Bis[platinum(II)] and Bis[palladium(II)] Complexes of α,ω-Dicarboxylic Acid Bis(1,2,4-triaminobutane-N^4) Amides†

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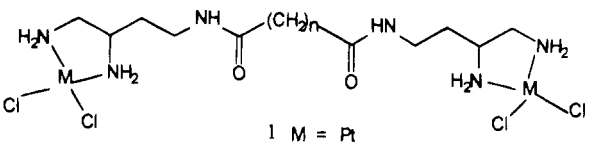
The synthesis and properties of bimetallic complexes $[Cl_2M(LL)MCl_2]$ (M = Pt, Pd) are reported (LL are two 1,2,4-triaminobutane units linked by nitrogens in position 4 as α,ω-dicarboxylic acid bis(amides) $H_2NCH_2CHNH_2$-$CH_2CH_2NHCO(CH_2)_nCONHCH_2CH_2CHNH_2CH_2NH_2$, $n = 3-6, 8$). In these complexes two *cis*-$PtCl_2$ fragments are bridged by a spacer. Their solvolysis in Me_2SO was studied by multinuclear (^1H, ^{13}C, and ^{195}Pt) NMR spectroscopy. The ionic compounds $[(DMSO)(Cl)Pt(LL)Pt(Cl)(DMSO)]Cl_2$ were isolated and characterized as mixtures of *cis/trans* isomers. The ligands containing two vicinal diamino units were prepared from N^1,N^2-bis-(*tert*-butoxycarbonyl)-N^4-(trifluoroacetyl)-1,2,4-triaminobutane, by basic removal of the trifluoroacetyl group and acylation of free amine with dicarboxylic acid dichlorides of variable chains. Subsequent splitting of Boc protecting groups and reaction with K_2PtCl_4 or Na_2PdCl_4 under controlled-pH conditions afforded the title compounds.

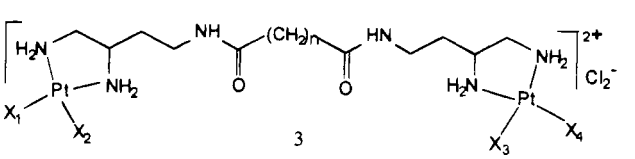
Introduction

Drugs as cross-linking agents capable of substantial DNA sequence recognition have been the subject of intensive research.[1] *cis*-Diamminedichloroplatinum(II) and diammine-(1,1-cyclobutanedicarboxylato)platinum(II) are powerful anticancer drugs[2] acting as intrastrand cross-linking agents.[3] Other second-generation Pt(II) analogues are undergoing clinical trials. Bis[platinum(II)] complexes in which two Pt(II) units are linked by a tether of variable chains are designed to act as intra- and interstrand cross-link agents. Peak et al.[4] first reported bis[*cis*-dichloro(diamine)platinum(II)] complexes in which the diamines were bridged using 3,4-diaminobenzoic acid *via* two amide linkages of cadaverine, spermidine, or spermine. Vlassov has demonstrated that the heterobifunctional complex $[BrPt(dien)-(CH_2)_6(dien)Pt(H_2O)](NO_3)_3$ was bound to short oligonucleotides and then cross-linked to sequence-specific complementary oligonucleotides.[5] Bis[platinum(II)] complexes in which two $Pt(NH_3)Cl_2$ units are bound by a bis(diamine) were shown by Farrell to exhibit anticancer activity against cell lines resistant to cisplatin.[6−10] On the other hand, dinuclear Pt(II) compounds having bulky substituents on nitrogen[11] or species which do not possess a primary or secondary amine do not show significant activity.[12] $[(Dien)Pt^{II}I]_2I$ complexes linked with $(CH_2)_n$ chains were designed by Taylor to discriminate between B and Z conformations of DNA.[13] Three *cis*-PtX_2(amine) units were linked in a linear fashion (amine: NH_3 and linear $H_2N-(CH_2)_nNH_2$ as linker),[14] and trinuclear complexes of spermidine were shown to interact with DNA.[15] The cation $[\{Pt(NH_3)_3\}_2-NH_2(CH_2)_nNH_2]^{4+}$ stabilizes the Z form of DNA,[16] and DMSO complexes $[\{trans\text{-}Pt(Me_2SO)(NH_3)_2\}_2NH_2(CH_2)_nNH_2]^{4+}$ induce the transition of DNA from the B to the Z form.[17]

We previously described mononuclear *cis*-$Pt(L)Cl_2$ complexes in which L are 1,2,4-triaminobutanes having different acyl substituents on nitrogen in position 4.[18] The trifluoroacetyl and isobutyryl compounds exhibited cytotoxic activity in *in vitro* and *in vivo* tests. Some mononuclear $[Pt(en)Cl_2]$ and $[PtCl(Me_2-SO)(en)]^+$ complexes react with nucleotides[19] and exhibit anticancer activity.[20,21] One of our previously prepared compounds, N^1,N^2-bis(*tert*-butoxycarbonyl)-N^4-(trifluoroacetyl)-1,2,4-triaminobutane, with its easily and preferentially removable protecting groups, appeared to be a suitable intermediate to design a series of bis(platinum) and bis(palladium) complexes **1**−**3**.



1 M = Pt
2 M = Pd



3

$X_1 = X_3 = Cl$, $X_2 = X_4 = DMSO$
$X_1 = X_4 = DMSO$; $X_2 = X_3 = Cl$
$X_1 = X_4 = Cl$; $X_2 = X_3 = DMSO$

$n = 3-6, 8$

Experimental Section

Starting Materials and Physical Methods. Histamine dihydrochloride, glutaryl chloride, adipoyl chloride, and di-*tert*-butyl dicarbonate were commercially available (Aldrich, Fluka). Histamine

† Dedicated to Professor Dr. Hubert Schmidbaur on the occasion of his 60th birthday.

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dihydrochloride was dried *in vacuo* over P_4O_{10} before use. K_2PtCl_4 and Na_2PdCl_4 were gifts from Degussa. N^{α}-(Trifluoroacetyl)histamine (**4**) as the trifluoroacetate salt was prepared by published methods.[22] Solvents of analytical grade were purchased from Fluka; a suspension of Raney nickel in water was purchased from Aldrich. Flash chromatography was carried out on silica gel (Merck, 70−230 mesh); TLC was performed on Merck Kieselgel 60 F_{254} plates using 0.2% ethanolic solution of ninhydrin for visualization. Melting points up to 200 °C were determined on a Büchi melting point apparatus and above 200 °C on an electrothermal digital melting point apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL FX 90Q at 90 MHz and a JEOL EX-400 spectrometer at 399.65 and 100.4 MHz, respectively. ^{195}Pt-NMR spectra were recorded using a JEOL GSX-270 spectrometer operating at 57.8 MHz. ^{1}H and ^{13}C chemical shifts are given with respect to $Si(CH_3)_4$ as internal standard. ^{195}Pt chemical shifts are quoted *vs* K_2PtCl_6 as external standard. IR spectra were measured on a Nicolet 520 FT-IR spectrometer. Conductivity was measured on a Schoth Instrument CG854 digital conductometer. C,H,N analyses were performed by the Microanalytical Laboratory of our institute.

