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Synthesis and Characterization of Antitumor-Active Platinum 2,2-Dimethyl-1,3-diaminopropane Compounds. Crystal and Molecular Structure of (Malonato)(2,2-dimethyl-1,3-diaminopropane)platinum(II)

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The synthesis and characterization of a series of platinum compounds containing 2,2-dimethyl-1,3-diaminopropane (DMDAP) are described. The compounds are Pt(DMDAP)X_2 with X_2 = Cl_2, Br_2, I_2, or malonate and Pt(DMDAP)Cl_4. The crystal structure of the malonate compound has been determined from three-dimensional single-crystal X-ray data. The complex crystallizes in space group $P2_1/m$ of the monoclinic system with two formula units in a unit cell of dimensions a = 5.807 (2) Å, b = 9.980 (5) Å, c = 9.667 (2) Å, and β = 96.31 (3)°. The structure was solved by standard Patterson and Fourier methods and refined by full-matrix least-squares techniques to a value of the conventional R_F factor of 0.021 (R_{wF} = 0.034) by using 1260 observed reflections. The molecule lies on a crystallographic mirror plane passing through the platinum atom, the methylene group of the malonate ion, and the $C(CH_3)_2$ group of the amine. The coordination geometry around Pt is square planar with two oxygen atoms at 2.029 (4) Å and two nitrogen atoms at 2.022 (4) Å. The N–Pt–N angle is 97.2 (2)°, and the O–Pt–O angle is 90.1 (2)°. The crystal structure consists of layers perpendicular to the c axis in which the molecules are pseudohexagonally stacked and coupled through hydrogen bonds of the type N–H···O. The Pt–amine chelate ring adopts a chair conformation strongly flattened at the PtN_2 end while the Pt–malonate chelate ring has a boat conformation. The chloro compounds and the malonate compound show significant activity against the L-1210 leukemia in mice. Some remarks concerning the relation between structure and activity of the platinum compounds are made.

Introduction

In 1969 Rosenberg and co-workers reported on the capacity of *cis*-dichloro(diammine)platinum(II) and some related compounds to inhibit the growth of certain tumors in mice.[2] The antitumor activity of cis platinum compounds with N-donor ligands and anions like Cl^-, SO_4^{2-}, or malonate is now well established,[3] and a large number of platinum compounds with a wide variety of N-donor ligands have been tested.[3c]

It appears from the literature that compounds with $-NH_2$ donor groups can have significant antitumor activity. Compounds with heterocyclic N-donor ligands like pyridines only showed a weak activity.[4] We have synthesized a number of platinum compounds with imidazoles and pyrazoles with and without an N–H group in the heterocyclic ring.[5] These compounds did not show more than marginal activity.[6] However, a compound with histamine, containing an imidazole group and an NH_2 group bound to platinum, has some activity.[7] These results support the conclusion that the presence of NH_2 groups of aliphatic amines is likely to be essential for activity.

Now we have synthesized and tested a number of platinum compounds with aliphatic diamines which are able to form six-membered chelate rings with metal ions. Only a few compounds with six-membered chelate rings have been investigated for possible antitumor activity, like (malonato)(1,3-diaminopropane)platinum,[8] dichloro(1-amino-2-aminomethylcyclopentane)platinum,[9] and dichloro(*N*-aminoethylpyrrolidine)platinum.[9] All of these compounds show significant activity in animal tests.[8,9]

This paper reports on the synthesis and characterization and activity of platinum compounds with 2,2-dimethyl-1,3-diaminopropane (abbreviated as DMDAP) and the crystal and molecular structure of malonato(2,2-dimethyl-1,3-diaminopropane)platinum(II). The synthesis of Cl_2(DMDAP)Pt^{II} and a few other compounds with this ligand has been described earlier.[10] So far, only a few platinum complexes having antitumor properties have been structurally investigated, i.e., *cis*-Pt$(NH_3)_2Cl_2$,[11] dichloro(ethylenediamine)platinum,[12] *cis*-dichlorobis(ethylenimine)platinum,[13] *cis*-dichlorobis(cyclohexylamine)platinum,[14] and *cis*-dichlorobis(cyclopropylamine)platinum.[15] For this reason, and in order to obtain more information on the conformations of the two six-membered chelate rings, we have determined the structure of the malonato compound.

