Hydrocarbon-bridged Metal Complexes, LII [1]. N^1,N^2-Di(*tert*-butoxycarbonyl)-1,2,4-triaminobutane, a Useful Reagent for the Synthesis of Hydrocarbon-bridged Bis(ethylenediamine) Ligands by Reactions with Dicarboxylic Acids

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Dedicated to Professor Gérard Jaouen on the occasion of his 65th birthday

The reactions of N^1,N^2-Di-boc-1,2,4-triaminobutane with bridged dicarboxylic acids afford the corresponding bis-amides from which – after removal of the Boc groups – bis(*N,N′*-bidendate) ligands $H_2NCH_2CH(NH_2)(CH_2)_2NHCO$-X-$CONH(CH_2)_2CH(NH_2)CH_2NH_2$ can be obtained. New examples are the reactions of the triaminobutane with pyridine-2,6-dicarboxylic acid, with phenylene-1,4-diacetic acid, with terephthalic acid dichloride and with benzene-1,2,4,5-tetracarboxylic acid. From the new ligands with two terminal ethylenediamine groups, the bis(dichloroplatinum) complexes were synthesized.

Key words: 1,2,4-Triaminobutane, Dicarboxylic Acids, Bis(ethylenediamine) Ligands, Platinum

Introduction

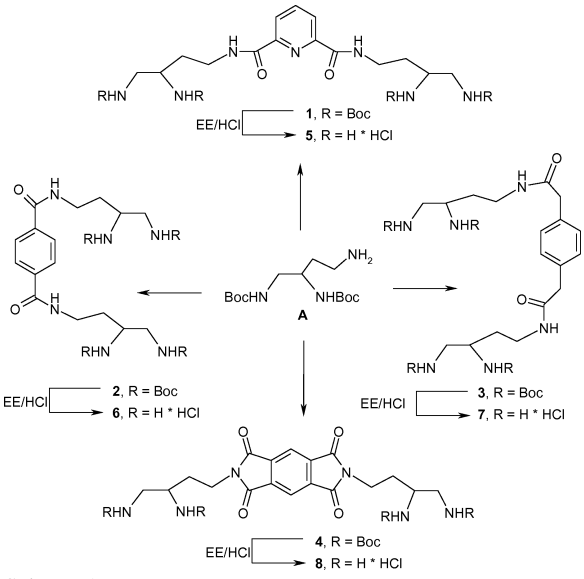
N^1,N^2-Di-boc-1,2,4-triaminobutane **A** was prepared by Bamberger ring cleavage of *N*-trifluoroacetyl histamine with di-*tert*-butylcarbonate, reduction with H_2/Raney nickel and removal of the trifluoroacetyl group with NaOH [2, 3]. Triaminobutane **A** (in non-racemic form) was obtained also from pyroglutamic acid ester by several steps [4]. Recently another – five step – synthesis of the selectively protected triaminobutane, (2*S*)-N^1,N^2-dibenzyloxycarbonyl-1,2,4-triaminobutane in optically pure form, was reported, starting with glutamic acid [5].

The selectively protected triaminobutane **A** provides a rational route to hydrocarbon-bridged bis(ethylenediamine) ligands from which bis(dichloroplatinum) complexes could be obtained. The reactions of **A** with several α,ω-dicarboxylic acids afforded the corresponding bis-amides $H_2NCH_2CH(NH_2)(CH_2)_2$-$NHCO(CH_2)_nCONH(CH_2)_2CH(NH_2)CH_2NH_2$ [3], and the interaction of their bis(dichloroplatinum) complexes with DNA has been studied [6]. Similarly, bis(ethylenediamine) ligands and their platinum complexes could be obtained from **A** and pyrrole-dicarboxylic acids [7]. In continuation of these studies we report in the following new reactions of **A** with various dicarboxylic acids.

