.85. IR (KBr, cm^{-1}): $\nu(COO)_{asym}$, 1636, 1618; $\nu(COO)_{sym}$, 1396. ^1H NMR (DMF-d_7, ppm): 0.93 (s, CH_3, 6H), 2.33 (br, s, CH_2N, 4H), 2.58 (t, CH_2, 2H, J = 6.8 Hz), 3.69 (t, CH, 1H, J = 6.8 Hz), 4.92 (d, =CH_2, 1H, J = 9.9 Hz), 5.05 (d, =CH_2, 1H, J = 16.2 Hz), 5.45 (br, s, NH, 4H), 5.86−5.99 (m, =CH, 1H). ^1H NMR (Me_2SO-d_6, ppm): 0.78 (s, CH_3, 6H), 2.01 (br, s, CH_2N, 4H), 2.42 (t, CH_2, 2H, J = 7.2 Hz), 3.68 (t, CH, 1H, J = 7.2 Hz), 4.90 (d, =CH_2, 1H, J = 9.9 Hz), 5.01 (d, =CH_2, 1H, J = 17.6 Hz), 5.22−5.43 (br, s, NH, 4H), 5.73−5.87 (m, =CH, 1H). ^1H NMR (CD_3OD, ppm): 0.91 (s, CH_3, 6H), 2.23 (br, s, CH_2N, 4H), 2.85 (t, CH_2, 2H, J = 7.0 Hz), 3.80 (t, CH, 1H, J = 7.3 Hz), 5.00 (d, =CH_2, 1H, J = 9.9 Hz), 5.14 (d, =CH_2, 1H, J = 17.6 Hz), 5.71−5.95 (m, =CH, 1H). ^1H NMR (D_2O, ppm): δ 0.94 (s, CH_3, 3H), 0.95 (s, CH_3, 3H), 2.01 (dd, CH_2, 1H, J = 14.3/7.4 Hz), 2.25 (d, CH_2N, 2H, J = 4.7 Hz), 2.62 (d, CH_2N, 2H, J = 4.7 Hz), 2.79 (dd, CH_2, 1H, J = 14.3/5.7 Hz), 3.52−3.56 (m, CH, 1H), 4.37 (d, =CH_2, 1H, J = 14.9 Hz), 4.66 (d, =CH_2, 1H, J = 7.7 Hz), 5.56−5.68 (m, =CH, 1H). ^{13}C NMR (DMF-d_7, ppm): 23.8, 34.8, 35.5, 53.5, 58.1, 115.1 (C=C), 139.1 (C=C), 176.1 (C=O). ^{13}C NMR (D_2O, ppm): 21.5, 24.1, 29.7, 33.8, 51.1, 51.5, 76.7 (C=C, $^1J_{Pt-C}$ = 137.8 Hz), 96.6 (C=C, $^1J_{Pt-C}$ = 108.2 Hz), 175.6 (C=O, coordinated to Pt), 179.8 (C=O, not coordinated to Pt).

Synthesis of (DACH)Pt(AM). This compound was prepared in 75.7% yield by the same procedure used for (DMPDA)Pt(AM). Mp 209 °C (dec). Anal. Calcd for $C_{12}H_{20}N_2O_4Pt \cdot 2H_2O$: C, 29.6; H, 4.96; N, 5.75. Found: C, 30.1; H, 4.87; N, 5.92. IR (KBr, cm^{-1}): $\nu(COO)_{asym}$, 1664, 1624; $\nu(COO)_{sym}$, 1396. ^1H NMR (Me_2SO-d_6, ppm): 0.96−1.08 (m, CH_2 in DACH, 2H), 1.12−1.31 (m, CH_2 in DACH, 2H), 1.42−1.53 (m, CH_2 in DACH, 2H), 1.76−1.84 (m, CH_2 in DACH, 2H), 2.02−2.14 (m, CHN in DACH, 2H), 2.42 (t, CH_2 in AM, 2H, J = 7.0 Hz), 3.71 (t, CH in AM, 1H, J = 7.0 Hz), 4.90 (d, =CH_2, 1H, J = 10.2 Hz), 5.01 (d, =CH_2, 1H, J = 17.3 Hz), 5.18−5.33 (m, NH, 4H), 5.75−5.92 (m, =CH, 1H). ^1H NMR (D_2O, ppm): 1.14−1.48 (m, 8H), 1.58−1.72 (m, 4H), 2.01−2.19 (m, 6H), 2.54−2.72 (m, 4H), 2.78−2.94 (m, 2H), 3.58 (d, 2H, J = 6.12 Hz), 4.35 (d, 1H, J = 14.55 Hz), 4.43 (d, 1H, J = 14.76 Hz), 4.82 (d, 1H, J = 11.97 Hz), 5.02 (d, 1H, J = 7.8 Hz), 5.56−5.71 (m, 2H). ^{13}C NMR (D_2O, ppm): 24.0, 24.1, 29.8, 32.0, 32.2, 57.3, 57.6, 59.9, 64.2, 75.5 (C=C, $^1J_{Pt-C}$ = 141.7 Hz), 95.2 (C=C), 176.1 (C=O, coordinated to Pt), 181.3 (C=O, uncoordinated to Pt).