Experimental Part

Starting Materials. Platinum was commercially available as the tetrachloroplatinate K_2PtCl_4 (Drijfhout, Amsterdam). A sample of 2,2-dimethyl-1,3-diaminopropane was kindly provided by BASF, The Netherlands.

Synthesis of the Compounds. Pt(DMDAP)I_2. A 415-mg (1-mmol) sample of K_2PtCl_4 was dissolved in 20 mL of water, and 4 g (about 24 mmol) of KI was added to yield a solution of 0.05 M PtI_4^{2-} and 1 M I^-. To this solution was added 102 mg (1 mmol) of DMDAP in a few milliliters water. The compound precipitated immediately. The product was filtered, washed with water, and dried at 60 °C.

Pt(DMDAP)X_2 with X = Cl, Br. A 551-mg (1-mmol) sample of the diiodo compound was suspended in a 1 M solution of $NaNO_3$ in water containing about 20% acetone, and a solution of 323 mg (1.9

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Table I. Final Positional[a] and Anisotropic (×100) Thermal Parameters[b] for Pt(DMDAP)(mal)

atom	x/a	y/b	z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Pt(1)	0.15738 (3)	0.25000 (–)	0.06871 (2)	2.75 (2)	2.11 (2)	2.52 (2)	0.00 (–)	0.06 (1)	0.00 (–)
O(1)	0.2242 (7)	0.1061 (4)	−0.0698 (4)	4.3 (2)	3.0 (2)	3.3 (2)	−0.3 (2)	0.6 (1)	−0.5 (1)
O(2)	0.4537 (7)	0.0361 (4)	−0.2210 (4)	4.9 (2)	4.5 (2)	4.6 (2)	0.8 (2)	0.4 (1)	−2.0 (2)
N(1)	0.1016 (7)	0.0981 (4)	0.1993 (4)	4.0 (2)	2.5 (2)	2.8 (2)	−0.3 (2)	0.5 (1)	0.1 (1)
C(1)	0.4013 (8)	0.1214 (5)	−0.1370 (5)	3.3 (2)	3.0 (2)	3.2 (2)	0.7 (2)	−0.7 (2)	0.1 (2)
C(2)	0.5440 (11)	0.2500 (–)	−0.1173 (8)	2.6 (3)	4.5 (4)	4.8 (4)	0.0 (–)	0.2 (3)	0.0 (–)
C(3)	0.0304 (9)	0.1250 (5)	0.3394 (5)	4.7 (2)	3.3 (2)	2.6 (2)	−0.9 (2)	0.7 (2)	0.1 (2)
C(4)	0.1291 (10)	0.2500 (–)	0.4111 (6)	2.6 (3)	2.8 (3)	2.7 (3)	0.0 (–)	−0.3 (2)	0.0 (–)
C(5)	0.0471 (15)	0.2500 (–)	0.5577 (6)	5.8 (4)	4.4 (4)	2.3 (3)	0.0 (–)	0.0 (3)	0.0 (–)
C(6)	0.3926 (14)	0.2500 (–)	0.4249 (8)	3.3 (3)	5.1 (5)	5.3 (4)	0.0 (–)	−1.0 (3)	0.0 (–)

atom	x/a	y/b	z/c	atom	x/a	y/b	z/c
H(1)[c]	0.0000	0.0359	0.1439	H(6)	−0.1176	0.1202	0.3275
H(2)	0.2394	0.0507	0.2051	H(7)	−0.1269	0.2500	0.5506
H(3)	0.6036	0.2500	−0.0238	H(8)	0.0931	0.1765	0.6036
H(4)	0.6971	0.2500	−0.1771	H(9)	0.4642	0.2500	0.3407
H(5)	0.0695	0.0313	0.3908	H(10)	0.4693	0.1558	0.4741

[a] The estimated standard deviations in the least significant figures are given in parentheses here and in other tables. [b] The thermal parameters are in the form $T = \exp[-2\pi^2\Sigma_i\Sigma_j U_{ij}h_ih_ja_i^*a_j^*]$. [c] Parameters for all hydrogens are not refined; $U_{iso} = 2.67$ Å^2.

mmol) of $AgNO_3$ in water was added. The suspension was stirred for 0.5 h, and the precipitate of AgI was filtered. The filtrate is assumed to contain the diaquo species. After addition of a 20-fold excess of NaBr or NaCl, respectively, the dibromo or the dichloro compound precipitated. The product was filtered, washed with ethanol and dry diethyl ether, and dried in vacuo at room temperature.