Results and Discussion

By use of the Steglich [8] reagent DMAP or by use of the standard peptide coupling agent TBTU, respectively, the triaminobutane **A** was reacted with pyridine-2,6-dicarboxylic acid, terephthalic acid dichloride, phenylene 1,4-diacetic acid and benzene-1,2,4,5-tetracarboxylic acid to give the Boc-protected ligands **1** – **4** (Scheme 1). Removal of the Boc groups was performed with a solution of hydrogen chloride in acetic acid ethyl ester to afford the bis(ethylenediamine) ligands as tetrahydrochlorides **5** – **8** from which the bis(*cis*-dichloroplatinum) complexes **9** – **12** – by reaction with K_2PtCl_4 and NaOH – could be obtained (Fig. 1).

The complexes **9** – **12** have been characterized unequivocally by their IR and NMR spectra (see Experimental Section). Characteristic IR absorptions are observed for ν(Pt–Cl) = 320 cm^{-1} and ν(Pt–N) = 550 cm^{-1}, ν(N–H) = 3200 cm^{-1}, δ(N–H) = 1530 cm^{-1}, and ν(amide) = 1650 cm^{-1}. In the ^1H NMR spectra of **9** – **12** (solutions in DMSO) the



Scheme 1.

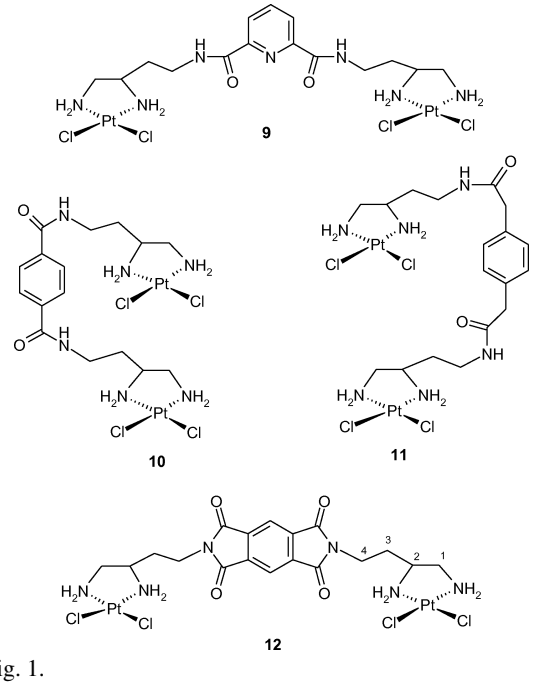


Fig. 1.

typical signals of the triaminobutane [2] are found. The low field shift of the signals of the amino protons from 5.7 – 6.1 to 6.3 – 6.9 ppm is remarkable and is due to the gradual exchange of the chloro ligands by DMSO. By solvolysis of one chloro ligand per Pt in **9** – **12** in DMSO two isomers can be formed [2] which give a complex pattern of the amino signals.

At present, di- and multinuclear platinum complexes find much interest as a novel class of anticancer agents [9, 10] which may circumvent cisplatinum resistance. Among others, Farrell and coworkers are pioneers in this area. In our group several bis(*cis*-dichloroplatinum) complexes have been studied [2, 3, 6, 11]. The study of the biological properties of **9** – **12** is limited by their low solubility in water.

In conclusion, the 1,2,4-triaminobutane **A** has been proven to be a useful reagent for the synthesis of bis(bidendate ethylenediamine) ligands through condensation of its 4-amino group with carboxylic groups.

Experimental Section

rac-N^1,N^2-Dibenzyloxycarbonyl-1,2,4-triaminobutane **A** was synthesized from *N*-trifluoro-acetylhistidine [2, 3].

*General procedure for the preparation of **1**, **3** and **4***

The carboxylic acid, 1,2-di(*tert*-butoxycarbonyl amino)-4-amino-butane, triethylamine and TBTU were suspended in 5 mL of acetonitrile at 0 °C. After 2 h the mixture was warmed up to r. t. and stirred for 12 h. Then, the mixture was heated under reflux for 1 h and stirred for another 30 min. The volatiles were removed *in vacuo*, and the residue was dissolved in acetic acid ethyl ester and was treated three times with 1.1 M aqueous $KHSO_4$ solution and three times with saturated aqueous $NaHCO_3$ solution (with alternation). The organic phase was dried with $MgSO_4$, and the solvent was removed *in vacuo*. The brown residue was purified by chromatography (SiO_2, $CHCl_3$/MeOH = 10/1) and finally by recrystallization from EtOAc/*n*-hexane to give a colorless product.