Synthesis of (DMPDA)Pt(DAM). This compound was prepared in 81.3% yield by the same procedure used for (DMPDA)Pt(AM). Mp 172 °C (dec). Anal. Calcd for $C_{14}H_{24}N_2O_4Pt \cdot 2H_2O$: C, 32.6; H, 5.47; N, 5.43. Found: C, 32.6; H, 5.45; N, 5.40. IR (KBr, cm^{-1}): $\nu(COO)_{asym}$, 1652, 1574; $\nu(COO)_{sym}$, 1368, 1322. ^1H NMR (DMF-d_7, ppm): 0.94 (s, CH_3, 6H), 2.33 (br, s, CH_2N, 4H), 2.97 (d, CH_2, 4H, J = 7.1 Hz), 4.94 (d, =CH_2, 2H, J = 9.9 Hz), 5.04 (d, =CH_2, 2H, J = 17.3 Hz), 5.49 (br, s, NH, 4H), 5.78−5.93 (m, =CH, 2H). ^1H NMR (Me_2SO-d_6, ppm): 0.79 (s, CH_3, 6H), 2.03 (br, s, CH_2N, 4H), 2.88 (d, CH_2, 4H, J = 6.8 Hz), 4.94 (d, =CH_2, 2H, J = 11.0 Hz), 5.01 (d, =CH_2, 2H, J = 17.0 Hz), 5.28 (br, s, NH, 4H), 5.67−5.82 (m, =CH, 2H). ^1H NMR (CD_3OD, ppm): (major) 0.97 (s, CH_3, 6H), 1.56 (dd, CH_2, 1H, J = 13.0, 7.7 Hz), 2.13−2.94 (m, CH_2 and CH_2N, 7H), 4.09 (d, =CH_2, 1H, J = 14.9 Hz), 4.50 (d, =CH_2, 1H, J = 7.7 Hz), 5.01 (d, =CH_2, 1H, J = 10.7 Hz), 5.06 (d, =CH_2, 1H, J = 16.9 Hz), 5.59−5.71 (m, =CH, 1H), 5.77−6.02 (m, =CH, 1H); (minor) 0.92 (s, CH_3, 6H), 2.26 (s, CH_2N, 4H), 2.91 (d, CH_2, 4H, J = 7.2 Hz), 5.01−5.13 (m, =CH_2, 4H), 5.69−5.84 (m, =CH, 2H). ^1H NMR (D_2O, ppm): 0.96 (s, CH_3, 6H), 1.70 (dd, CH_2, 1H, J = 13.4, 7.8 Hz), 2.25−2.70 (m, CH_2 and CH_2N, 7H), 4.26 (d, =CH_2, 1H, J = 14.8 Hz), 4.67 (d, =CH_2, 1H, J = 7.7 Hz), 5.12 (d, =CH_2, 1H, J = 8.0 Hz), 5.16 (d, =CH_2, 1H, J = 11.8 Hz), 5.54−5.67 (m, =CH, 1H), 5.78−5.93 (m, =CH, 1H). ^{13}C NMR (D_2O, ppm): 21.5, 24.2, 33.8, 34.8, 41.3, 51.1, 51.6, 64.7, 77.4 (C=C, coordinated to Pt), 95.4 (C=C, coordinated to Pt), 118.5 (C=C, uncoordinated to Pt), 134.6 (C=C, uncoordinated to Pt), 177.3 (C=O, coordinated to Pt), 180.7 (C=O, uncoordinated to Pt). ^{195}Pt NMR (DMF-d_7, ppm): −1932.3. ^{195}Pt NMR (Me_2SO-d_6, ppm): −1921.9. ^{195}Pt NMR (CD_3OD, ppm): −1147.9, −1939.0. ^{195}Pt NMR (D_2O, ppm): −1166.2.

Synthesis of (DACH)Pt(DAM). This compound was prepared in 73.2% yield by the same procedure used for (DACH)Pt(AM). Mp 190 °C (dec). Anal. Calcd for $C_{15}H_{24}N_2O_4Pt \cdot 2H_2O$: C, 34.2; H, 5.35; N, 5.31. Found: C, 34.8; H, 5.17; N, 5.55. IR (KBr, cm^{-1}): $\nu(COO)_{asym}$, 1664, 1624, 1578; $\nu(COO)_{sym}$, 1378, 1328. ^1H NMR (D_2O, ppm): 1.18−1.49 (m, 8H), 1.62−1.76 (m, 4H), 2.03−2.18 (m, 4H), 2.43−2.70 (m, 8H), 4.22 (d, 1H, J = 14.62 Hz), 4.36 (d, 1H, J = 14.87 Hz), 4.86 (d, 1H, J = 8.19 Hz), 5.04 (d, 1H, J = 6.42 Hz), 5.14−5.21 (m, 4H), 5.62−5.96 (m, 4H).