***N*^{1},*N*^{2}-Bis(*tert*-butoxycarbonyl)-*N*^{4}-(trifluoroacetyl)-1,2,4-triaminobutane (6).** N^{α}-(Trifluoroacetyl)histamine[22] (7.4 g, 23.2 mmol) was suspended in acetonitrile (130 mL) and neutralized with aqueous 1 M $NaHCO_3$ (23 mL). After addition of aqueous 15% potassium acetate (92 mL) and di-*tert*-butyl dicarbonate (21.8 g, 0.1 mol), the reaction mixture was stirred for 5 d at ambient temperature. The organic layer was separated from the mixture and the solvent removed *in vacuo*. The residue was dissolved in ethyl acetate; the solution was washed with aqueous 5% $NaHCO_3$ and water and dried over Na_2SO_4. The ethyl acetate was evaporated, and the solution of the residue in a small volume of ethyl acetate/hexane was introduced into a silica gel column (120 g) prepared in hexane. Elution with hexane removed the unreacted di-*tert*-butyl dicarbonate. Elution with ethyl acetate/hexane (1:3) afforded **5**: colorless oil; yield 6.1 g (82%). IR (film): ν = 3330 (NH), 1670−1760 (CO), 1213, 1183, 1163 cm^{-1} (CF_3). **5** (10.0 g, 30.7 mmol) in ethanol (80 mL) was hydrogenated in an autoclave in the presence of Raney nickel (5 mL aqueous suspension, washed with 3 × 5 mL of ethanol) at 80 bar hydrogen pressure and 45 °C for 60 h. The solution was filtered from the catalyst and the ethanol removed *in vacuo*. The residue was redissolved in ethyl acetate, and the solution was filtered through a silica gel column (30 g) to remove $Al(OH)_3$ stemming from the catalyst, afforded **6**: yield 7.6 g (62%); mp (120−121 °C (lit.[18] 120−121 °C). The IR and ^{1}H-, ^{13}C-NMR spectroscopic data were identical to those described in ref 18.

***N*^{1},*N*^{2}-Bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane (7).** The removal of the trifluoroacetyl group with NaOH was performed according to a published procedure.[18]

Acylation of *N*^{1},*N*^{2}-Bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane (7) with α,ω-Dicarboxylic Acid Dichlorides. General Procedure. Freshly distilled α,ω-dicarboxylic acid dichloride (3.0 mmol) in dry CH_2Cl_2 (5 mL) was slowly added with stirring to a mixture of **7** (6.0 mmol), NEt_3 (12.0 mmol), and DMAP (0.5 mmol) in CH_2Cl_2 (70 mL) at 0 °C (ice bath). Stirring was continued for 1 h at 0 °C and for an additional 12 h at ambient temperature. The precipitate was filtered out and washed with CH_2Cl_2. The combined CH_2Cl_2 solutions were washed with water, dried, and evaporated to dryness. The residue was recrystallized from hot ethyl acetate to give pure **8**.

***N*^{4},*N*$'^4$-Glutarylbis[*N*^{1},*N*^{2}-bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane] (8a)**: colorless crystalline solid; yield 379 mg (90%); mp 144 °C. IR (Nujol): ν = 3342 (NH), 1682, 1642, (CO), 1531 cm^{-1} (NH). ^{1}H-NMR (DMSO-d_6): δ = 1.34 (s, 36 H, $C(CH_3)_3$), 1.36, 1.49 (m, 4H, 3-CH_2), 1.66 (m, 2H, 7-CH_2), 2.00 (m, 4H, 6-CH_2), 2.8−3.0 (m, 6H, 1-CH_2, 4-CH_2), 3.03 (m, 2H, 4-CH_2), 3.42 (m, 2H, 2-CH), 6.50 (m, 2H, 2-NH), 6.64 (m, 2H, 1-NH), 7.70 (m, 1H, 4-NH). ^{13}C-{^{1}H}-NMR (DMSO-d_6): δ = 21.9 (C-7), 28.5 ($C(CH_3)_3$), 32.0 (C-3), 35.1 (C-6), 36.1 (C-4), 78.1, 78.2 ($C(CH_3)_3$), 155.9, 156.2 (CO_2), 172.2 (C-5). Anal. Calcd for $C_{33}H_{62}N_6O_{10}$: C, 56.39; H, 8.89; N, 11.96. Found: C, 56.04; H, 9.01; N, 11.79.

***N*^{4},*N*$'^4$-Adipoylbis[*N*^{1},*N*^{2}-bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane] (8b)**: colorless crystalline solid; yield 374 mg (87%); mp 194 °C. IR (Nujol): ν = 3354, 3332 (NH), 1682, 1642 (CO), 1531 cm^{-1} (NH). ^{1}H-NMR (CD_2Cl_2): δ = 1.42, 1.43 (two s, 36H, $C(CH_3)_3$), 1.45, 1.65 (m, 4H, 3-CH_2), 1.61 (m, 4H 7-CH_2), 2.19 (m, 4H, 6-CH_2), 3.0−3.1 (m, 6H, 1-CH_2, 4-CH_2), 3.32 (m, 2H, 4-CH_2), 3.58 (m, 2H, 2-CH). ^{13}C{^{1}H}-NMR (CD_2Cl_2): δ = 26.4 (C-7), 28.8 ($C(CH_3)_3$), 33.0 (C-3), 37.2 (C-4), 36.7 (C-6), 45.3 (C-1), 50.0 (C-2), 80.0 ($C(CH_3)_3$), 158.2, 158.5 (CO_2), 175.5 (C-5). Anal. Calcd for $C_{34}H_{64}N_6O_{10}$: C, 56.96; H, 9.00; N, 11.72. Found: C, 56.98; H, 8.86; N, 11.68.

***N*^{4},*N*$'^4$-Pimeloylbis[*N*^{1},*N*^{2}-bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane] (8c)**: colorless crystalline solid; yield 1. 7 g (77%); mp 117−120 °C (from ethyl acetate/hexane). IR (Nujol): ν = 3351 (NH), 1683, 1643 (CO), 1535 cm^{-1} (NH). ^{1}H-NMR (DMSO-d_6): δ = 1.18 (m, 2H, 8-CH_2), 1.30−1.55 (m, 44H, $C(CH_3)_3$, 3-CH_2, 7-CH_2), 2.00 (m, 4H, 6-CH_2), 2.8−2.9 (m, 6H, 1-CH_2, 4-CH_2), 3.05 (m, 2H, 4-CH_2), 3.44 (m, 2H, 2-CH), 6.58 (m, 2H, 2-NH), 6.72 (m, 2H, 1-NH), 7.65 (m, 2H, 4-NH). ^{13}C{^{1}H}-NMR (DMSO-d_6): δ = 25.0 (C-7), 28.2 ($C(CH_3)_3$), 28.3 (C-8), 31.8 (C-3), 35.3 (C-6), 35.8 (C-4), 43.8 (C-1), 48.4 (C-2), 77.5, 77.6 ($C(CH_3)_3$), 155.3, 155.7 (CO_2), 171.8 (C-5). Anal. Calcd for $C_{35}H_{66}N_6O_{10}$: C, 57.51; H, 9.10; N, 11.50. Found: C, 57.38; H, 9.12; N, 11.48.

***N*^{4},*N*$'^4$-Suberoylbis[*N*^{1},*N*^{2}-bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane] (8d)**: colorless crystalline solid; yield 1.48 g (66%); mp 159−163 °C. IR (Nujol): ν = 3355, 3333 (NH), 1681, 1647 (CO), 1535 cm^{-1} (NH). ^{1}H-NMR (CD_2Cl_2/CD_3OD): δ = 1.33 (m, 4H, 8-CH_2), 1.43 (m, 38H, $C(CH_3)_3$, 3-CH_2), 1.6−1.7 (m, 6H, 3-CH_2, 7-CH_2), 2.16 (m, 4H, 6-CH_2), 2.9−3.0, 3.4−3.5 (m, 4H, 4-CH_2), 3.1−3.2 (m, 4H, 1-CH_2), 3.5−3.7 (m, 2H, 2-CH), 5.95 (broad, NH). ^{13}C{^{1}H}-NMR (CD_2Cl_2/CD_3OD): δ = 26.5 (C-8), 28.7 (CH_3), 29.0 (C-7), 33.2 (C-3), 36.8 (C-4), 44.6 (C-1), 49.4 (C-2), 80.0, 80.1 ($C(CH_3)_3$), 157.8, 158.0 (CO_2), 175.2 (C-5). Anal. Calcd for $C_{36}H_{68}N_6O_{10}$: C, 58.04; H, 9.20; N, 11.28. Found: C, 58.02; H, 9.17; N, 11.27.