*Bisamide **1***

932 mg (3.07 mmol) of 1,2-di(*tert*-butoxycarbonyl-amino)-4-aminobutane, 814 μL (5.84 mmol) of triethylamine, 244 mg (1.46 mmol) of pyridine-2,6-dicarboxylic acid and 938 mg (2.92 mmol) TBTU were used. – Yield 580 mg (54 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3357 (s, ν NH), 3341 (s, ν NH), 3065 (w), 2979 (s), 2932 (m), 2877 (w), 1719 (s), 1696 (s, COO), 1682 (s, CON), 1665 (s), 1541 (s, CON), 1479 (w), 1450 (m), 1392 (m), 1367 (s), 1322 (w), 1289 (m), 1272 (m), 1251 (s), 1170 (s), 1108 (w), 1074 (m), 1054 (sh), 1036 (sh), 1001 (m), 981 (w), 960 (w), 899 (w), 869 (m, NH), 845 (m), 781 (m), 751 (w), 724 (w), 709 (w), 679 (m), 647 (m), 463 (w), 433 (w), 348 (sh), 330 (w), 303 (w) cm^{-1}. – ^1H NMR (400 MHz, [D_6]acetone): δ = 9.09 – 9.08 (m, 2 H, N4-H), 8.28 (d, ^3J = 6.8 Hz, 2 H, CH), 8.16 (t, ^3J = 8.0 Hz, 1 H, CH), 7.41 (s, 2 H, CH), 6.28 (s, 2 H, N1-H), 6.14 (d, ^3J = 8.8 Hz, 2 H, N2-H), 3.88 (m, 4 H, C4-H),

3.73 (m, 2 H, C2-H), 3.37 – 3.22 (m, 4 H, C1-H), 1.67 – 1.84 (m, 4 H, C3-H), 1.39 (s, 18 H, CH_3), 1.35 (s, 18 H, CH_3). – ^{13}C NMR (101 MHz, [D$_6$]acetone): δ = 163.10 (2 C, CON), 156.76 (COO), 156.52 (COO), 149.17 (2 C, qC), 139.26 (CH), 124.21 (2 C, CH), 78.10 (4 C, qC_{Boc}), 49.23 (2 C, C2), 44.43 (2 C, C1), 35.66 (2 C, C4), 32.70 (2 C, C3), 27.98 (12 C, CH_3). – $C_{35}H_{39}N_7O_{10}$ (739.89): calcd. C 56.96, H 8.06, N 13.28; found C 56. 62, H 8.20, N 13.06.