X-ray Analyses of (DMPDA)Pt(AM)·2H₂O and (DMPDA)Pt(DAM)·2H₂O. A single crystal of each compound was wedged in a Lindemann capillary with mother liquor. All X-ray data were collected on an Enraf-Nonius CAD4 automatic diffractometer with graphite-monochromated Mo Kα (λ = 0.710 73 Å) at ambient temperature. Unit cell dimensions were based on 25 well-centered reflections by using a least-squares procedure. During the data collection, three standard reflections monitored every hour did not show any significant intensity variation. The data were corrected for Lorentz and polarization effects. Absorption effects were corrected for by the empirical ψ-scan method. The structures were solved by the Patterson method (SHELXS-86) and were refined by full-matrix least-squares techniques (SHELXL-93).[19] All non-hydrogen atoms were refined anisotropically and hydrogen atoms were added at calculated positions. The largest peak in the final difference synthesis was close to the heavy platinum atom. Crystal

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Table 1. Crystallographic Data for (DMPDA)Pt(AM)·2H_2O and (DMPDA)Pt(DAM)·2H_2O

	(DMPDA)Pt(AM)	(DMPDA)Pt(DAM)
formula	$C_{11}H_{20}N_2O_4Pt·2H_2O$	$C_{14}H_{24}N_2O_4Pt·2H_2O$
fw	475.41	515.47
T, °C	25(2)	25(2)
λ, Å	0.710 73	0.710 73
space group	$P4_2/m$ (No. 84)	$P2_1/n$ (No. 14)
a, Å	13.614(3)	11.021(3)
b, Å	13.614(3)	8.996(2)
c, Å	8.451(4)	18.765(7)
β, deg	90.0	106.92(3)
V, Å^3	1566.3(9)	1780.0(9)
Z	4	4
d_{calcd}, g/cm^3	2.016	1.923
abs coeff, mm^{-1}	8.983	7.913
final R indices, $[I > 2\sigma(I)]^a$	R1 = 0.0472, wR2 = 0.1167	R1 = 0.0531, wR2 = 0.1333

^{a} $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. $wR2 = \{\sum w(F_o^2 - F_c^2)^2/\sum wF_o^4\}^{1/2}$.

parameters and procedural information corresponding to data collection and structure refinement are given in Table 1. Final atomic coordinates and isotropic thermal parameters of (DMPDA)Pt(AM)·2H_2O and (DMPDA)Pt(DAM)·2H_2O are available in the Supporting Information.

Results

Synthesis. The reaction of diamineplatinum(II) sulfates with barium salts of the AM or DAM ligand in aqueous solution at room temperature smoothly afforded the product, A_2PtL_2 (eq 1). Recrystallization of the complexes in a solvent pair of water

$$A_2PtSO_4 + BaL_2 \xrightarrow[\text{room temp.}]{H_2O} A_2PtL_2 + BaSO_4\downarrow \qquad (1)$$

$$A_2 = \text{DMPDA, DACH; } L_2 = \text{AM, DAM}$$

and acetone resulted in colorless crystalline solid products in high yields (73.2−81.3%), but attempts to recrystallize in other solvent pairs failed to obtain crystalline products. The products are moderately soluble not only in water but also in polar organic solvents such as methanol, ethanol, DMF, and Me_2SO. The title complexes decompose in the temperature range of 172−209 °C but are stable in both water and polar organic solvents at room temperature. The stability of the present complexes in solutions seems to be ascribed to the chelation effects of both the amine and anionic ligands.

Crystal Structures of (DMPDA)Pt(AM)·2H_2O and (DMPDA)Pt(DAM)·2H_2O. The molecular structure of (DMPDA)Pt(AM)·2H_2O is depicted in Figure 1, and the relevant bond distances and angles are listed in Table 2. The crystal consists of centrosymmetric discrete molecules. The most striking feature of its molecular structure is that the anionic AM ligand is coordinated to the platinum atom through two carboxylate groups with the allyl group uncoordinated. Ethylene group is known to be a soft base and generally is preferred to the carboxylate group for coordination to the platinum atom, which is a soft acid. The two carboxylate groups are coordinated to platinum in a monodentate fashion (C(1)−O(1), 1.27(1) Å; C(1)−O(2), 1.22(1) Å), resulting in a (O,O′)-chelation. The DMPDA amine ligand is chelated to the metal atom in cis positions. The C(4)−C(5) distance of the alkene group (1.31(3) Å) is similar to that of a normal double bond (1.33 Å).[20]

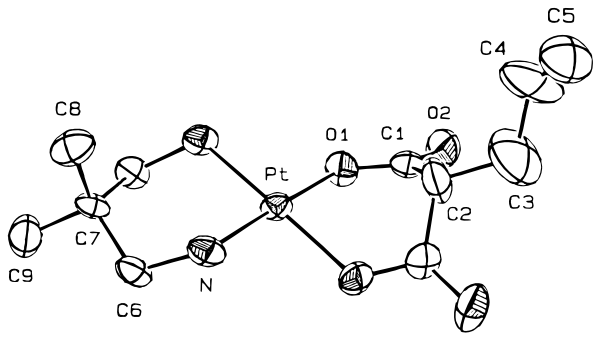

Figure 1. ORTEP drawing of (DMPDA)Pt(AM)·2H_2O showing the atomic labeling scheme and thermal ellipsoids at the 50% level.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for (DMPDA)Pt(AM)·2H_2O[a]

Pt−N	2.003(8)	N′−Pt−N	90.8(5)
Pt−O(1)	2.014(7)	N′−Pt−O(1)′	177.6(3)
O(1)−C(1)	1.27(1)	N−Pt−O(1)′	90.1(3)
O(2)−C(1)	1.22(1)	O(1)′−Pt−O(1)	88.9(4)
N−C(6)	1.49(1)	C(1)−O(1)−Pt	121.0(6)
C(1)−C(2)	1.52(2)	C(6)−N−Pt	115.9(6)
C(2)−C(3)	1.48(3)	O(2)−C(1)−O(1)	121(1)
C(3)−C(4)	1.41(3)	O(2)−C(1)−C(2)	124(1)
C(4)−C(5)	1.31(3)	O(1)−C(1)−C(2)	116(1)
C(6)−C(7)	1.53(1)	C(3)−C(2)−C(1)	114(1)

[a] Slanted primes (′) denote the symmetry transformation used to generate equivalent atoms: $x, y, -z$.