***N*^{4},*N*$'^4$-Sebacoylbis[*N*^{1},*N*^{2}-bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane] (8e)**: colorless crystalline solid; yield 1.92 g (83%); mp 169−170 °C. IR (Nujol): ν = 3353, 3331 (NH), 1682, 1646 (CO), 1534 cm^{-1} (NH). ^{1}H-NMR (DMSO-d_6): δ 1.24 (m, 8H, 8-CH_2, 9-CH_2), 1.35 (s, 36H, $C(CH_3)_3$, 1.39−1.51 (m, 8H, 3-CH_2, 7-CH_2), 1.99 (m, 4H, 6-CH_2), 2.90−3.05 (m, 6H, 1-CH_2, 4-CH_2), 3.10 (m, 2H, 4-CH_2), 3.47 (m, 2H, 2-CH), 6.43 (m, 2H, 2-NH), 6.54 (m, 2H, 1-NH), 7.53 (m, 2H, 4-NH). ^{13}C{^{1}H}-NMR (DMSO-d_6): δ = 25.3 (C-9), 28.2 (CH_3), 28.7 (C-7, C-8), 31.8 (C-3), 35.6 (C-6), 36.0 (C-4), 43.8 (C-1), 48.4 (C-2), 77.6, 79.0 ($C(CH_3)_3$), 155.4, 155.8 (CO_2), 172.0 (C-5). Anal. Calcd for $C_{38}H_{72}N_6O_{10}$: C, 59.04; H, 9.39; N, 10.87. Found: C, 58.97; H, 9.36; N, 10.84.

Acylation of Histamine with Glutaryl and Adipoyl Chloride. General Procedure. Histamine dihydrochloride (1.0 g, 5.4 mmol) and NEt_3 (2.2 g, 21.7 mmol) were stirred for 2 h in dry DMF (100 mL) at ambient temperature. Glutaryl or adipoyl chloride (5.4 mmol) in DMF (2 mL) was added with stirring dropwise at 0 °C (ice bath), and stirring was continued for an additional 2 h at 0 °C and for 18 h at ambient temperature. Another solution of histamine dihydrochloride (1.0 g, 5.4 mmol) and NEt_3 (1.1 g, 10.9 mmol) in DMF (50 mL) was added, and the reaction mixture was stirred for 3 d at ambient temperature. The solution was filtered from the partially precipitated triethylammonium chloride and the DMF removed *in vacuo*. The solution of the residue in water (200 mL) was saturated with Na_2CO_3 to precipitate crude **1**. The precipitate was isolated by filtration, dried *in vacuo*, and extracted

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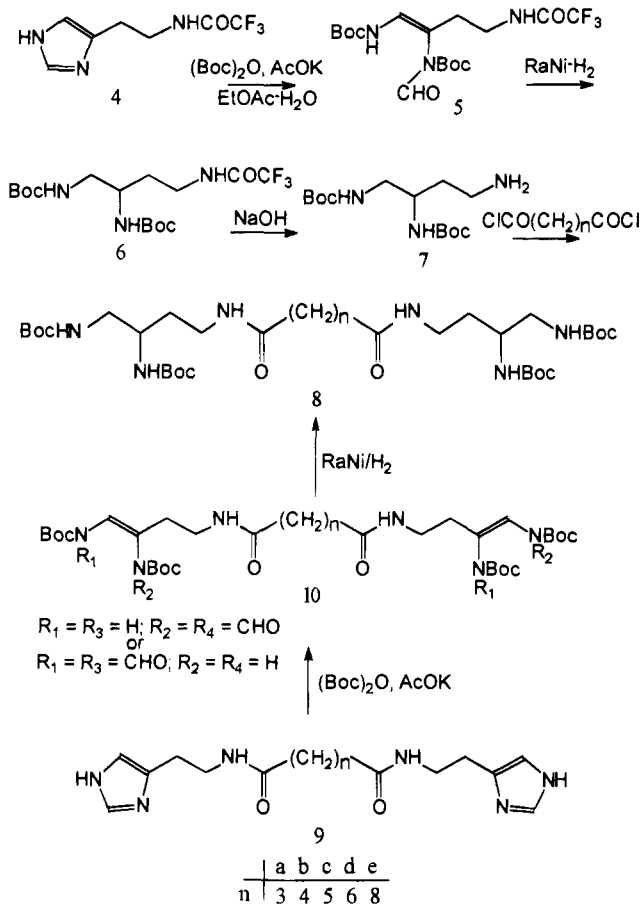
Scheme 1



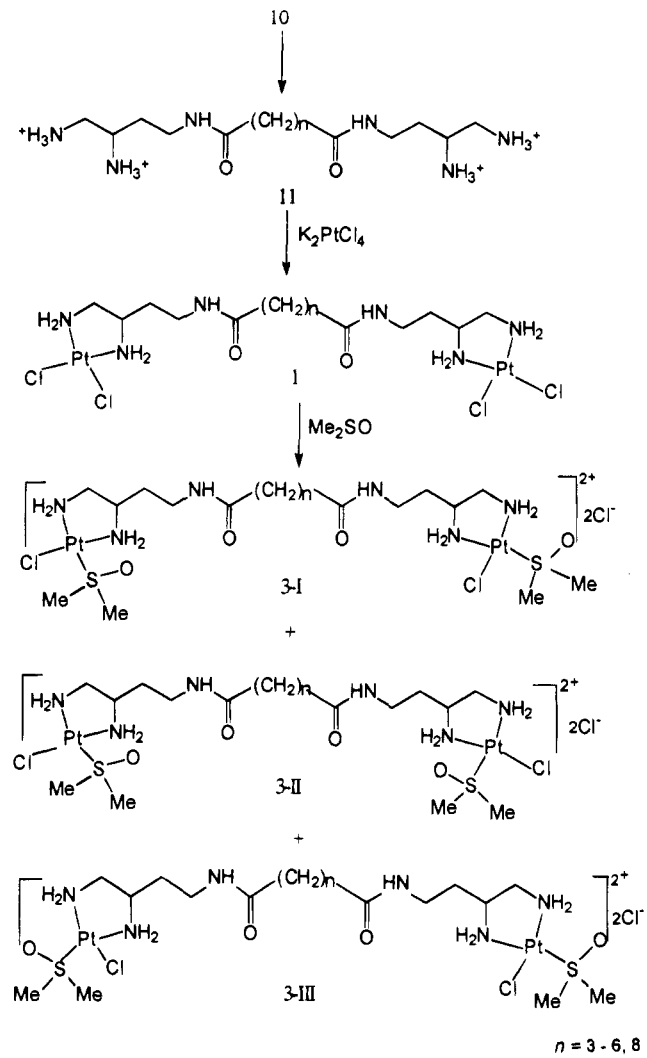
with hot 2-propanol. **1** crystallized from the *i*PrOH solution upon addition of diethyl ether and was recrystallized from ethanol/diethyl ether to give the analytically pure product.