Bisamide ***2***

To a solution of 1.50 g (4.95 mmol) of 1,2-di(*tert*-butoxycarbonyl-amino)-4-amino-butane, 1.3 mL (9.2 mmol) of triethylamine, and 84.3 mg (0.69 mmol) of DMAP in 10 mL of dichloromethane a suspension of 467 mg (2.30 mmol) of terephthalic acid dichloride in 5 mL of dichloromethane was added dropwise at 0 °C. The mixture was warmed up to r. t. under stirring for 12 h. Then, the mixture was heated under reflux for 1 h and stirred for another 30 min. After addition of 50 mL of acetic acid ethyl ester the mixture was washed twice with 1.1 M $KHSO_4$ solution, twice with saturated $NaHCO_3$ solution and with water. The milky organic phase contained the product. The precipitate formed was separated and washed with acetic acid ethyl ester. – Yield 1.02 g (60 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3443 (sh), 3363 (br, ν NH), 3084 (w), 2982 (m), 2931 (m), 2872 (sh), 1692 (s, COO), 1643 (s, CON), 1534 (br, CON), 1455 (m), 1393 (m), 1367 (s), 1318 (sh), 1283 (m), 1252 (s), 1172 (s), 1066 (m), 1017 (w), 1000 (w), 903 (w), 868 (m, ρ NH), 781 (w), 731 (w), 644 (w), 630 (w), 605 (w), 462 (w), 436 (w), 331 (w) cm^{-1}. – ^{1}H NMR (400 MHz, CDCl3): δ = 7.87 (s, 4 H, CH), 7.41 (s, 2 H, N4-H), 5.96 (br, 2 H, NH), 5.90 (br, 2 H, NH), 3.70 – 3.61 (m, 2 H, C2-H), 3.31 – 3.29 (m, 2 H, C1-H), 3.16 – 3.08 (m, 2 H, C1-H), 1.75 – 1.71 (m, 2 H, C3-H), 1.54 – 1.51 (m, 2 H, C3-H), 1.40 (s, 18 H, CH_3), 1.39 (s, 18 H, CH_3). – ^{13}C NMR (101 MHz, $CDCl_3$): δ = 190.50 (2 C, CON), 157.47 (2 C, COO), 157.40 (2 C, COO), 136.93 (2 C, qC), 127.33 (4 C, 4 CH), 79.74 (2 C, qC_{Boc}), 79.63 (2 C, qC_{Boc}), 49.24 (2 C, C2), 44.21 (2 C, C1), 36.60 (2 C, C4), 32.18 (2 C, C3), 28.22 (6 C, CH_3), 28.10 (6 C, CH_3). – $C_{36}H_{60}N_6O_{10}$ (736.91): calcd. C 58.68, H 8.21, N 11.40; found C 58.08, H 8.02, N 11.19.

Bisamide ***3***

750 mg (2.47 mmol) of di(*tert*-butoxycarbonyl-amino)-4-aminobutane, 0.69 mL (4.95 mmol) of triethylamine, 240 mg (1.24 mmol) of 1.4-phenylene-diacetic acid, and 794 mg (2.47 mmol) of TBTU were used. – Yield 918 mg (97 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3342 (br, ν NH), 3092 (w), 3063 (w), 2982 (s), 2931 (m), 1694 (s, COO), 1655 (s, CON), 1521 (br, CON), 1479 (w), 1455 (m), 1441 (sh), 1393 (m), 1367 (s), 1273 (sh), 1252 (s), 1172 (s), 1065 (m), 998 (w), 902 (w), 866 (m, ρ NH), 782 (m), 758 (w), 722 (w), 680 (w), 643 (w), 635 (w), 624 (w), 600 (w), 461 (w), 441 (w), 435 (w), 333 (m) cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (s, 4 H, CH), 6.58 (br, 2 H, N4-H), 5.07 – 4.95 (m, 4 H, NH), 3.58 (s, 4 H, CH_2), 3.12 (t, ^3J = 7.0 Hz, 4 H, C4-H), 3.06 (m, 2 H, C2-H), 2.85 – 2.79 (m, 4 H, C1-H), 1.59 – 1.57 (m, 4 H, C3-H), 1.38 (s, 18 H, CH_3), 1.35 (s, 18 H, CH_3). – ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.11 (2 C, CON), 157.20 (COO), 157.08 (COO), 133.81 (2 C, qC), 129.65 (4 C, CH), 79.62 (4 C, qCBoc), 49.62 (2 C, CH2), 44.12 (2 C, C2), 42.98 (2 C, C1), 36.11 (2 C, C4), 32.20 (2 C, C3), 28.25 (12 C, CH_3). – $C_{38}H_{64}N_6O_{10}$ (764.93): calcd. C 59.67, H 8.43, N 10.99; found C 58.70, H 8.46, N 10.74.