Pt(DMDAP)(mal). To a solution containing the diaquo species, obtained as described above, was added a fivefold excess of malonic acid neutralized with an equivalent amount of KOH. The pH of the solution was adjusted to 5. Within 1 day the desired compound crystallized. The crystals were filtered, washed with an ethanol/water (1:1) mixture, ethanol, and dry diethyl ether, and dried in vacuo at room temperature.

Pt(DMDAP)Cl$_4$. A mixture of 368 mg (1 mmol) of Pt(DMDAP)Cl$_2$, 10 mL of 2 N HCl, and 4 mL of 30% H_2O_2 solution was boiled until a clear yellow solution was obtained. When the solution was cooled, the desired compound crystallized. The product was filtered, washed with an ethanol/water mixture (1:1), ethanol, and dry diethyl ether, and dried in vacuo at room temperature.

Physical Methods. Chemical analyses were carried out by using standard procedures. Infrared spectra of the compounds, pressed in KBr disks and as Nujol mulls, were recorded on a Beckman Acculab instrument (4000–250 cm^{-1}). No decomposition of the compounds occurs in KBr as can be seen from the spectra recorded in Nujol, which are identical with those recorded in KBr. Far-infrared spectra of the compounds pressed in polyethylene disks were recorded on a Beckman IR-720 interferometer (500–20 cm^{-1}).

X-Ray Structure Determination and Refinement. Crystal data for Pt(DMDAP)(mal) are as follows: $C_8H_{16}N_2O_4Pt$, monoclinic, space group $P2_1/m$, $Z = 2$, $a = 5.807$ (2) Å, $b = 9.980$ (5) Å, $c = 9.667$ (2) Å, $\beta = 96.31$ (3)°, $V = 556.87$ Å^3, mol wt = 399.32, $F(000) = 376$, μ(Mo Kα) = 132.5 cm^{-1}, d(X) = 2.381 g cm^{-3}, d(exptl) = 2.36 g cm^{-3}.

Accurate values of the unit cell parameters and the crystal orientation matrix were determined at ambient temperatures from a least-squares treatment of the angular settings of 12 reflections, carefully centered on an Enraf-Nonius CAD4 diffractometer using Mo Kα radiation ($\lambda = 0.71069$ Å).[16] The standard deviations in the lattice parameters were derived from a comparison of the deviations from integer values of the indices, calculated with the orientational matrix, for the angular settings of the orientation reflections as described by Duisenberg.[17]

The unit cell parameters and systematic absences ($0k0$, $k = 2n + 1$) allowed for two space groups, $P2_1$ and $P2_1/m$. Structure determination excluded $P2_1$. The crystal selected for data collection was a regular parallelepiped bounded by six planes. Dimensions were measured under a binocular microscope and were as follows: (001) to (00$\bar{1}$), 0.17 mm; (110) to ($\bar{1}\bar{1}$0), 0.20 mm; (1$\bar{1}$0) to ($\bar{1}$10), 0.19 mm. The crystal volume amounts to 7.45×10^{-3} mm^3. The crystal was mounted on top of a Lindemann capillary with 001 and 110 approximately in a plane perpendicular to the spindle axis and $\bar{1}$10 as "top-plane".

Intensity data were collected with a CAD4 diffractometer equipped with a scintillation counter in the $\omega/2\theta$ scan mode by using zirconium-filtered Mo Kα radiation, up to $\theta = 27.5°$. The applied scan angle was $\Delta\omega = 0.60 + 0.35 \tan(\theta)°$. The background was measured in an additional scan angle of $\Delta\omega/4°$ on both sides of the main scan and with the same speed. The scan speed was selected such as to obtain $\sigma(I)/I = 0.02$, subject to a maximum time per reflection of 2 min. The intensity of a standard reflection was monitored every 30 min of X-ray exposure time. There was no indication for decay during data collection.