***N*¹,*N*'¹-Glutarylbis(histamine) (9a)**: colorless crystals; yield 481 mg (28%); mp 161 °C. IR (Nujol): ν = 3294−3012 (NH), 1638 (CO), 1563 cm^{-1} (NH). ^{1}H-NMR (CD_3OD): δ = 1.84 (quint, $^3J_{HH}$ = 7.3 Hz, 2H, CH_2), 2.16 (t, $^3J_{HH}$ = 7.3 Hz, 4H, $COCH_2$), 2.77 (t, $^3J_{HH}$ = 7.2 Hz, 4H, CH_2), 3.41 (t, $^3J_{HH}$ = 7.2 Hz, 4H, NCH_2), 6.84 (s, 2H, imidazole H), 7.57 (s, 2H, imidazole H). ^{13}C{^{1}H}-NMR (CD_3OD): δ = 23.2 ($COCH_2CH_2$), 27.8 (NCH_2CH_2), 36.2 (NCH_2CH_2), 40.4 ($COCH_2CH_2$), 118.0 (*C*H=C), 136.0 (CH=*C*), 136.1 (N*C*H=N), 175.3 (CO). Anal. Calcd for $C_{15}H_{22}N_6O_2$: C, 56.59; H, 6.96; N, 26.40. Found: 56.33; H, 7.25; N, 26.28.

***N*¹,*N*'¹-Adipoylbis(histamine) (9b)**: colorless crystals; yield 684 mg (36%); mp 135 °C. IR (Nujol): ν = 3518−3026 (NH), 1634 (CO), 1580 cm^{-1} (NH). ^{1}H-NMR (CD_3OD/D_2O): δ = 1.50 (m, 4H, $COCH_2CH_2$), 2.19 (m, 4H, $COCH_2CH_2$), 2.80 (t, $^3J_{HH}$ = 6.8 Hz, 4H, NCH_2CH_2), 3.45 (t, $^3J_{HH}$ = 6.8 Hz, 4 H, NCH_2CH_2), 6.91 (s, 2H, imidazole H), 7.66 (s, 2H, imidazole H). ^{13}C{^{1}H}-NMR (CD_3OD/D_2O): δ = 24.9 ($COCH_2CH_2$), 27.1 (NCH_2CH_2), 36.4 (NCH_2CH_2), 40.0 ($COCH_2CH_2$), 117.7 (*C*H=C), 135.6 (CH=*C*), 136.4 (N*C*H=N), 176.9 (CO). Anal. Calcd for $C_{16}H_{24}N_6O_2{\cdot}H_2O$: C, 54.84; H, 7.48; N, 23.98. Found: C, 54.49; H, 7.51; N, 23.95.

Ring-Cleavage *tert*-Butoxycarbonylation of 9. General Procedure. To a suspension of **11** (4.0 mmol) in acetonitrile (50 mL) and 15% aqueous potassium acetate solution (40 mL) was added di-*tert*-butyl dicarbonate (8.7 g, 40.0 mmol), and the reaction mixture was stirred for 5 d at ambient temperature. The progress of the reaction was monitored by TLC using a 9:1 mixture of ethyl acetate/2-propanol. The organic layer was separated from the mixture and the acetonitrile removed *in vacuo*. The residue was dissolved in ethyl acetate (150 mL); the solution was washed with 5% aqueous $NaHCO_3$ and water and dried over Na_2SO_4. Silica gel (10 g) was added to the solution, and after 20 min of stirring, the solvent was removed *in vacuo*. The residue was introduced on the top of a column prepared from silica gel (30 g) in ethyl acetate/hexane (1:9). The excess of di-*tert*-butyl carbonate was eluted with ethyl acetate/hexane (1:9). **10** was obtained upon elution with ethyl acetate/2-propanol (95:5).

Scheme 2



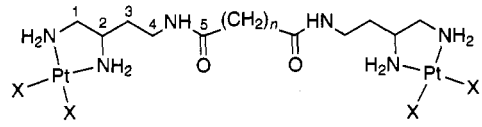
10a: colorless crystalline solid; yield 1.29 g (43%). R_f = 0.62 (TLC—silica gel, 0.2 mm, 254 mm, ethyl acetate/ethanol, 9:1). IR (Nujol): ν = 3299 (NH), 1750, 1728, 1697, 1654 cm^{-1} (CO). Anal. Calcd for $C_{35}H_{58}N_6O_{12}$: C, 55.69; H, 7.74; N, 11.13. Found: C, 55.81; H, 8.32; N, 11.03.

10b: colorless crystalline solid; yield 1.73 g (56%). R_f = 0.76 (TLC—silica gel, 0.2 mm, 254 nm, ethyl acetate/ethanol, 9:1). IR (Nujol): ν = 3391 (NH), 1750, 1727, 1697, 1647 cm^{-1} (CO). Anal. Calcd for $C_{36}H_{60}N_6O_{12}$: C, 56.23; H, 7.86; N, 10.93. Found: C, 56.17; H, 8.15; N, 10.65.

Hydrogenation of 10. General Procedure. A water suspension of Raney nickel (1 mL) was introduced into the hydrogenation vessel and washed with 3 × 5 mL of ethanol. **12** (0.6 mmol) in ethanol (50 mL) was added. Hydrogenation was performed slightly above atmospheric pressure for 24 h at 40 °C. The solution was filtered from the catalyst, concentrated, and passed through a silica gel column (10 g) to remove traces of $Al(OH)_3$ stemming from the catalyst. **10** was precipitated by addition of diethyl ether and recrystallized from ethanol/diethyl ether.

Removal of the *tert*-Butoxycarbonyl (Boc) Protecting Groups. General Procedure. To a solution of **10** (1.0 mmol) in dry ethanol (8 mL) was added a 20% solution (8 mL) of dry HCl in ethanol, and the reaction mixture was stirred for 6 h at ambient temperature. After 1 h, a precipitate of **11** was formed. Dry diethyl ether (20 mL) was added to complete precipitation. The crystalline **11** was isolated by filtration, washed three times with diethyl ether, and dried *in vacuo*.

Table 1. ^{195}Pt, ^{1}H, and ^{13}C NMR Chemical Shifts of the Pt(II) and Pd(II) Complexes 1a, 2a, 3a, and 13 in DMSO-d_6



		1a	2a	3a	13
$\delta(^{195}Pt)$		−2312		−3286, −3289	−3286, −3290
$\delta(^{1}H)$	1-H	2.35	2.40	2.71, 2.65	2.69, 2.62
		2.10	2.35	2.41, 2.41	2.40, 2.40
	2-H	2.56	2.76	2.90	2.82
	3-H	1.65	1.61	1.65	1.62
		1.53	1.54	1.73	1.70
	4-H	3.03	3.06	3.10	3.06, 3.04
	1-NH_2[a]	5.37	4.77	6.50, 6.10	6.44, 6.01
		5.24		6.26, 6.05	6.26
	2-NH_2[b]	5.43	4.92	6.46, 6.15	6.44, 6.05
		5.14	4.75	6.28, 5.90	6.29, 5.88
	4-NH	7.86	7.93	8.24, 8.11	8.03, 7.87
$\delta(^{13}C)$	C-1	52.4	51.2	50.9, 50.7	50.9, 50.7
	C-2	58.2	57.2	57.3, 57.2	57.3, 57.2
	C-3	30.0	31.2	30.4, 30.1	30.5, 30.1
	C-4	35.4	35.6	35.3, 35.2	35.3
	C-5	172.0	172.9	172.2, 172.1	174.3, 174.2

[a] AB part of ABX system; $^{2}J_{HNH}$ = 9.8 Hz (**1a**), broad, unresolved (**2b**), 10.0 Hz (**3a**), 9.9 Hz (**13**). [b] $^{2}J_{HNCH}$ = 5.9 Hz (**1a**), broad unresolved (**2a**), 5.8 Hz (**3a**), 5.8 Hz (**13**). Data for **3c** and **13** with coordinated $(CH_3)_2SO$ in D_2O at 90 MHz: ^{1}H NMR δ = 3.34, $(CH_3)_2SO$, J_{PtH} = 22 Hz.