Bisamide ***4***

1.31 g (4.33 mmol) of 1.1,2-di(*tert*-butoxycarbonyl-amino)-4-aminobutane, 1.15 mL (8.22 mmol) of triethylamine, 261 mg (1.03 mmol) of benzene-1,2,4,5-tetracarboxylic acid, and 1.32 g (4.11 mmol) of TBTU were used. – Yield 604 mg (42 %). – M. p. > 60 °C (dec.). – IR (KBr): ν = 3541 (sh), 3468 (sh, ν NH), 3369 (s, ν NH), 2982 (m), 2932 (m), 2888 (sh), 1773 (m), 1720 (s, COO), 1686 (s, CON), 1526 (s, CON), 1477 (w), 1458 (m), 1451 (m), 1435 (sh), 1397 (s), 1367 (s), 1342 (w), 1326 (m), 1297 (sh), 1271 (m), 1248 (s), 1170 (s), 1123 (sh), 1066 (m), 1056 (sh), 1021 (w), 999 (w), 960 (w), 948 (w), 921 (w), 890 (w), 866 (w), 857 (sh), 830 (m, ρ NH), 781 (w), 763 (w), 729 (m), 648 (w), 621 (w), 557 (w), 473 (w), 463 (w), 433 (w), 397 (w), 348 (w) cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (s, 2 H, CH), 4.81 (s, 4 H, NH), 3.85 – 3.80 (m, 4 H, C4), 3.65 (m, 2 H, C2), 3.24 – 3.19 (m, 4 H, C1), 1.96 – 1.68 (m, 4 H, C3), 1.41 (s, 36 H, CH_3). – ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.16 (4 C, CON), 156.58 (4 C, COO), 137.30 (4 C, qC), 118.26 (2 C, CH), 79.73 (4 C, qCBoc), 49.52 (2 C, C2), 44.48 (2 C, C1), 35.84 (2 C, C4), 31.24 (2 C, C3), 28.41 (12 C, CH_3). – $C_{38}H_{56}N_6O_{12}$ (788.86): calcd. C 57.86, H 7.16, N 10.65; found C 57.72, H 7.28, N 10.63.

General procedure for the removal of Boc groups from ***1 – 4***

Compound **1 – 4** was dissolved in 3 mL of acetic acid ethyl ester, and 10 mL of HCl-saturated EtOAc solution was added. With evolution of gas a colorless precipitate was formed within 2 h which was washed three times with EtOAc and once with diethyl ether.

Tetrahydrochloride ***5***

150 mg (207 mmol) of compound **1** was used. – Yield 93 mg (93 %). – IR (KBr): ν = 3413 (s), 3293 (s, ν NH), 2953 (br), 2671 (sh), 2594 (sh), 2020 (w), 1742 (m), 1709 (w), 1660 (s, CON), 1612 (w), 1590 (w), 1542 (s, CON), 1498

(sh), 1448 (m), 1394 (sh), 1374 (m), 1325 (m), 1311 (sh), 1243 (m), 1177 (m), 1159 (m), 1076 (m), 1048 (m), 1001 (w), 971 (w), 939 (w), 918 (w), 902 (w), 845 (m, ρ NH), 819 (w), 778 (w), 745 (m), 681 (m), 647 (m), 637 (w), 608 (w), 570 (w), 461 (w), 429 (w), 379 (w), 323 (w) cm^{-1}. – ^1H NMR (400 MHz, D_2O): δ = 8.13 – 8.10 (m, 3 H, CH), 3.77 (quint., ^3J = 6.0 Hz, 2 H, C4-H), 3.65 (t, ^3J = 6.4 Hz, 2 H, C2-H), 3.51 – 3.42 (m, 4 H, C1-H), 2.23 – 2.06 (m, 4 H, C3-H). – ^{13}C NMR (101 MHz, D_2O): δ = 166.08 (2 C, CON), 147.54 (2 C, qC), 140.23 (CH), 125.47 (2 C, CH), 47.37 (2 C, C2), 41.03 (2 C, C1), 35.28 (2 C, C4), 30.53 (2 C, C3). – $C_{15}H_{31}Cl_4$ N7O2 · 2 H_2O (474.23): calcd. C 35.94, H 6.23, N 19.55; found C 35.75, H 6.47, N 19.34.

