Synthesis of Meso- and Racemic 1,3-Diamino-1,3-diphenylpropanes*)

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The Pt-complexes **2a, b** are synthesized according to Scheme 2 including oximation of and 1,4-addition of H_2N-OH to the chalcone **3** and separation of the diastereomers either as bis-acetamides **5** or - less favourable - at the diamine stage **6**.

Synthese von meso- und racemischen 1,3-Diamino-1,3-diphenylpropanen

Die Pt-Komplexe **2a, b** wurden nach Schema 2 hergestellt, u.a. durch Oximierung und 1,4-Addition von H_2N-OH an das Chalcon **3** und Trennung der Diastereomere entweder als Bis-Acetamide **5** oder - schwieriger - als Diamine **6**.

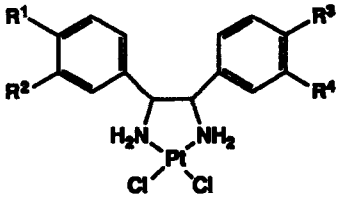
Schönenberger et al. have reported on the Pt-complexes of 1,2-diamino-1,2-diphenylethanes (Typ **1**), cytostatic compounds with affinity to the estrogen receptor possessing a cisplatinum increment as a cytotoxic entity[1]. Moreover, some of the ligands show estrogenic properties by themselves depending *inter alia* on their stereochemistry[1]. Meso-1,2-Diamino-1,2-bis-(2,6-dichloro-4-hydroxyphenyl)-ethane shows very remarkable tumor inhibiting effects in pharmacological tests[1].

By correlation of ^{1}H-NMR data defining the conformation of 1,2-diamino-1,2-diphenyl-Pt-complexes **1** with their ability to bind to the estrogen receptor *Schönenberger* et al.[1] have found that the conception of an antiperiplanar arrangement of the aromatic increments in hexestrole (10 - 12 Å distance of the phenolic OH-groups) cannot be transferred to estrogenic Pt-complexes (in erythro 1-(2,6-dichloro-4-hydroxyphenyl)-2-(2-chloro-4-hydroxyphenyl)-1,2-diaminoethane-Pt-complex the phenyl groups are arranged synclinally).

Schönenberger et al.[1] discuss the contribution of λ- and δ-conformers of 5-membered Pt-complexes of type **1**. The conformational flexibility of cyclic diamino-Pt-complexes should be enhanced when extending the 5-membered ring to a 6-membered one, in other words: comparing the efficacy of 1,3-diamino-1,3-diphenylpropane-Pt-complexes looks interesting. On the other hand the stability of the complexes and the property of the (inorganic) leaving groups to be substituted by bionucleophiles should be of comparable magnitude in both classes of complexes.

Here we describe the synthesis of the diastereomeric complexes **2a, b** which are to be compared with the analogously substituted 1,2-diamino-1,2-diphenylethanes **1a, b** [2] as far as their biochemical and pharmacological properties are concerned.

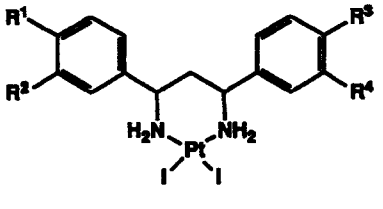
The strategies of *Schönenberger's* group for the synthesis of compounds **1** [3] (aza-*Cope*-rearrangements of stilbenes) cannot be used for the preparation of compounds **2**. The chalcones **3** were obtained by OH^--catalyzed condensation of anisaldehyde with p-methoxyacetophenone (for **3a**) following the general procedure of *Kohler*[4]. - 3,4-Dimethoxybenzaldehyde and 3,4-dimethoxyacetophenone were used for **3b**. - Reaction of compounds **3** with 2 moles of H_2N-OH under basic conditions led to the hydroxyamino-hydroxyimino-compounds **4** (method: *Arakawa*[5], *v. Auwers*[6]), which were reduced with $NaBH_4/TiCl_4$[7] to afford the bis-amides **5** after acetylation. At this stage of the reaction sequence the diastereomers of **5** (meso/racemic) were separated.