N^4,N'^4-Glutaroylbis(1,2,4-triaminobutane) Tetrahydrochloride (11a): colorless crystalline hygroscopic solid; yield 412 mg (92%). IR (Hostaflon): ν = 3255−2600 cm^{-1} (NH). IR (Nujol): 1640 (CO), 1553 cm^{-1} (NH). ^{1}H-NMR (D_2O): δ = 1.79 (m, 2H, 7-CH_2), 1.87, 1.92 (m, 4H, 3-CH_2), 2.22 (t, $^{3}J_{HH}$ = 7.7 Hz, 4H, 6-CH_2), 3.2−3.4 (m, 8H, 1-CH_2, 4-CH_2), 3.54 (m, 2H, 2-CH). $^{13}C\{^{1}H\}$-NMR (D_2O): δ = 22.5 (C-7), 31.2 (C-3), 35.7 (C-6), 35.8 (C-4), 41.8 (C-1), 48.2 (C-2), 177.5 (C-5). Anal. Calcd for $C_{13}H_{34}Cl_4N_6O_2$: C, 34.83; H, 7.64. Found: C, 34.87; H, 8.35.

N^4,N'^4-Adipoylbis(1,2,4-triaminobutane) Tetrahydrochloride (11b): colorless crystalline hygroscopic solid; yield 456 mg (95%). IR (Hostaflon): ν = 3250−2600 cm^{-1} (NH). IR (Nujol): 1639, 1612 (CO), 1551 cm^{-1} (NH). ^{1}H-NMR (D_2O): δ = 1.61 (m, 4H, 7-CH_2), 1.96, 2.03 (m, 4H, 3-CH_2), 2.32 (m, 4H, 6-CH_2), 3.3−3.5 (m, 8H, 1-CH_2, 4-CH_2), 3.64 (m, 2H, 2-CH). $^{13}C\{^{1}H\}$-NMR (D_2O): δ = 25.4 (C-7), 31.0 (C-3), 35.5 (C-4), 35.9 (C-6), 41.5 (C-1), 47.9 (C-2), 178.0 (C-5). Anal. Calcd for $C_{14}H_{36}Cl_4N_6O_2{\cdot}H_2O$: C, 35.01; H, 7.97. Found: C, 34.91; H, 8.08.

N^4,N'^4-Pimeloylbis(1,2,4-triaminobutane) Tetrahydrochloride (11c): colorless crystalline hygroscopic solid; yield 470 mg (90%). IR (Nujol): ν = 3260−2600 (NH), 1639 (CO), 1550 cm^{-1} (NH). ^{1}H-NMR (D_2O): δ = 1.17 (m, 2H, 8-CH_2), 1.45 (m, 4H, 7-CH_2), 1.74, 1.84 (m, 4H, 3-CH_2), 2.81 (m, 4H, 6-CH_2), 3.1−3.3 (m, 8H, 1-CH_2, 4-CH_2), 3.47 (m, 2H, 2-CH). $^{13}C\{^{1}H\}$-NMR (CD_3OD): δ = 26.3 (C-7), 29.7 (C-8), 31.3 (C-3), 35.8 (C-4), 35.9 (C-6), 42.3 (C-1), 48.6 (C-2), 177.5 (C-5). Anal. Calcd for $C_{15}H_{38}Cl_4N_6O_2{\cdot}C_2H_5OH$: C, 39.09; H, 8.49; N, 16.09. Found: C, 38.42; H, 8.47; N, 15.72.

N^4,N'^4-Suberoylbis(1,2,4-triaminobutane) Tetrahydrochloride (11d): colorless crystalline hygroscopic solid; yield 413 mg (77%). IR (Nujol): ν = 3200−2600 (NH), 1639 (CO), 1550 cm^{-1} (NH). Anal. Calcd for $C_{16}H_{40}Cl_4N_6O_2{\cdot}C_2H_5OH$: C, 40.31; H, 8.64; N, 15.67. Found: C, 40.12; H, 8.50; N, 15.02.

N^4,N'^4-Sebacoylbis(1,2,4-triaminobutane) Tetrahydrochloride (11e): colorless crystalline hygroscopic solid; yield 526 mg (98%). IR (Nujol): ν = 3253−2500 (NH), 1638 (CO), 1548 cm^{-1} (NH). ^{1}H-NMR (CD_3OD): δ = 1.22 (m, 8H, 8-CH_2, 9-CH_2), 1.51 (m, 4H, 7-CH_2), 1.78, 1.89 (m, 4H, 3-CH_2), 2.14 (m, 4H, 6-CH_2), 3.16−3.52 (m, 10H, 1-CH_2, 2-CH, 4-CH_2). $^{13}C\{^{1}H\}$-NMR (CD_3OD): δ = 26.7 (C-7), 30.1 (C-9), 30.3 (C-8), 32.2 (C-3), 35.8 (C-4), 36.8 (C-6), 42.2 (C-1), 48.4 (C-2). Anal. Calcd for $C_{18}H_{44}Cl_4N_6O_2{\cdot}2H_2O$: C, 39.09; H, 8.74. Found: C, 39.98; H, 8.98.

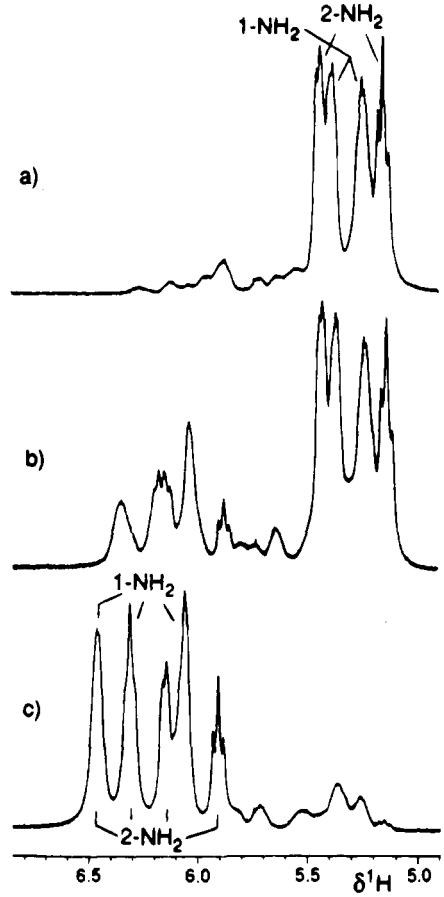


Figure 1. ^{1}H-NMR spectra in DMSO-d_6 of the NH_2 signal region: (a) freshly prepared solution of the pure bis(dichloroplatinum) complex **1e**; (b) same solution after 1 h; (c) equilibrated solution of the solvato species **3e** after 12 h.

Preparation of $[Cl_2Pt(LL)PtCl_2]$ (1) and $[Cl_2Pd(LL)PdCl_2]$ (2). General Procedure. A solution of **11** (1.0 mmol) and K_2PtCl_4 or Na_2PdCl_4 (2.0 mmol) in distilled water (12 mL) was heated to 65−70 °C with stirring. The pH of the reaction solution was checked continuously with a pH electrode and dropped as the reaction progressed. With the help of a syringe, 1 M NaOH (3.6 mL) was added in intervals to keep the pH in the range 3−4. Toward the end of the reaction, pH was adjusted to 5 with 0.1 M NaOH. After the mixture was cooled to ambient temperature, the yellow precipitate of **1** or **2** was centrifugated, washed three times with cold water, twice with ethanol, and once with diethyl ether, and dried *in vacuo*. For the ^{1}H-, ^{13}C-, and ^{195}Pt-NMR spectroscopy, complexes **1** and **2** were dissolved in DMSO-d_6 immediately before recording the spectra. The ^{1}H-, ^{13}C-, and ^{195}Pt-NMR data are given in Table 1.

1a: yellow solid; yield 597 mg (70%); mp 225 °C dec. IR (Nujol): ν = 3273, 3206, 3109, 1640, 1561, 350 sh, 312 cm^{-1}. Anal. Calcd for $C_{13}H_{30}Cl_4N_6O_2Pt_2{\cdot}H_2O$: C, 18.32; H, 3.78; N, 9.86. Found: C, 18.24; H, 3.96; N, 9.61.