Tetrahydrochloride ***6***

400 mg (543 mmol) of compound **2** was used. – Yield 249 mg (95 %). – IR (KBr): ν = 3419 (br), 3353 (br, ν NH), 2963 (s), 2674 (sh), 2582 (sh), 2004 (w), 1741 (m), 1631 (s, CON), 1549 (s, CON), 1499 (s), 1450 (m), 1393 (sh), 1374 (m), 1300 (m), 1246 (m), 1205 (w), 1164 (m), 1126 (w), 1047 (m), 965 (w), 868 (m, ρ NH), 845 (w), 819 (w), 792 (w), 731 (m), 696 (w), 628 (w), 608 (w), 526 (w), 499 (w), 461 (w) cm^{-1}. – ^1H NMR (400 MHz, D_2O): δ = 7.87 (s, 2 H, CH), 7.86 (s, 2 H, CH), 3.78 (quint., ^3J = 6.0 Hz, 4 H, C4-H), 3.67 – 3.57 (m, 2 H, C2-H), 3.48 – 3.46 (m, 4 H, C1-H), 2.21 – 2.06 (m, 4 H, C3-H). – ^{13}C NMR (101 MHz, D_2O): δ = 170.34 (2 C, CON), 136.37 (2 C, qC), 127.94 (2 C, CH), 127.71 (2 C, CH), 47.52 (2 C, C2), 41.08 (2 C, C1), 35.73 (2 C, C4), 30.51 (2 C, C3). – $C_{16}H_{28}N_6O_2$ (336.41): calcd. C 57.13, H 8.39, N 24.97; found C 56. 84, H 8.26, N 25.08.

Tetrahydrochloride ***7***

400 mg (523 μmol) of bisamide **3** was used. – Yield 246 mg (92 %). – IR (KBr): ν = 3429 (s), 3274 (sh, ν NH), 2985 (s), 2940 (s), 2671 (sh), 2586 (sh), 2017 (w), 1640 (s, CON), 1550 (s, CON), 1515 (s), 1448 (m), 1375 (m), 1350 (w), 1299 (w), 1250 (m), 1208 (w), 1161 (w), 1107 (w), 1048 (m), 1027 (sh), 980 (w), 939 (w), 921 (w), 845 (w, ρ NH), 816 (w), 786 (w), 634 (w), 628 (w), 587 (w), 479 (w), 455 (w), 379 (w) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29 (s, 2 H, CH), 7.28 (s, 2 H, CH), 3.62 (s, 4 H, C2-H), 3.68 – 3.57 (m, 6 H, C4-H, C2-H), 3.37 (d, ^3J = 5.9 Hz, 4 H, C1-H), 2.01 – 1.92 (m, 4 H, C3-H). – $C_{18}H_{32}N_6O_2$ (364.45): calcd. C 59.32, H 8.85, N 23.05; found C 59. 04, H 8.98, N 23.01.

Tetrahydrochloride ***8***

388 mg (500 μmol) of bisamide **4** was used. – Yield 232 mg (87 %). – IR (KBr): ν = 3426 (br, ν NH), 2946 (br), 2662 (sh), 2577 (sh), 1980 (w), 1771 (m), 1715 (s, CON), 1603 (m, CON), 1578 (sh), 1505 (m), 1503 (m), 1473 (w), 1459 (m), 1449 (sh), 1399 (sh), 1389 (s), 1371 (s), 1314 (sh), 1275 (w), 1202 (w), 1169 (w), 1157 (w), 1127 (w), 1100 (m), 1043 (br), 984 (w), 945 (w), 915 (w), 818 (w), 802 (sh), 751 (w), 729 (s), 645 (w), 624 (w), 603 (w), 561 (m), 527 (w), 503 (w), 473 (w), 454 (w), 418 (w), 394 (w) cm^{-1}. – ^1H NMR (400 MHz, D_2O): δ = 8.35 (s, 2 H, CH), 4.05 – 3.94 (m, 4 H, C4-H), 3.88 – 3.81 (m, 2 H, C2-H), 3.58 – 3.47 (m, 4 H, C1-H), 2.26 (t, ^3J = 6.3 Hz, 4 H, C3-H). – ^{13}C NMR (101 MHz, D_2O): δ = 168.30 (2 C, 2 CON), 137.41 (2 C, CH), 118.87 (2 C, qC), 118.70 (2 C, qC), 47.69 (2 C, C2), 40.93 (2 C, C1), 34.30 (2 C, C4), 29.42 (2 C, C3). – $C_{18}H_{28}Cl_4N_6O_4$ · 2 H_2O (570.23): calcd. C 37.91, H 5.66, N 14.74; found C 38.26, H 6.04, N 14.69.