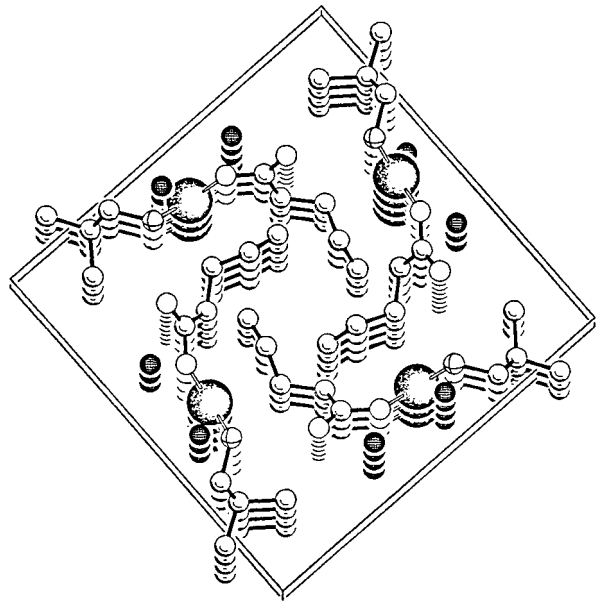

Figure 2. Perspective view of (DMPDA)Pt(AM)·2H_2O as a PLUTON drawing including the unit cell, viewed along the c axis. Hydrogen atoms are omitted for clarity.

Thus, the local geometry around the platinum atom approximates to a square planar arrangement: distances of Pt−N and Pt−O(1) are 2.003(8) and 2.014(7) Å, respectively, and the bond angles of N′−Pt−N, N−Pt−O(1), and O(1)′−Pt−O(1) are 90.8(5), 177.6(3), and 88.9(4)°, respectively. The packing diagram in Figure 2 shows a very interesting molecular assembly. The molecules are assembled in a propeller-like hydrophobic tunnel (4.03(4) × 4.12(4) Å) created by the four different arrays of alkene groups that form its inner wall. As expected, the tunnel constructed by the alkene groups does not contain solvate water molecules, so it may be considered a lipophilic channel. The water molecules are instead positioned around hydrophilic

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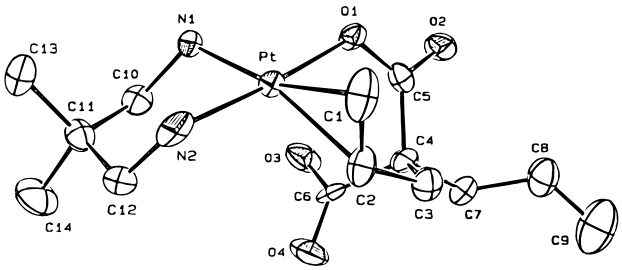

Figure 3. ORTEP drawing of (DMPDA)Pt(DAM)·2H_2O showing the atomic labeling scheme and thermal ellipsoids at the 50% level.

Table 3. Selected Bond Lengths (Å) and Angles (deg) for (DMPDA)Pt(DAM)·2H_2O

Pt−O(1)	2.017(8)	O(1)−Pt−N(2)	176.3(3)
Pt−N(2)	2.03(1)	O(1)−Pt−N(1)	89.2(3)
Pt−N(1)	2.068(9)	N(2)−Pt−N(1)	88.5(4)
Pt−C(1)	2.13(1)	O(1)−Pt−C(1)	90.0(4)
Pt−C(2)	2.15(1)	N(2)−Pt−C(1)	91.4(4)
O(1)−C(5)	1.31(1)	N(1)−Pt−C(1)	163.4(5)
O(2)−C(5)	1.25(1)	O(1)−Pt−C(2)	90.9(4)
O(3)−C(6)	1.25(1)	N(2)−Pt−C(2)	92.3(4)
O(4)−C(6)	1.22(1)	N(1)−Pt−C(2)	159.6(4)
N(1)−C(10)	1.48(1)	C(1)−Pt−C(2)	37.0(5)
N(2)−C(12)	1.49(2)	C(2)−C(1)−Pt	72.4(7)
C(1)−C(2)	1.36(2)	C(1)−C(2)−Pt	70.6(7)
C(2)−C(3)	1.54(2)	O(1)−C(5)−C(4)	119.7(9)
C(7)−C(8)	1.50(2)	O(3)−C(6)−C(4)	115.3(9)
C(8)−C(9)	1.29(2)	C(10)−C(11)−C(12)	112.7(9)

groups such as nitrogen atoms and carboxylate groups. There is no prominent $\pi-\pi$ interaction between the alkene groups, and the separation between the planes is 8.50 Å.