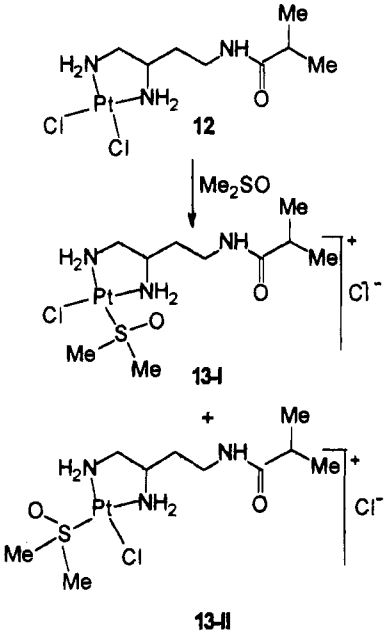
1b: yellow solid; yield 546 mg (63%); mp 254 °C dec. IR (Nujol): ν = 3273, 3198, 3109, 1643, 1559, 338 sh, 310 cm^{-1}. Anal. Calcd for $C_{14}H_{32}Cl_4N_6O_2Pt_2{\cdot}H_2O$: C, 19.41; H, 3.96; N, 9.70. Found: C, 19.56; H, 4.16; N, 9.49.

1c: yellow solid; yield 650 mg (74%); mp 234 °C dec. IR (Nujol): ν = 3270, 3197, 3102, 1644, 1559, 325 sh, 303 cm^{-1}. Anal. Calcd for $C_{15}H_{34}Cl_4N_6O_2Pt_2{\cdot}H_2O$: C, 20.46; H, 4.12; N, 9.54. Found: C, 20.27; H, 4.39; N, 9.26.

1d: yellow solid; yield 733 mg (82%); mp 250 °C dec. IR (Nujol): ν = 3270, 3198, 3107, 1647, 1559, 310 br cm^{-1}. Anal. Calcd for $C_{16}H_{36}Cl_4N_6O_2Pt_2{\cdot}H_2O$: C, 21.48; H, 4.28; N, 9.40. Found: C, 21.24; H, 4.33; N, 9.19.

1e: yellow solid; yield 720 mg (78%); mp 242 °C dec. IR (Nujol): ν = 3268, 3196, 1646, 1559, 310 br cm^{-1}. Anal. Calcd for $C_{18}H_{40}Cl_4N_6O_2Pt_2{\cdot}H_2O$: C, 23.43; H, 4.59; N, 9.11. Found: C, 23.31; H, 4.61; N, 9.01.

Scheme 3



2a: yellow solid; yield 520 mg (77%); mp 240 °C dec. IR (Nujol): ν = 3282, 3202, 3116, 1649, 1559, 340 sh, 304 cm^{-1}. Anal. Calcd for $C_{13}H_{30}Cl_4N_6O_2Pd_2 \cdot H_2O$: C, 23.13; H, 4.78; N, 12.45. Found: C, 22.98; H, 4.91; N, 12.06.

2b: yellow solid; yield 474 mg (67%); mp 255 °C dec. IR (Nujol): ν = 3282, 3203, 3099, 1645, 1556, 349 sh, 303 cm^{-1}. Anal. Calcd for $C_{14}H_{32}Cl_4N_6O_2Pd_2 \cdot 2H_2O$: C, 23.78; H, 5.13; N, 11.88. Found: C, 23.81; H, 5.08; N, 11.63.

Solvolysis of Complexes 1 and 12 in DMSO-d_6. **1** or **14** (0.05 mmol) was dissolved in DMSO-d_6 (0.5 mL) at ambient temperature. Immediately after dissolution and after 1 h, the ^{1}H-NMR spectra were recorded, and after 12 h, the ^{1}H-, ^{13}C-, and ^{195}Pt-NMR spectra were recorded.

Isolation of [(DMSO)(Cl)Pt(LL)Pt(Cl)(DMSO)]Cl_2 (3) and [Pt(L)(DMSO)Cl]Cl (13). General Procedure. **1** (0.1 mmol) was dissolved in DMSO (1 mL). After 12 h, the product was precipitated by addition of ether (10 mL) and purified by dissolving in MeOH (1 mL) and precipitating with ether.

3c: white solid; yield 95 mg (93%); mp 95 °C (change to yellow—displacement of DMSO by chlorine). IR (Nujol): ν = 3356, 3213, 3066, 1643, 1550, 1129, 441, 344 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6; freshly prepared sample): δ = 1.22 (m, 2H, 8-CH_2), 1.50 (m, 4H, 7-CH_2), 1.66, 1.73 (m, 4H, 3-CH_2), 2.09 (t, 4H, 6-CH_2), 2.44, 2.65, 2.72 (m, 4H, 1-CH_2), 2.82 (m, 2H, 2-CH), 3.05 (m, 2H, 4-CH_2N), 3.39, 3.40, 3.41, 3.44 (6H, $(CH_3)_2$S), 5.89, 6.40 (m, 4H, 2-NH_2), 6.05, 6.13, 6.23 (m, 4H, 1-NH_2), 7.96 (t, 1H, NH), 8.13 (t, 1H, NH). The signals at 3.39−3.44 disappear upon standing owing to exchange with molecules of solvent. ^{1}H-NMR (90 MHz, D_2O): δ = 3.35 (s and two satellites, J_{PtH} = 22 Hz, CH_3S). ^{13}C-NMR (DMSO-d_6; freshly prepared sample: δ = 24.9 (C-7), 28.3 (C-8), 29.6, 30.1 (C-3), 31.5 (C-6), 35.2 (C-4), 43.1, 43.2, 43.3, 43.4 ($(CH_3)_2$S); 50.7, 50.9 (C-1), 57.2, 57.4 (C-2), 176.3, 176.4 (CO); the signals at δ 43.1−43.4 disappear upon standing owing to exchange with molecules of solvent. Anal. Calcd for $C_{19}H_{46}Cl_4N_6O_4S_2Pt_2$: C, 22.40; H, 4.55; N, 8.25; S, 6.19. Found: C, 21.98; H, 4.67; N, 7.99; S, 6.03.

3d: white solid; yield 90 mg (87%); mp 102 °C (change to yellow—displacement of DMSO by chlorine). IR (Nujol): ν = 1644, 1547, 1129, 441, 344 cm^{-1}. ^{1}H-NMR (90 MHz, D_2O): δ = 3.35 (s and two satellites, J_{PtH} = 22 Hz, CH_3S). Anal. Calcd for $C_{20}H_{48}Cl_4N_6O_4S_2Pt_2$: C, 23.26; H, 4.68; N, 8.13; S, 6.21. Found: C, 23.59; H, 4.86; N, 7.78; S, 5.95.

3e: white solid; yield 97 mg (88%); mp 90 °C (change to yellow). IR (Nujol): ν = 1644, 1549, 1130, 441, 347 cm^{-1}. ^{1}H-NMR (90 MHz, D2O): δ = 3.35 (s and two satellites, J_{PtH} = 22 Hz, CH_3S). Anal. Calcd for $C_{22}H_{52}Cl_4N_6O_4S_2Pt_2$: C, 24.91; H, 4.94; N, 7.92; S, 6.02. Found: C, 25.13; H, 5.11; N, 7.70; S, 5.86.