Absorption correction was performed with a Gaussian integration technique by using a $8 \times 8 \times 8$ grid. The observed absorption corrections were in the range 4.95–7.94. The data were averaged to a unique set of 1342 reflections of which 82 have intensities with $I < 2.5\sigma(I)$ and corrected for Lorentz and polarization effects.

The structure was solved by standard Patterson and Fourier methods and refined by least-squares techniques. Hydrogen atom positions could be located from a difference Fourier synthesis. A final full-matrix least-squares refinement converged at $R_F = 0.021$ ($R_{wF} = 0.034$) for 1260 observed reflections.[18] Weights were included as $w^{-1} = \sigma^2(F_o) + 0.0007F_o^2$.

Positional and anisotropic thermal parameters for all nonhydrogen atoms were refined. Hydrogen atoms were fixed on their observed positions with $B = 2.1$ and not refined. Table I lists the final positional and anisotropic thermal parameters. A final electron density difference map showed no significant features higher than 0.5 e Å^{-3}, apart from two satellite peaks near Pt as high as 1 e Å^{-3} that are attributed to "model errors".

Scattering factors were taken from ref 19. Except those for H that were taken from ref 20. The anomalous dispersion correction for Pt was taken from ref 21. Most calculations were performed on a CDC CYBER-73 at the computer center of the University of Utrecht. Programs used in this structural analysis included ORTEP[22] and an extended version of the X-RAY76 SYSTEM.[23] A listing of

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Table II. New Compounds with Their Color and Analytical Data

compd	color	% C calcd	% C found	% H calcd	% H found	% N calcd	% N found
$Pt(DMDAP)Cl_2$	light yellow	16.3	16.3	3.8	3.8	7.6	7.5
$Pt(DMDAP)Br_2$	light yellow	13.1	13.4	3.1	2.9	6.1	6.1
$Pt(DMDAP)I_2$	yellow	10.9	10.9	2.5	2.5	5.1	5.2
Pt(DMDAP)(mal)	white	24.1	24.2	4.0	4.0	7.0	7.1
$Pt(DMDAP)Cl_4$	yellow	13.7	13.8	3.2	3.0	6.4	6.3

Table III. Far-Infrared Spectra of the Compounds in the 400–100 cm^{-1} Region[a]

compd	absorption bands, cm^{-1}
$Pt(DMDAP)Cl_2$	365 w, 323 s,[b] 312 s,[b] 285 s, 209 s, 157 m, 133 s
$Pt(DMDAP)Br_2$	370 w, 274 s, 235 s,[c] 220 s,[c] 195 s,[c] 135 s
$Pt(DMDAP)I_2$	370 vw, 271 s, 209 s, 178 s,[b] 170 s,[b] 131 s
Pt(DMDAP)(mal)	377 s, 323 s, 280 s, 261 s, 222 m, 193 s, 148 s, 132 m, 102 m
$Pt(DMDAP)Cl_4$	354 s,[b] 343 s,[b] 336 s,[b] 276 s, 219 s, 183 m, 170 s, 164 sh

[a] s = strong, m = medium, w = weak, vw = very weak, sh = shoulder. [b] Pt–halogen stretching vibration. [c] These vibrations have Pt–Br stretching character but also contain another vibration due to the ligand.

observed and calculated structural factors is available as supplementary material.

Results and Discussion

Characterization of the Compounds. Table II lists the compounds with their color and the analytical data. The results of the analyses are in agreement with the suggested formulas. The infrared spectra of the compounds show absorption bands due to ligand vibrations. The infrared spectrum of the malonato compound shows C–O stretching vibrations at 1658 and 1625 cm^{-1}. Other absorptions of the malonate ion could not be assigned with certainty, due to the presence of ligand absorptions.