The crystal structure of (DMPDA)Pt(DAM)·2H_2O is shown in Figure 3, and the relevant bond distances and angles are listed in Table 3. The local geometry around the platinum atom approximates to a square planar arrangement. The most interesting feature is that the bonding mode of the tetradentate anionic DAM ligand is chelated to the platinum atom through one carboxylate (Pt−O(1), 2.017(8) Å) and one alkene group (Pt−C(1), 2.13(1) Å; Pt−C(2), 2.15(1) Å), resulting in a (O,alkene)-chelation. Thus, another carboxylate and another alkene group are dangled. As expected for the coordinated carboxylate, the bond length of C(5)−O(1) (1.31(1) Å) is longer than that of C(5)−O(2) (1.25(1) Å). The corresponding bond lengths of the uncoordinated carboxylate are 1.25(1) Å (C(6)−O(3)) and 1.22(1) Å (C(6)−O(4)). The coordinated alkene group is positioned perpendicular to the platinum plane. The coordinated C(1)−C(2) bond length (1.36(2) Å) is longer than the uncoordinated C(8)−C(9) bond (1.29(9) Å). The C(1)−Pt−C(2) angle of 37.0(5)° is approximately the same as the values observed in other known alkeneplatinum(II) complexes.[21,22] There exist intermolecular hydrogen bondings between the oxygen of the coordinated carboxylate group and the amine group of its neighboring molecule (O(1)···N(1)′, 2.920 Å) and between the dangling carboxylate group and the amine group of its neighboring molecule (O(4)···N(2)′, 2.803 Å). These intermolecular hydrogen bonds may give rise to additional stability for (O,alkene)-chelation in the solid state.

IR Spectra. The IR spectra of the carboxylate group of the title complexes are informative to discern the bonding fashions of the carboxylate groups, since the spectral pattern and stretching frequencies of the carboxyl groups vs their bonding fashions are well established.[23−25] For (DMPDA)Pt(AM) showing (O,O′)-chelation in its X-ray structure (Figure 1), one symmetric carbonyl stretching frequency appears at 1396 cm^{-1}, but two asymmetric carbonyl stretching bands are observed at the slightly different frequencies of 1636 and 1618 cm^{-1}, indicating that the two coordinated carboxylate groups are not exactly equivalent. (DACH)Pt(AM) shows the same spectral pattern, and thus seems to have essentially the same molecular structure. For (DMPDA)Pt(DAM) exhibiting the (O,alkene)-chelation mode with one uncoordinated carboxylate group in its X-ray structure (Figure 3), two asymmetric carbonyl stretching frequencies are clearly observed at 1652 and 1574 cm^{-1} and two symmetric bands at 1378 and 1328 cm^{-1}. The bands at 1574 and 1328 cm^{-1} are presumed to be due to the uncoordinated carboxylate. (DACH)Pt(DAM) shows a spectral pattern similar to that of (DMPDA)Pt(DAM) but the asymmetric carbonyl stretching band of the coordinated carboxylate group is split into two sharp bands for an uncertain reason.

^{1}H and ^{13}C NMR Spectra of A_2Pt(AM). The (O,O′)-chelation in the solid state of A_2Pt(AM) was directly elucidated from X-ray analysis and IR spectra, as was mentioned above. Solvent effects on the chelation modes of (DMPDA)Pt(AM) were examined using ^{1}H and ^{13}C NMR spectroscopies, since the chelation modes of the complexes were found to be solvent-dependent. In DMF solution, the ^{13}C chemical shift of the two carboxylate groups shows a singlet at 176.1 ppm, and the alkene resonances (139.1 and 115.1 ppm) of the AM ligand are similar to those of sodium salt of AM (137.3 and 115.7 ppm), which indicates that the (O,O′)-chelation mode of AM is retained in DMF solution. In D_2O, however, the ^{13}C NMR spectrum shows quite a different resonance pattern: two resonances appear at 179.8 and 175.6 ppm due to the free and coordinated carboxylate groups, respectively, in contrast to a single resonance of sodium salt of AM (179.5 ppm in D_2O). The alkene ^{13}C resonances at 96.6 and 76.7 ppm in aqueous solution are significantly shifted upfield compared to those in DMF, and both resonances are accompanied by ^{195}Pt−carbon coupling, $^1J_{Pt-C}$ = 108.2 and 137.8 Hz, respectively. Such upfield shifts and the presence of ^{195}Pt satellites clearly indicate Pt−alkene coordination. As expected, the DMPDA region is more complicated in D_2O than in DMF due to the unsymmetrical ligation of the AM ligand. Thus, it may be concluded that the AM ligand in (DMPDA)-Pt(AM) is chelated to the platinum atom via (O,alkene)-chelation in an aqueous solution in contrast to the (O,O′)-chelation in the solid state and in DMF solution. The ^{1}H NMR spectra of (DMPDA)Pt(AM) at room temperature are presented in Figure 4. The $=CH_2$ protons of the AM ligand in DMF solution (Figure 4a) show two doublets at 5.05 ($^3J_{cis}$ = 16.2 Hz) and 4.92 ($^3J_{trans}$ = 9.9 Hz) ppm that are assigned as *cis*- and *trans*-protons to =CH, respectively. These chemical shifts are consistent with those of a free alkene group, disclosing that the alkene group of the AM ligand is dangled in DMF solution. The complex also shows the same proton resonance pattern also in Me_2SO solution as in DMF. However, the ^{1}H NMR spectrum of the complex in D_2O (Figure 4c) is significantly different from those in DMF and Me_2SO solutions: The $=CH_2$ protons of the AM ligand are shifted to a higher field compared to those in the aprotic solvents. The ^{1}H upfield shift difference (H_{trans} at 4.66