13: white solid; yield 45 mg (88%); mp 95 °C (change to yellow). IR (Nujol): ν = 1646, 1545, 1128, 441, 346 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6; freshly prepared sample): δ = 0.97, 1.00 (dd, 6H, $(CH(CH_3)_2$, 1.62, 1.70 (m, 2H, 3-CH_2), 2.34 (m, 1H, C$H(CH_3)_2$), 2.38, 2.62, 2.69 (m, 2H, 1-CH_2), 2.82 (m, 1H, 2-CH), 3.03 (m, 2H, 4-CH_2N), 3.39, 3.40, 3.41, 3.44 (6H, $(CH_3)_2$S), 5.80, 6.44 (m, 2H, 2-NH_2), 6.04, 6.13, 6.28 (m, 2H, 1-NH_2), 7.96 (t, 1H, NH), 8.13 (t, 1H, NH); the signals at δ 3.39−3.44 disappear upon standing owing to exchange with molecules of solvent. ^{1}H-NMR (90 MHz, D_2O): δ = 3.35 (s and two satellites, J_{PtH} = 22 Hz, CH_3S). ^{13}C-NMR (DMSO-d_6; freshly prepared sample): δ = 19.5, 19.6 (Me), 30.0, 30.4 (C-3), 34.0, 34.0 (C-4), 35.2 ($CH(CH_3)_2$, 43.1, 43.2, 43.3, 43.4 $(CH_3)_2$S, 50.7, 51.0 (C-1), 57.2, 57.3 (C-2), 176.3, 176.4 (CO); the signals 43.1−43.4 disappear upon standing owing to exchange with molecules of solvent. Anal. Calcd for $C_{10}H_{19}Cl_2N_3O_2SPt$: C, 23.21; H, 4.87; N, 8.12; S, 6.19. Found: C, 23.35; H, 5.05; N, 7.95; S, 6.03.

Results and Discussion

Synthesis of Bis(1,2,4-triaminobutane) Derivatives. We previously reported the two-step synthesis of N^1,N^2-bis(*tert*-butoxycarbonyl)-N^4-(trifluoroacetyl)-1,2,4-triaminobutane (**6**) involving ring cleavage by *tert*-butoxycarbonylation of N^{α}-(trifluoroacetyl)histamine (**4**) and catalytic reduction of the open-chain product **5**.[18] Removal of the trifluoroacetyl group with NaOH gives N^1,N^2-bis(*tert*-butoxycarbonyl)-1,2,4-triaminobutane (**7**); tethering together the two free amine functions of **7** as bis(amides) of α,ω-dicarboxylic acids of different chain lengths, **8** (n = 3−6, 8), and removal of Boc protecting groups, creates in one molecule two ethylenediamine units available for formation of bis(platinum) complexes at its ends (Scheme 1). Some difficulties previously encountered in the hydrogenation step were now overcome by performing hydrogenation at 80 bar hydrogen pressure and 45 °C. This synthetic pathway appears to be more general and easier than another approach which involves bridging of two histamine molecules by dicarboxylic acid dichlorides to give bis(amide) **9**, ring-opening *tert*-butoxycarbonylation to **10**, and reduction to **8**. Treatment of **10a**−**e** with dry hydrogen chloride in ethanol removes the Boc protecting groups, yielding tetraamines as hygroscopic colorless tetrahydrochlorides, **11**.

Preparation and Properties of Pt(II) and Pd(II) Complexes. Tetrahydrochlorides **11** react with 2 equiv of K_2PtCl_4 or Na_2PdCl_4 in water solution at 70 °C and pH 5 to form the yellow solid of the bis(dichloroplatinum) or bis(dichloropalladium) complex **1** or **2** (Scheme 2). The reaction requires well-controlled pH conditions to avoid formation of white tetraamineplatinum(II), which could be observed above pH 7. **1** and **2** are sparingly soluble in water and in DMF. They are soluble in Me_2SO, which involves solvolysis similar to that observed for mononuclear Pt(II) complexes with substituted ethylenediamines.[23] The process affords $[Pt(Cl)(Me_2SO)(en)]^+$ species in which the chelating amine does not undergo exchange.[23] In the solvolysis process of *cis*- and *trans*-$[Pt(am)_2Cl_2]$, where am is NH_3 or primary aliphatic amine, the formed *cis*- or *trans*-$[Pt(am)_2(DMSO)Cl]Cl$ complexes undergo further displacement of the amine ligand by chloride.[24−28]

NMR Spectra of the Metal Complexes. We run the NMR spectra of dinuclear complexes **1** and **2** in $(CD_3)_2SO$, avoiding

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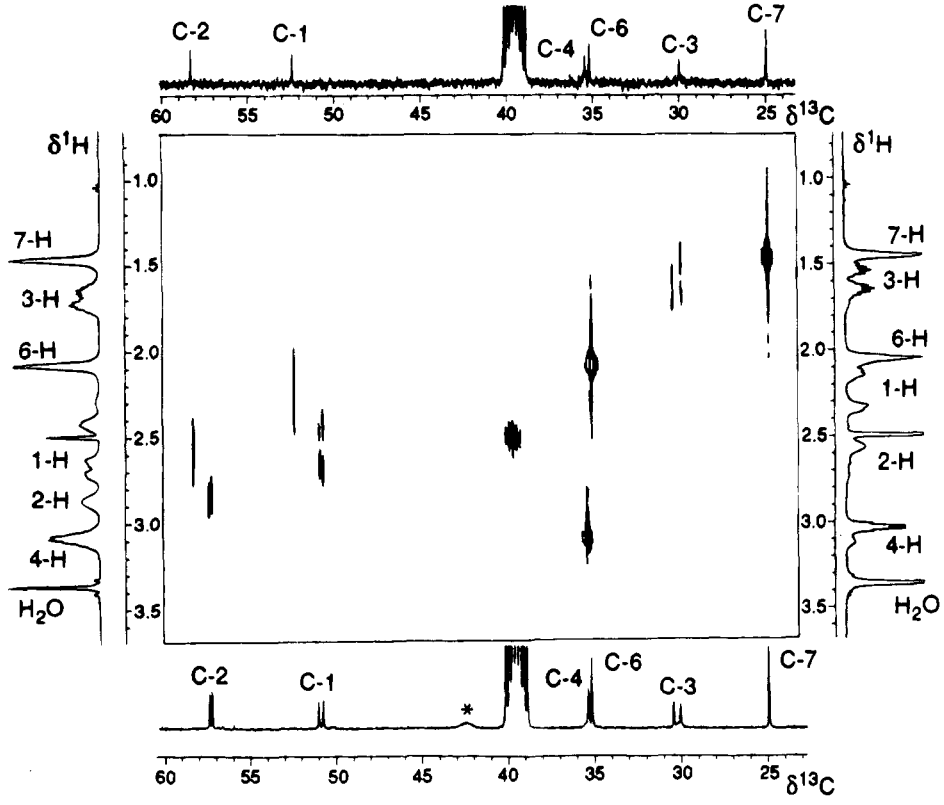

Figure 2. $^1H,^{13}C$-correlated NMR spectrum of the solution of **1b** in DMSO-d_6 scanned overnight. It shows the cross peaks of **1b** as well as of **3b**. The ^{13}C-NMR of **1b** (top) and **3b** (bottom) as well as their ^1H-NMR spectra (right and left sides, respectively) are also shown. The ^{13}C-NMR signal in the spectrum of **3b** marked with an asterisk is attributed to coordinated DMSO-d_6.

deuteration of amine groups of the ligands in order to follow changes in the absorptions of NH_2 protons. The freshly prepared solutions show the presence of a single species of the parent complex **1** or **2**. With the formation of the five-membered chelate ring, the protons of the coordinating NH_2 groups become diastereotopic because of the chiral center at C-2 in the triaminobutane ligand. The assignment of the signals belonging to one NH_2 group as well as of the other signals in the ^1H-NMR spectra follows unequivocally from the ^1H-COSY-45 NMR spectra. The dfference in the chemical shifts for the 2-NH_2 protons located next to the chiral center is larger than for the 1-NH_2 protons, and it is more strongly pronounced in the platinum complexes **1** than in the palladium complexes **2**. For the 2-NH_2 protons the geminal coupling is 9−10 Hz (Table 1).