General procedure for the preparation of the bisplatinum complexes ***9 – 12***

To a solution of **1 – 4** in 2 mL of water a concentrated aqueous solution of K_2PtCl_4 was added, and the solution was heated to 65 °C. The neutralization with 1 M NaOH (90 % of the hydrochloride) and finally with 1 M $NaHCO_3$ (10 %) was controlled by potentiometric pH measurements, and the base was added slowly at pH < 6 until pH = 5.5. The product was obtained as a light-beige precipitate which was centrifuged off, washed three times with ice cold water, and once with ice cold ethanol.

Bisplatinum complex ***9***

960 mg (205 μmol) of **5**, 170 mg (409 mmol) of K_2PtCl_4 and 818 μL (818 μmol) of 1 M NaOH were used. – Yield 80 mg (45 %). – IR (KBr): ν = 3455 (br), 3369 (br, ν NH), 3210 (s, ν NH), 3120 (s, ν NH), 2945 (m), 2894 (sh), 2477 (w), 2368 (w), 2022 (w), 1660 (s, CON), 1586 (m), 1569 (m), 1540 (s, CON), 1447 (m), 1384 (w), 1375 (w), 1311 (w), 1238 (w), 1191 (m), 1179 (m), 1059 (w), 1027 (w), 1000 (m), 845 (m, ρ NH), 789 (w), 754 (w), 719 (w), 668 (w), 647 (m), 570 (w), 470 (w), 429 (w), 323 (m), 322 (m, ν Pt–Cl), 319 (m) cm^{-1}. – $C_{15}H_{27}Cl_4N_7O_2Pt_2$ · 4 H_2O (941.37): calcd. C 19.13, H 3.32, N 10.42; found C 18.87, H 3.37, N 10.22.

Bisplatinum complex ***10***

200 mg (415 μmol) of **6**, 344 mg (830 μmol) of K_2PtCl_4, and 1.66 mL of 1 M NaOH were used. – M. p. 210 °C (dec.). – IR (KBr): ν = 3480 (br), 3392 (br, ν NH), 3246 (sh, ν NH), 3114 (m), 2953 (w), 2367 (w), 1631 (s, CON), 1547 (s, CON), 1498 (m), 1451 (m), 1402 (w), 1373 (w), 1321 (m), 1188 (w), 1161 (w), 1103 (w), 1055 (w), 1023 (w), 997 (w), 865 (m, ρ NH), 831 (w), 732 (w), 667 (w), 638 (w), 623 (w), 570 (w), 499 (w), 469 (w), 321 (m, ν Pt–Cl), 304 (w, ν Pt–Cl) cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ = 8.74 – 8.72 (m, 2 H, N4-H), 7.93 (s, 2 H, CH), 7.92 (s, 2 H, CH), 6.50 – 5.96 (m, 4 H, NH), 5.48 – 5.23 (m, 4 H,

NH), 3.40 – 3.23 (m, 4 H, C4-H), 2.94 – 2.55 (m, 2 H, C2-H), 2.43 – 2.16 (m, 4 H, C1-H), 1.88 – 1.62 (m, 4 H, C3-H). – ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 166.28 (CON), 166.10 (CON), 136.95 (2 C, qC), 127.78 (4 C, CH), 57.78 (2 C, C2), 51.50 (2 C, C1), 36.70 (2 C, C4), 30.82 (C3), 30.26 (C3). – $C_{16}H_{28}Cl_4N_6O_2Pt_2 \cdot H_2O$ (886.41): calcd. C 21.67, H 3.41, N 9.47; found C 21.51, H 3.31, N 9.24.