Table III lists the wavenumbers of the absorption bands in the far-infrared spectra of the compounds. For a cis square-planar geometry two Pt–halogen stretching vibrations are expected (A_1 and B_1 under C_{2v} symmetry). These vibrations in the spectra of $Pt(DMDAP)Cl_2$ and $Pt(DMDAP)I_2$ are assigned at 323 and 312 and at 178 and 170 cm^{-1}, respectively. The Pt–Br stretching vibrations (expected near 220 cm^{-1}) in the spectrum of $Pt(DMDAP)Br_2$ are rather complex due to the presence of another absorption band in the same region. The assignment of the absorption bands in the spectrum of Pt(DMDAP)(mal) is very difficult, as is the case for other compounds with bidentate oxygen donor ligands like acetyl acetonate or oxalate.[24] For a *cis*-PtN_2Cl_4 species four absorption bands are expected ($2A_1$, B_1, and B_2 under C_{2v} symmetry). In the spectra of other *cis*-tetrachloroplatinum(IV) complexes usually three of these absorption bands are found in the 350–300 cm^{-1} region, whereas the fourth band is found at about 200 cm^{-1}.[25] Therefore the absorption bands at 354–336 cm^{-1} in the spectrum of $Pt(DMDAP)Cl_4$ are all assigned to Pt–Cl stretching vibrations. A Pt–Cl stretching vibration expected at about 200 cm^{-1} could not be assigned due to the presence of another strong absorption band in this region (see spectra of the dichloro and diiodo compounds).

Description of the Structure of the Malonato Compound. The structure of Pt(DMDAP)(mal) consists of monomeric molecular units. An ORTEP drawing of the molecule with the atomic numbering scheme is given in Figure 1. The molecule

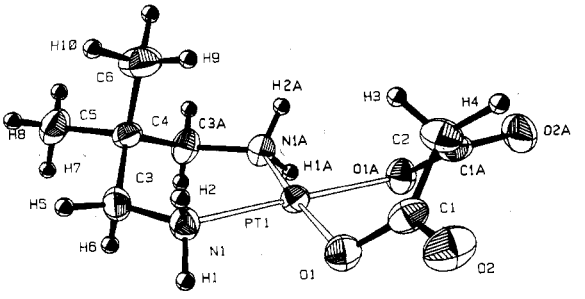

Figure 1. ORTEP drawing of Pt(DMDAP)(mal) scaled to include 50% probability. The hydrogen atoms are represented as artificially small spheres.

lies on a crystallographic mirror plane passing through C(2), Pt(1), C(4), C(5), and C(6). The bond distances and bond angles within the complex are listed in Table IV. (Atoms related by the mirror plane symmetry operation $x, {}^1/_2 - y, z$ are indicated by A.) Table V gives some least-squares planes in the molecule with the deviations of some atoms and the angles between some of these planes.

Coordination Geometry. The coordination around platinum is square planar with cis bond angles of 90.1 (2), 97.2 (2), 86.4 (2), and 86.4 (2)° and trans bond angles of 176.3 (2)°. The Pt–N distance of 2.022 (4) Å is similar to those reported for other platinum complexes with aliphatic amines as ligands.[26] The Pt–O distance of 2.029 (4) Å is slightly longer than the values of 2.00 Å found in $K_2Pt(C_2O_4)_2 \cdot 2H_2O$[27] and of 2.002 (4) Å found in *trans*-bis(glycinato)platinum(II).[28] The four donor atoms lie exactly in one plane as required by the symmetry plane. The deviation of the platinum atom from this plane is only 0.020 Å on the same side as the H1 atom.

Conformation of the Pt–Malonato Chelate Ring. The conformation of the Pt–malonato chelate ring can be compared with other structures in which a malonato anion acts as a bidentate ligand coordinating to one metal ion.[29] From these structures it appears that these chelate rings can adopt a variety of conformations like chair,[29c,g] boat,[29a,b,e] envelope,[29d] or flattened with a distortion toward a skewboat conformation.[29f] As concluded earlier,[29e] this type of a malonato chelate ring seems to have a high degree of conformational flexibility. The Pt–malonate ring in the new compound is another example of a boat conformation. The dihedral angle between the O(1)–Pt(1)–O(1A) plane and the plane through O(1), O(1A), C(1), and C(1A) is 37.7°. The angle between this latter plane and the plane through C(1), C(2), and C(1A) is 43.4°. The O(1)–Pt(1)–O(1A) angle of 90.1 (2)° and the Pt(1)–O–C

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Table IV. Bond Distances (Å) and Angles (Deg) for All Nonhydrogen Atoms in Pt(DMDAP)(mal)