The ^{13}C chemical shifts of **1** and **2** are assigned on the basis of ^1H, ^{13}C-correlated spectra and are given in Table 1. They prove that no migration of the acyl group took place and the ligand skeleton was preserved during the complex formation. On coordination, the resonances of C-1 and C-2 are shifted to lower field ($\Delta\delta \sim 10$) compared to those of the free ligands.[29]

The ^{195}Pt-NMR spectra of complexes **1** show a broad signal ($\Delta_{1/2} \sim 300$ Hz) at $\delta = -2312$ (Table 1).[30-32] The ^{195}Pt chemical shifts compare well with those of the analogous mononuclear N^4-acyl-1,2,4-triaminobutane complexes[18] and of other diamine $PtCl_2$ complexes.[20,21]

The progress of solvolysis may be conveniently followed by monitoring the ^1H-NMR signals of the NH_2 protons (Figure 2). A freshly prepared solution shows only the signals of **1**. After 1 h, two new sets of signals for each NH_2 group appear at lower field. Solvolysis is complete within 12 h (Figure 1). Since in the parent complex **1** the two chlorines at each Pt are not equivalent, the displacement of one chlorine at each Pt may lead to three possible square planar, ionic [(DMSO)(Cl)Pt(LL)-Pt(Cl)(DMSO)]Cl_2 isomers **3-I**, **3-II**, and **3-III**: X^1, X^3 = Cl, X^2, X^4 = $(CD_3)_2SO$; X^1, X^4 = $(CD_3)_2SO$, X^2, X^3 = Cl; X^1, X^4 = Cl, X^2, X^3 = $(CD_3)_2SO$ (Scheme 2). The solvolysis of the mononuclear complex **12**[18] in DMSO-d_6 yields **13-I**, X^1 = Cl, X^2 = $(CD_3)_2SO$, and **13-II**, X^1 = $(CD_3)_2SO$, X^2 = Cl. The side chain with the acyl function has no influence on the preference of chlorine toward exchange. In this respect, the platinum complexes of acyl-substituted triaminobutane ligands behave as ethylenediamine complexes substituted on carbon with alkyl groups[23] (Scheme 3). **3** and **13** were identified by their ^{195}Pt-, ^1H-, and ^{13}C-NMR spectra (Table 1). In both cases, the spectra show two sets of signals, corresponding to the two environments of the platinum atoms with the $(CD_3)_2SO$ ligand bonded *cis* or *trans* to the 1-NH_2 group. They do not differentiate between the two asymmetrically substituted chelate rings in **3-I** and a mixture of the two symmetric isomers **3-II** and **3-III**. The ^{195}Pt-NMR spectra of **3** and **13** show two broad ($\Delta_{1/2} \sim 300$ Hz) signals located close together around −3288 ppm (Table 1), a region characteristic of [Pt(amine)$_2$Cl(Me$_2$-SO)]Cl type complexes.[23] Compared to that of **1**, the ^{195}Pt signal of the ionic sulfoxides is shifted by ~1000 ppm to higher field, which is expected to occur when Cl^- at a platinum atom is substituted by Me_2SO.[23,27]

The ^1H- and ^{13}C-NMR spectra of **3** and **13** resemble those of $PtCl_2$ complexes **1** and **2**. The assignment of the NH_2 signals as well as the other signals in the ^1H-NMR spectra is based on ^1H-COSY-45 spectra. They demonstrate clearly the presence of two sets of diastereotopic 1-NH_2 and 2-NH_2 protons,

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confirming that the five-membered chelate ring has been preserved during solvolysis. The ^{13}C-NMR signals of **3** and **13** (Table 1) are assigned on the basis of $^{1}H,^{13}C$-correlated spectra. Figure 2 shows the $^{1}H,^{13}C$-correlated spectrum of a freshly prepared solution of **1b** in DMSO-d_6 and a spectrum of this solution recorded overnight. Since solvolysis is slow, but complete within 12 h, it shows the cross peaks of both **1b** and **3b**. As can be seen, replacement of Cl^- by $(CD_3)_2SO$ at the platinum atom shifts the signals of the C-1 and C-2 carbon atoms of $(CD_3)_2SO$, coordinated to platinum, to a slightly higher field, while the signals of the protons at these carbon atoms experience a slight shift in the opposite direction. The broad signal in the ^{13}C spectrum of **1b** in Figure 4 and $\delta = 42.5$ is attributed to the carbon atoms of $(CD_3)_2SO$, coordinated to platinum.

The DMSO complexes **3c**, **3d**, and **3e** were isolated as white solids when the exchange was performed in $(CH_3)_2SO$. For the freshly prepared solutions in DMSO-d_6, four very close signals of the diastereotopic methyls of the two Pt−S bound $(CH_3)_2SO$ ligands are observed in ^{1}H NMR, shifted downfield by 0.9 ppm is compared to the signals of the noncoordinated ligand. In the ^{13}C NMR spectrum, the four signals of corresponding coordinated DMSO methyls appear in the 43.1−43.4 ppm region. Upon standing, these signals disappear as a result of equilibration with deuterated molecules of the solvent which gives rise in the same region to the very broad absorption of the coordinated DMSO-d_6. **3** and **13** are soluble in water. In the ^{1}H NMR spectra in D_2O at 90 MHz all methyls of coordinated $(CH_3)_2SO$ appear as a singlet at 3.33 ppm with the characteristic satellites of J_{PtH} coupling of 22 Hz.[33] At 400 MHz the satellites are not observed;[29] the coordinated $(CH_3)_2SO$ of **3c** gives rise to three signals and of **13** to two, in a ratio 1:3, owing to superposition of the expected four signals whereas in ^{13}C NMR all four are observed.

Conductivity. Water solutions (2.5×10^{-4} M) of **3c**, **3d**, and **3e** exhibit at 25 °C conductivity of 231, 227, and 225 Ω^{-1} cm^{-1} mol^{-1}, respectively, whereas the conductivity of the mononuclear complex **13** is 99 Ω^{-1} cm^{-1} mol^{-1}. When the sample is heated at 90−110 °C at atmospheric pressure, the ionic chlorine slowly reenters the coordination sphere, displacing Me_2SO. The reported mononuclear $[Pt(Me_2SO)(en)Cl]^+Cl^-$ lost Me_2SO at 138 °C at 20 mmHg.[23]

IR Spectra of Metal Complexes. In the IR spectra of complexes **1** and **2**, the NH absorptions are observed in the 3100−3280 cm^{-1} region, the δNH bands of the amide groups and of the $M-NH_2$ groups at 1556−1561 cm^{-1}, and the carbonyl absorptions at 1640−1649 cm^{-1}. The M−Cl absorptions appear as strong broad bands in the 303−350 cm^{-1} region with a maximum between 303 and 310 cm^{-1} and a shoulder between 335 and 350 cm^{-1}. The ionic complexes **3** and **13** exhibit a weak Pt−Cl band at 346 cm^{-1}, a weak Pt−S band at 440 cm^{-1}, and a strong stretching frequency of coordinated SO at 1128 cm^{-1}.[33,34]

Conclusion

We have described the synthesis and the properties of a series of bis(platinum) complexes **1** and **3** in which two 1,2,4-triaminobutane units are bridged as α,ω-dicarboxylic acid bis(amides) of variable length ($n = 3-6, 8$). They are at present under study as DNA interstrand cross-linking agents.[35]

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Supplementary Material Available: ^{1}H-COSY-45 NMR spectra of **1e** and **3a** and two tables of NMR data for all complexes **1a−e** and **3a−e** (4 pages). Ordering information is given on any current masthead page.

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(35) The efficiency of the bis(platinum) complexes **1** and **3** to form interhelical cross-linking of the double-strand DNA is currently being analyzed by H. Büning and Dr. H. Zorbas at the Institute of Biochemistry, University of Munich, and will be reported in due course.