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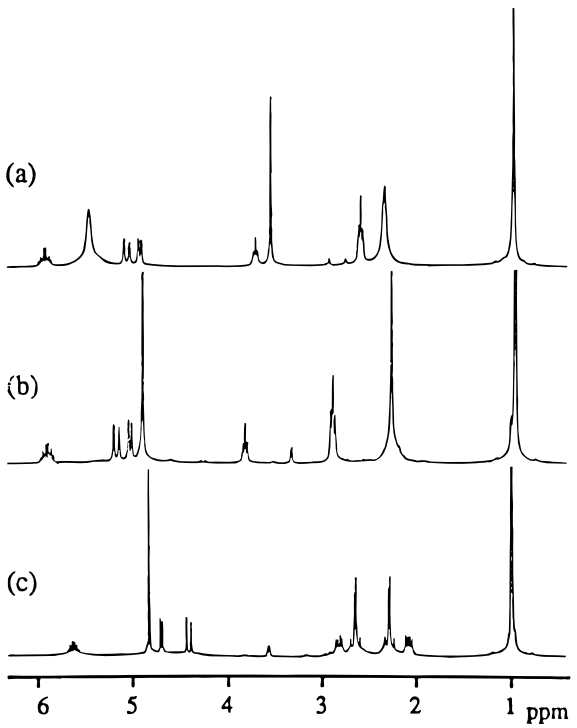
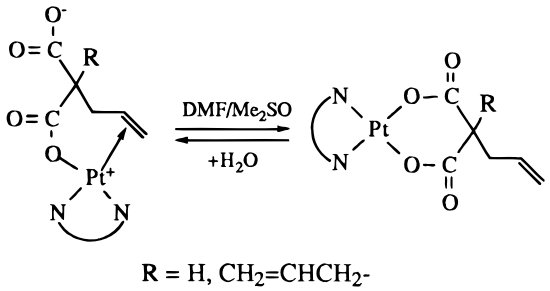


Figure 4. ^{1}H NMR spectra of (DMPDA)Pt(AM) in DMF-d_7 (a), CD_3OD (b), and D_2O (c).

ppm, $\Delta\delta = 0.26$ ppm) and (H_{cis} at 4.37 ppm, $\Delta\delta = 0.68$ ppm) is an additional evidence for the Pt−alkene coordination. The methylene protons of the AM ligand in D_2O also appear as two distinct resonances of a doublet of a doublet at 2.79 and 2.01 ppm. Appearance of the two chemical shifts would be expected if the AM chelate ring adopted a rigid conformation placing two protons in different environments. For the DMPDA ligand, two methylene groups adjacent to the nitrogen atoms appear as two different resonances at 2.62 and 2.25 ppm, and the two terminal methyl groups exhibit two different chemical shifts at 0.94 and 0.95 ppm in aqueous solution due to unsymmetric ligation of the AM ligand, that is, (O,alkene)-chelation. Adding a small quantity of water to the DMF or DMSO solution of the complex resulted in conversion of the (O,O′) isomer to (O,-alkene) isomer. The chemical shifts and the spectral pattern of the complex in CD_3OD (Figure 4b) show an equilibrium between the two species in methanol at room temperature. For the DACH analogue of AM, a similar spectral pattern and trend were observed.

^{1}H and ^{195}Pt NMR Spectra of A_2Pt(DAM). It has been shown from the aforementioned X-ray structure of (DMPDA)-Pt(DAM) that the DAM ligand was coordinated to the platinum atom via (O,alkene)-mode in the solid state, but the chelation mode of the DAM ligand was also found to be solvent-dependent. The $=CH_2$ protons of DAM in DMF solution appear as two doublets at 5.04 ($^3J_{cis} = 17.3$ Hz) and 4.94 ($^3J_{trans} = 9.9$ Hz) ppm that are assigned as *cis*- and *trans*-protons to =CH, respectively. The CH_2 protons of the DAM ligand appear as a doublet at 2.97 ppm ($J = 7.1$ Hz). The chemical shifts and integral ratios disclose that the DAM ligand is coordinated to the platinum atom via (O,O′)-chelation through two carboxylate group in DMF solution in contrast to (O,alkene)-chelation in the solid state. The chemical shifts and peak pattern of the complex in Me_2SO solution is similar to those in DMF solution. However, in D_2O, the =CH protons of the DAM ligand appear as two distinct quartets in the range of 5.5−6.0 ppm, and the $=CH_2$ protons are observed as two sets of doublets, one set at 5.12 and 5.16 ppm, the other at 4.26 and 4.67 ppm. The methylene proton regions of the DAM and DMPDA ligands are very complicated, reflecting the unsymmetrical (O,alkene)-chelation of the DAM ligand. Thus, the structure of the complex in aqueous solution seems to be consistent with the structure in the solid state. The chemical shifts and peak patterns of the complex in CD_3OD is similar to those in D_2O, but the spectrum in CD_3OD shows another set of resonances corresponding to (O,O′)-isomer. Addition of water to DMF, Me_2SO, or CD_3OD solution changes the coordination mode exclusively to (O,-alkene)-chelation: the conversion process is greatly dependent on the presence or absence of water (eq 2).