Distances					
Pt(1)-O(1)	2.029 (4)	C(3)-C(4)	1.509 (6)	O(2)-C(1)	1.237 (6)
Pt(1)-N(1)	2.022 (4)	C(4)-C(5)	1.545 (9)	O(1)-C(1)	1.284 (6)
N(1)-C(3)	1.483 (6)	C(4)-C(6)	1.521 (10)	C(1)-C(2)	1.529 (6)

Angles					
O(1)-Pt(1)-N(1)	86.4 (2)	O(1)-C(1)-O(2)	121.3 (4)	N(1)-C(3)-C(4)	116.0 (4)
O(1)-Pt(1)-O(1A)	90.1 (2)	O(1)-C(1)-C(2)	119.3 (5)	C(3)-C(4)-C(3A)	111.6 (4)
N(1)-Pt(1)-N(1A)	97.2 (2)	O(2)-C(1)-C(2)	119.4 (5)	C(3)-C(4)-C(6)	111.6 (3)
O(1)-Pt(1)-N(1A)	176.3 (2)	C(1)-C(2)-C(1A)	114.2 (5)	C(3)-C(4)-C(5)	106.3 (4)
Pt(1)-O(1)-C(1)	118.2 (3)	Pt(1)-N(1)-C(3)	121.0 (3)	C(5)-C(4)-C(6)	109.1 (5)

Table V

Least-Squares Planes in Pt(DMDAP)(mal)[a]

plane no.	atoms defining the plane	*A*	*B*	*C*	*D*
1	C(1), C(2), C(1A) dev: O(2), −0.876	−1.325	0.000	9.599	−1.847
2	O(1), O(1A), C(1), C(1A) dev: O(2), −0.498; C(2), 0.573; Pt(1), 0.878	2.945	0.000	7.760	0.119
3	O(1), Pt(1), O(1A)	5.413	0.000	2.611	1.031
4	N(1), N(1A), O(1), O(1A) dev: Pt(1), −0.020	5.443	0.000	2.480	1.047
5	N(1), Pt(1), N(1A)	5.474	0.000	2.338	1.022
6	N(1), N(1A), C(3), C(3A) dev: Pt(1), −0.057; C(4), 0.727	5.383	0.000	2.736	1.092
7	C(3), C(4), C(3A)	−4.724	0.000	6.503	2.063

Angles between Planes, Deg

1-2	43.4	5-6	2.4
2-3	37.7	6-7	58.7

[a] Equations of the planes are expressed as $Ax + By + Cz = D$. Deviations from planes are in Å.

angle of 118.2 (3)° are the smallest found thus far compared with the corresponding angles in the above-mentioned structures. The smallest values found in these structures are 90.5° and 90.6° for the O–M–O angle in $Na_4(Cr(mal)_2OH)_2$[29b] and $Cu(N,N\text{-}Et_2\text{-}en)(H_2O)(mal)$,[29c] respectively, and 122.5° and 123.5° for the M–O–C angle in one of the chelate rings in $Na(Co(en)(mal)_2)\cdot 2H_2O$.[29e] The other bond lengths and angles are well within the range observed in the other malonato complexes.[29]

Conformation of the Pt–Amine Chelate Ring. The Pt–amine chelate ring adopts a chair conformation strongly flattened at the PtN_2 end. The dihedral angle between the N(1)–Pt(1)–N(1A) plane and the plane through N(1), N(1A), C(3), and C(3A) is only 2.4°. The angle between this latter plane and the plane through C(3), C(4), and C(3A) is 58.7° and is very close to the expected value of 60°. A similar flattened chair conformation has also been observed in dichloro(1,3-diaminopropane)cadmium[30] and in dichlorobis(1,3-diaminocyclohexane)palladium.[31] The N(1)–Pt(1)–N(1A) angle of 97.2 (2)° is the largest value so far observed in platinum or palladium complexes with chelating diamines.[12,31] For comparison, this value amounts to 94.8 (2)° in the Pd–1,3-diaminocyclohexane complex[31] and to less than 90° in $M(en)Cl_2$ (M = Pd, Pt) compounds containing a five-membered chelate ring.[12]

Although the Pt(1)–N–C bond angle (121.0 (3)°) and the N–C–C bond angle (116.0 (4)°) are much larger than the tetrahedral angle, these values are within the range observed in other complexes containing six-membered chelate rings formed by aliphatic diamines.[30-32]