*Bisplatinum complex **11***

200 mg (395 μmol) of **7**, 328 mg (789 μmol) of K_2PtCl_4, and 1.58 mL (1.58 mmol) of 1 M NaOH were used. – Yield 180 mg (51 %). – IR (KBr): ν = 3414 (br), 3246 (s, ν NH), 3121 (m, ν NH), 2367 (w), 1645 (s, CON), 1576 (sh), 1540 (s, CON), 1514 (m), 1439 (m), 1370 (w), 1389 (w), 1314 (w), 1260 (w), 1205 (sh), 1189 (m), 1161 (sh), 1098 (w), 1023 (w), 790 (w), 761 (w), 718 (w), 570 (w), 519 (w), 465 (w), 441 (w), 421 (w), 387 (w), 320 (m, Pt–Cl) cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.08 – 8.05 (m, 2 H, NH), 7.17 (s, 4 H, CH), 5.63 – 5.38 (m, 4 H, NH), 5.24 – 5.13 (m, 4 H, NH), 3.30 (s, 4 H, CH$_2$), 3.09 – 3.03 (m, 4 H, C4-H), 2.51 (s, 2 H, C2-H), 2.33 – 2.08 (m, 4 H, C1-H), 1.66 – 1.55 (m, 4 H, C3-H). – ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 171.16 (CON), 171.13 (CON), 134.87 (2 C, qC), 129.46 (4 C, CH), 57.88 (2 C, C2), 51.24 (2 C, C1), 42.54 (s, 4 H, CH2), 39.85 (2 C, C1), 31.00 (C3), 30.54 (C3). – $C_{18}H_{32}Cl_4N_6O_2Pt_2 \cdot 2\ H_2O$ (932.46): calcd. C 23.19, H 3.89, N 9.01; found C 23.17, H 3.61, N 8.72.

*Bisplatinum complex **12***

105 mg (197 μmol) of **8**, 82 mg (197 μmol) of K_2PtCl_4, and 0.75 mL of 1 M NaOH were used. – Yield l91 mg (51 %). – IR (KBr): ν = 3427 (br), 3248 (s, ν NH), 3201 (s, ν NH), 3127 (s, ν NH), 2948 (br), 1630 (s, CON), 1592 (s, CON), 1560 (s), 1492 (sh), 1460 (m), 1392 (sh), 1355 (s, br), 1449 (sh), 1194 (w), 1138 (w), 1076 (w), 1050 (sh), 927 (w), 857 (w), 816 (w), 807 (w), 775 (w), 763 (w), 748 (w), 722 (w), 619 (w), 572 (w), 505 (w), 461 (sh), 321 (m, ν Pt–Cl) cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.15 – 8.01 (m, 2 H, N4-H), 7.47 (s, 2 H, CH), 5.43 – 5.24 (m, 4 H, NH), 5.22 – 5.12 (m, 4 H, NH), 3.33 (s, 4 H, CH2), 3.12 – 3.04 (m, 4 H, C4-H), 2.59 (s, 2 H, C2-H), 2.25 – 2.06 (m, 4 H, C1-H), 1.60 (m, 4 H, C3-H). – ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 171.18 (CON), 171.15 (CON), 136.87 (4 C, qC), 130.46 (2 C, CH), 56.95 (2 C, C2), 51.44 (2 C, C4), 39.85 (2 C, C1), 31.21 (C3), 30.94 (C3). – $C_{18}H_{24}Cl_4N_6O4Pt_2 \cdot 2\ H_2O$ (956.36): calcd. C 22.61, H 2.95, N 8.78; found C 22.90, H 3.47, N 9.46.

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