(2)

The ^{195}Pt NMR spectra of the complex demonstrate more clearly the structural variation dependent on solvents. The ^{195}Pt NMR spectrum of (DMPDA)Pt(DAM) was measured in various solvents. Each spectrum in DMF or Me_2SO solution exhibits only one ^{195}Pt resonance, reflecting the presence of one platinum species in each solution. The chemical shifts at −1932 (in DMF-d_7) and −1922 ppm (in Me_2SO-d_6) lie in a similar region to that (−1930 to −1950 ppm) of (DACH)Pt(steroids), which was already elucidated as (N,N′-amine)Pt(O,O′-carboxylate).[26] However, the ^{195}Pt NMR spectrum in CD_3OD shows two resonances at −1939 and −1148 ppm with the ratio of 1:8 at room temperature, indicating that two isomers coexist in methanol solution. The signal at −1939 ppm corresponds to the (O,O′)-chelate while the chemical shift at −1148 ppm to (O,alkene)-chelate. The ^{195}Pt NMR spectrum in D_2O shows a single resonance at −1166 ppm, indicating the presence of only (O,-alkene)-isomer. Thus, for the present platinum complexes, the variation of medium critically affects the coordination modes of the anionic ligands.

Temperature-Dependent ^{1}H NMR Spectra of (DMPDA)-Pt(DAM). As mentioned above, the present complexes were found to exist in methanol as a mixture of linkage isomers, although the major isomer is the (O,alkene)-chelate. The proton spectrum of (DMPDA)Pt(DAM) in CD_3OD exhibits a marked temperature-dependence in the range of 188−328 K (Figure 5). (DMPDA)Pt(DAM) in methanol solution at room temperature (at 298 K) shows two sets of resonance signals, indicating the coexistence of the linkage isomeric mixture of (O,O′)- and (O,-alkene)-chelates in the ratio of approximately 1:8, as was confirmed by previous ^{195}Pt NMR spectra. Although the solution was cooled to 188 K, the ratio of two linkage isomers was not significantly changed, but some peaks were somewhat broadened at low temperature. However, warming up the solution above room-temperature resulted in a gradual increase of the (O,alkene)-chelate (indicated as ↓in Figure 5), and at 328 K (the limit temperature of CH_3OH) the ratio of the (O,O′)- and (O,-alkene)-chelates becomes approximately 1:2. An interesting feature is that such a temperature-dependent isomerism is

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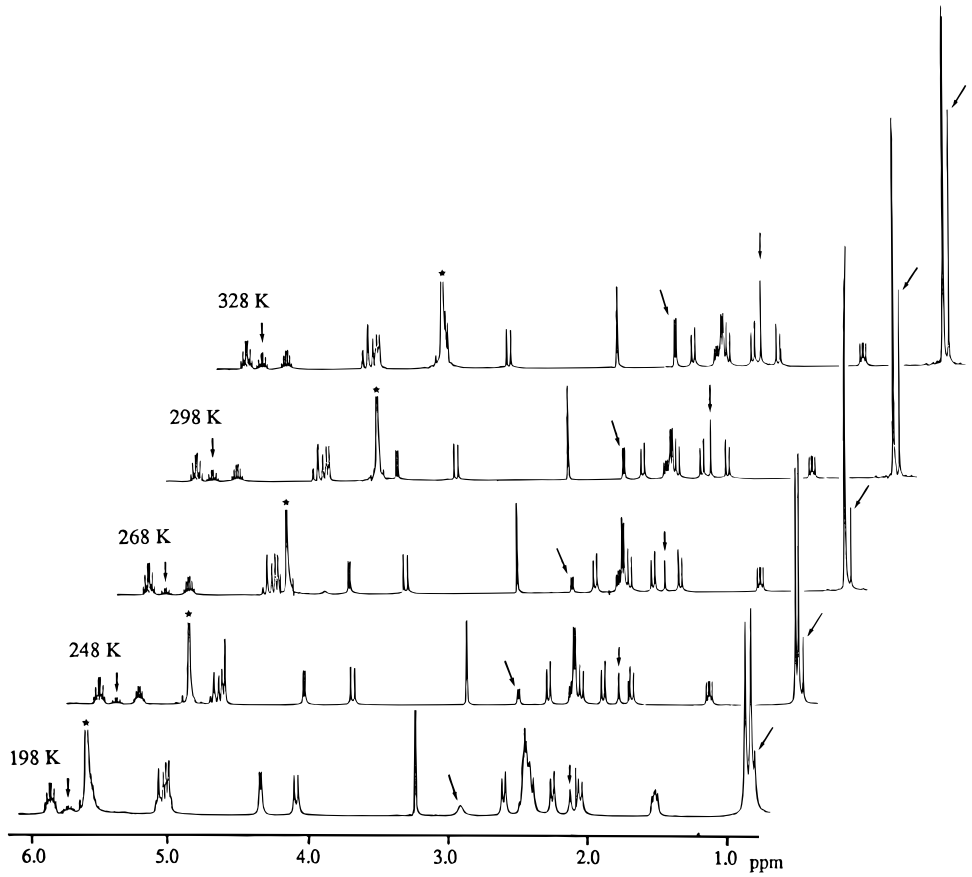
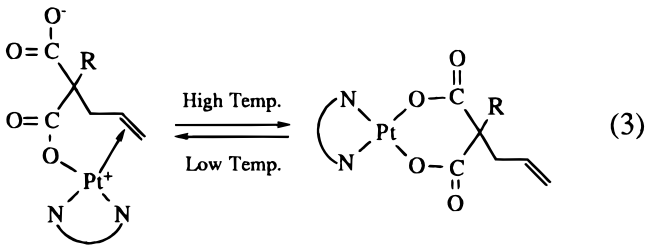


Figure 5. Variable-temperature ^{1}H NMR spectra of (DMPDA)Pt(DAM) in CD_3OD (500 MHz). The star-marked peak is due to water molecule.

essentially reversible: at low temperature the DAM ligand strongly prefers the (O,alkene)-chelation mode, as is expected from its thermodynamic parameters (ΔH = 38 kJ/mol, ΔS = 109 J/K·mol) calculated from the equilibrium constants whereas at elevated temperature the equilibrium shifts to the (O,O′)-chelate (eq 3).