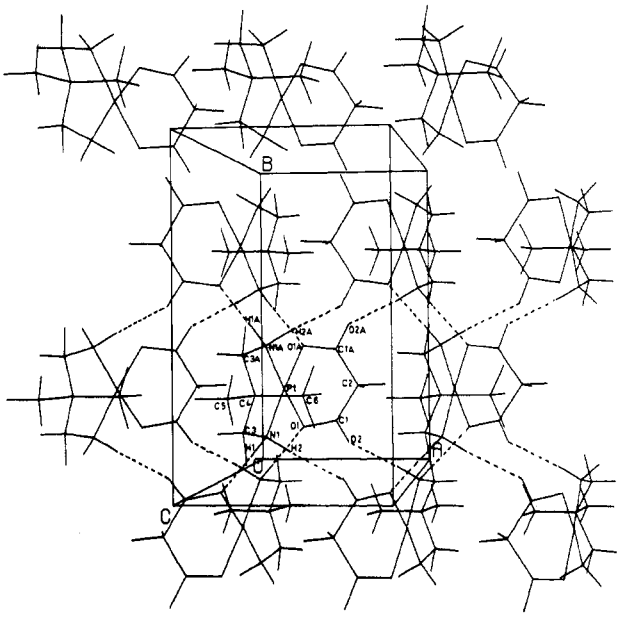

Figure 2. Projection of the unit cell content of Pt(DMDAP)(mal) (approximately down the *c* axis) showing part of the hydrogen bonding scheme and the pseudohexagonal layer structure.

Table VI. Hydrogen Bond Distances (Å) and Angles (Deg) in Pt(DMDAP)(mal)

atoms N, H, O	N-H	H···O	N·····O	N-H···O
N(1), H(1), O(1)	0.975 (4)	2.003 (4)	2.963 (6)	167.7
N(1), H(2), O(2)	0.926 (4)	1.973 (4)	2.896 (5)	174.4

Crystal Structure and Hydrogen Bonding. Figure 2 gives a view of the packing and part of the hydrogen bonding scheme of the molecules in the crystal structure. It consists of layers perpendicular to the *c* axis in which the molecules are pseudohexagonally stacked and coupled through hydrogen bonds of the type N–H···O. Each molecule is doubly hydrogen bonded to four neighboring molecules in the layer. The hydrogen bridges are almost linear (N(1)–H(1)···O(1) = 167.7° and N(1)–H(2)···O(2) = 174.4°). The distances and angles of the hydrogen bridges are presented in Table VI.

Structure–Activity Relationships. The compounds Pt(DMDAP)Cl_2, Pt(DMDAP)(mal) and Pt(DMDAP)Cl_4 show significant activity against the leukemia L1210 in mice.[33] The malonato and tetrachloro compounds are especially interesting because their water solubility is approximately twice that of *cis*-$Pt(NH_3)_2Cl_2$, which is of great value for practical application. This result again demonstrates that apparently only complexes with $-NH_2$ donor groups exhibit significant anti-

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tumor activity. It is difficult to explain this within the present knowledge of the biological properties of these platinum compounds. A great number of factors may determine the activity of the platinum compounds. Among these are toxic side effects, water solubility, lipid solubility, membrane transport, side reactions inside and outside the cell, the reactions with the DNA of the cell (which is known[3] to cause the cytostatic effect in the case of *cis*-$Pt(NH_3)_2Cl_2$), and possible repair mechanisms. An illustration of the difficulties encountered in explaining the wide variation in activity of the different platinum compounds is the question whether or not all platinum–DNA complexes formed with different platinum compounds are the same.[34]

Since NH_2 groups can form hydrogen bonds it seems likely that hydrogen bond formation plays an important role in one or more of the above mentioned factors. For example Marzilli, Bau, and co-workers have shown that hydrogen bonding plays an important role in the interaction of metal ions with nucleic acid constituents.[35] However much work has to be done to verify this idea and to determine the relative importance of the above-mentioned factors. Determination of the pharmacokinetics and distribution in- and outside the cell of different platinum compounds and investigation of the type and number of lesions produced on the DNA by these platinum complexes are very important to obtain more information on the relation between structure and activity.

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Registry No. Pt(DMDAP)(mal), 72968-07-1; $Pt(DMDAP)I_2$, 72968-08-2; $Pt(DMDAP)Br_2$, 72968-09-3; $Pt(DMDAP)Cl_2$, 28866-75-3; $Pt(DMDAP)Cl_4$, 72968-10-6; $Pt(DMDAP)(OH_2)_2^{2+}$, 72968-11-7; K_2PtCl_4, 10025-99-7.

Supplementary Material Available: A listing of observed and calculated structural factors (10 pages). Ordering information is given on any current masthead page.

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Preparation and Chemistry of the $B_9H_{12}Se^-$ and $B_9H_{12}Te^-$ Ions

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Aqueous polyselenide or polytelluride solutions react with $B_9H_{13}{\cdot}S(CH_3)_2$ to form the $B_9H_{12}X^-$ (X = Se or Te) anions, which can be isolated as tetramethylammonium salts. Oxidation of these salts with iodine produces the $B_9H_{11}X$ molecules in benzene or the $B_9H_{11}X{\cdot}CH_3CN$ molecules in the presence of acetonitrile. Reaction of $B_9H_{11}Se{\cdot}CH_3CN$ with triethylamine produces $B_9H_{11}Se{\cdot}N(C_2H_5)_3$. Pyrolysis of $B_9H_{11}Se$ produces mixtures of B_9H_9Se and $B_{11}H_{11}Se$. The $B_8H_{10}Se_2$ molecule is formed as a coproduct during the isolation of the $B_9H_{12}Se^-$ ion.

Introduction

The thiaborane anion $B_9H_{12}S^-$ has previously been prepared by a degradation–insertion reaction of decaborane with an aqueous polysulfide solution.[1] Studies of its derivative chemistry[2,3] and the ^{11}B NMR assignment of this anion have been published.[4] Reactions of decaborane with aqueous polyselenide and polytelluride solutions formed mainly the insertion product $B_{10}H_{11}X^-$ (X = Se or Te).[5] We report in this article syntheses of the $B_9H_{12}Se^-$ and $B_9H_{12}Te^-$ anions and some of their derivative chemistry. A preliminary communication has been published concerning the $B_8H_{10}Se_2$ molecule which is produced as a coproduct in the $B_9H_{12}Se^-$ ion synthesis.[6]

Experimental Section

General Procedures and Instrumentation. All reactions were run under an atmosphere of prepurified nitrogen. The organic solvents used as reaction solvents were dried and distilled prior to use. All other reagants were used as received. Melting points were obtained in sealed, evacuated capillaries and are uncorrected.

Boron (^{11}B) NMR spectra at 70.6 MHz were obtained with a Varian HR-220 spectrometer and were externally referenced to $BF_3{\cdot}O(C_2H_5)_2$. Proton NMR spectra were obtained on a Varian T-60A spectrometer. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N.Y. High-resolution mass spectral data were obtained on an AEI MS-902 spectrometer.[15] Infrared data, contained in Table I, were obtained as KBr disks, or as indicated, on a Perkin-Elmer 283 instrument.

$(CH_3)_4N[B_9H_{12}Se]$ (I) and $B_8H_{10}Se_2$ (II). An aqueous ammonium polyselenide solution was prepared by using the procedure described previously,[5] with 50 mL of ammonia, 0.67 g (29 mmol) of sodium metal, and 4.6 g (58 mmol) of selenium powder in a 100-mL, three-neck flask fitted with a magnetic stirrer, dry ice condenser, and nitrogen inlet. Reduction of sputtering was accomplished by packing dry ice around the reaction flask during the addition of sodium and selenium. The material $B_9H_{13}{\cdot}S(CH_3)_2$ was prepared by using the literature method described for the synthesis of $B_9H_{13}{\cdot}S(C_2H_5)_2$.[7] $B_9H_{13}{\cdot}S(CH_3)_2$, 2.00 g (11.6 mmol), was added rapidly to the reaction flask, and the solution was stirred 12 h. Excess tetramethylammonium chloride in deoxygenated water was added to the reaction mixture, and the resulting air sensitive precipitate was filtered, washed with 2 × 10 mL portions of deoxygenated water, and dried under a nitrogen

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