(3)

Discussion

It is suprising from the viewpoint of the hard/soft rule that the allylmalonate ligand coordinates to platinum via (O,O′)-chelation mode in the solid state with the alkene group uncoordinated, since ethylene is classified as a soft base, like the phosphorus or sulfur-donating ligands, and platinum(II) cation is classified as a soft acid. Furthermore, among the three possible bonding modes of (O,O′)-, (O,alkene)-, or (alkene,-alkene′)-chelation for the diallymalonate ligands, only (O,O′)- and (O,alkene)-modes were observed, and no (alkene,alkene′)-chelation was observed on any occasions despite no unfavorable electronic or steric reasons. On the other hand, we have seen from our multinuclear NMR studies and X-ray analysis on both allyl-and diallylmalonate complexes that the alkene group is competitive with the carboxylate group in coordination to the platinum(II) ion probably due to crystal packing energy as well as intermolecular hydrogen bondings, which results in linkage isomerism. However, it is still unclear why the hard/soft rule is overridden by such intermolecular interactions in the title complexes.

Table 4. Bonding Modes of AM and DAM Complexes in the Solid State and in Solutions

		solution			
compounds	solid	D_2O	CD_3OD	Me_2SO-d_6	DMF-d_7
A_2Pt^{II}(AM)	(O,O′)	(O,alkene)	(O,O′) (O,alkene)	(O,O′)	(O,O′)
A_2Pt^{II}(DAM)	(O,alkene)	(O,alkene)	(O,alkene) (O,O′)	(O,O′)	(O,O′)

Structural characterization on the title complexes of allyl- and diallylmalonate ligands both in the solid state and in solutions have shown that interconversion between (O,O′)- and (O,-alkene)-isomers via linkage isomerism is subtly dependent on the solvent and temperature. The bonding modes are summarized in Table 4. The bonding fashions were not changed depending on the amine coligands (DMPDA and DACH) either in solution or in the solid state. It was also observed that, regardless of the chelation modes in solution, only (O,O′)- and (O,alkene)-chelates were exclusively obtained in the solid state for the AM and DAM complexes, respectively. Why do the AM and DAM complexes have different bonding modes in the solid state? The answer may be sought from the stabilization energy induced by crystal packing rather than electronic effects. The (O,alkene)-chelation in the solid state of (DMPDA)Pt(DAM) seems to be induced by intermolecular hydrogen bondings between the carboxylates and neighboring amines (NH···O, 2.84 and 2.89

Å) as well as between the solvated water molecules and amine or carboxylate groups (NH···O or OH···O, 2.84−2.89 Å).

Even in solution, the hydrogen bonding ability of solvent with the molecules of the platinum complexes seems to play an important role in controlling the coordination mode of the anionic ligands. What is the major factor for determining the bonding mode in each solvent? The (O,alkene)-chelated species of the complexes have zwitterionic forms, and thus there seems to be hydrogen bonds between protic solvent molecules and the zwitterionic dipole molecules. Therefore, the (O,alkene)-chelate seems to be more stable in the protic solvent whereas the (O,O′)-mode is relatively more stable in aprotic solvent such as Me_2SO and DMF. Such systems are good examples that the solvent molecules play a key role in determining the coordination mode of the complexes. Thus, it can be concluded that the equilibrium between the two linkage isomers is solvent-dependent. A solvent is not a simple inert matrix in the present system but a very important factor along with the central metal and the ligands. Methanol is intermediate in polarity, dielectric constant, and hydrogen bonding ability between two extremes, protic solvent H_2O and aprotic solvent Me_2SO, and thus the two chelation modes coexist in MeOH at room temperature.

Temperature-dependent NMR spectra have been used to determine the transition temperature and reversibility. For instance, (DMPDA)Pt(DAM) in CD_3OD exhibits an equilibrium between the isomers at room temperature. Warming up the sample gives rise to shift from the (O,alkene)-mode to the (O,O′)-mode probably because the increased thermal energy at elevated temperatures contributes to less stabilization by H-bonding. Thus, the (O,O′)-chelation seems to be favored at high temperatures.

In conclusion, the title complexes are one of the rare examples exhibiting linkage isomerism between (O,O′) and (O,alkene) chelation modes that subtly depend on solvent and temperature. Since the bonding mode of anionic leaving groups of the diamineplatinum(II) complexes is pharmacokinetically important and as such closely related to their antitumor activity, various factors including linkage isomerism should be taken into account when new platinum complexes are designed using multidentate ligands. We will show that the antitumor activities of the title complexes are greatly dependent on their chelation modes in our paper to be published later separately.

Acknowledgment. This research was financially supported by the Ministry of Science and Technology in Korea.

Supporting Information Available: Details of atomic coordinates, anisotropic thermal parameters, lists of bond lengths and angles, ^{13}C NMR spectrum of (DMPDA)Pt(AM), and ^{1}H and ^{195}Pt NMR spectra of (DMPDA)Pt(DAM) and two X-ray crystallographic files, in CIF format, are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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