1

1a : $R^1 = R^3 = OH$, $R^2 = R^4 = H$

1b : $R^1 = R^2 = R^3 = R^4 = OH$



2

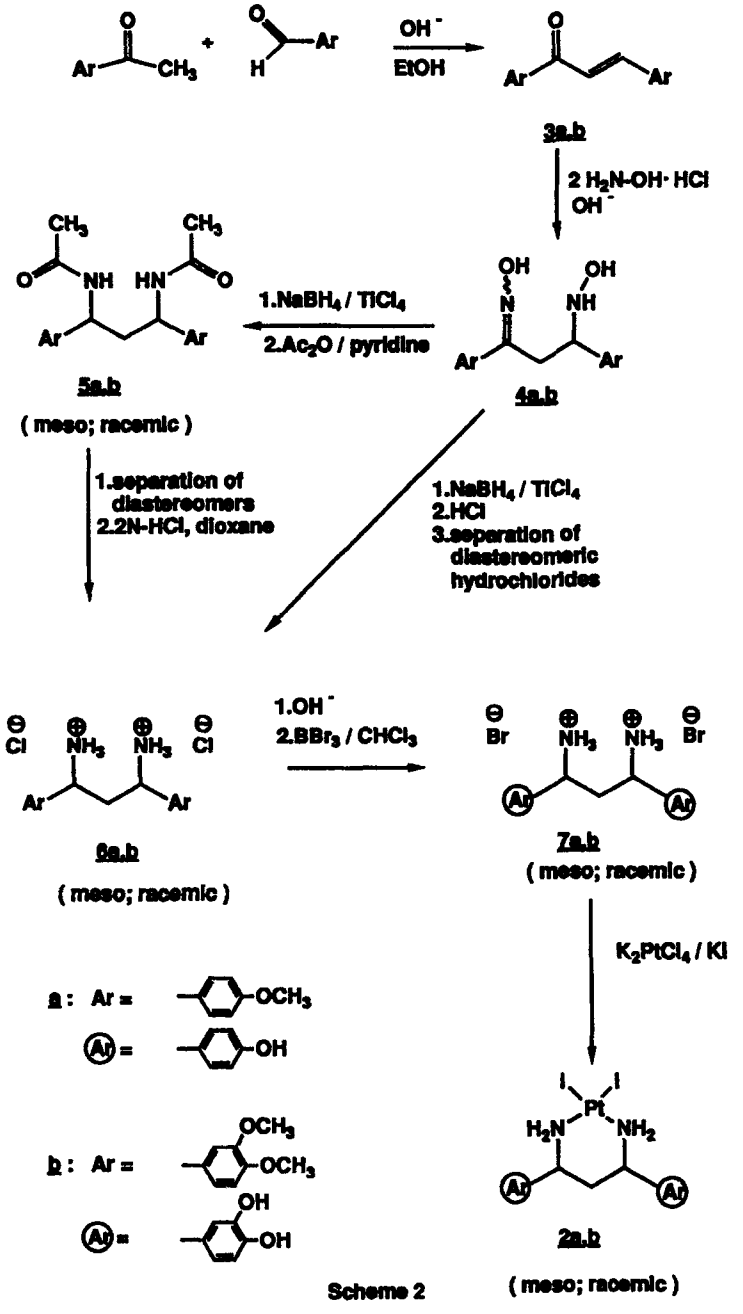
2a : $R^1 = R^3 = OH$, $R^2 = R^4 = H$

2b : $R^1 - R^4 = OH$

Scheme 1

*) Dedicated to Prof. Dr. *H. Möhrle*, Düsseldorf, on the occasion of his 60th birthday.

  0365-6233/91/0303-0177 $ 3.50 + .25/0



Scheme 2

In the course of the conversion of compounds **4** to the bis-acetamides **5** the crude diastereomeric bis-amines **6** are acetylated for separation. - Alternatively the isomers of **6a** can be separated by fractional crystallization as di-hydrochlorides from EtOH (meso-**6a**·2 HCl) and glacial acetic acid (racem.-**6a**·2 HCl), respectively. This procedure does not work with **6b**.

In the case of **5a** the diastereomers were assigned meso or racemic, respectively, by reason of their ^{1}H-NMR-spectra showing the multiplet for the CH_2-group of meso-**5**, and the triplet of racem.-**5**, contrary to lit.[5]. - Unequivocal assignment stems from separation of one diastereomer into enantiomers (racem.-**5**) by HPLC on a chiral column (Fig. 1) (cf. Experimental Part), whilst the other diastereomer remained unresolved under identical conditions (meso-**5**). - The hydroxyamino-hydroxyimino-compound **4a** was reduced and separated to the diastereomers of **6** without acetylation. - After converting the bis-hydrochlorides of compounds **6** to the free bases (a critical step!), the bisamines **6** were cleaved to the biphenols **7** by BBr_3, yielding compounds **7** as bis-hydrobromides. Treatment with K_2PtCl_4/KI afforded the Pt-complexes **2a, b**. Curiously enough this step works nicely with the racemic diastereomers whilst meso-**7a, b** are obtained after laborious work-up only.

During the preparation of **4b** the corresponding bis-hydroxyimino-analogue (formal dehydrogenation product of **4b** with two oxime increments) was obtained as a by-product (cf. [5][6]). This mixture, however, when being reduced

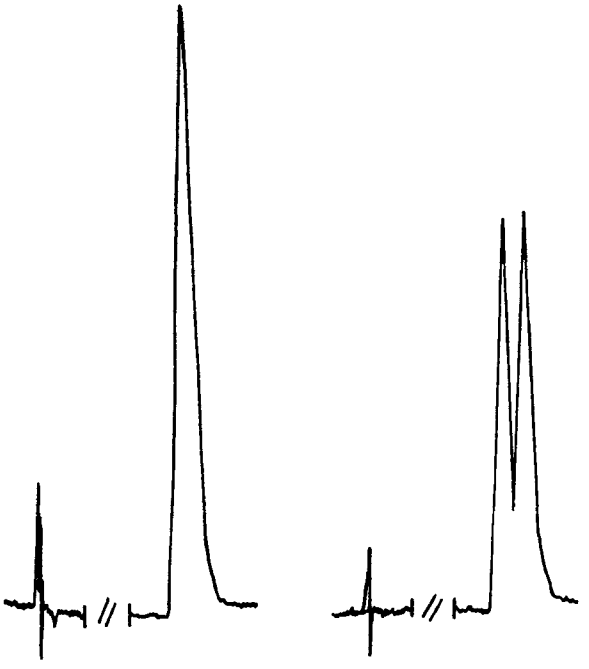


Fig. 1: HPLC-experiments with meso-**5a** (left) and racem.-**5a** (right) on a chiral column.

with $NaBH_4/TiCl_4$, followed by acetylation, afforded **5b** as a mixture of diastereomers, which was separated as described for **5a**.

Experimental Part

General procedures: m. ps. (uncorrected): apparatus according to Dr. *Tottoli* (Büchi). - Elemental analysis: Microanalysis Laboratory, University of Regensburg. - IR-spectra (in KBr): Beckman Acculab 3. - ^{1}H-NMR spectra: Varian EM 390 (90 MHz) or Bruker WM 250 (250 MHz). - Mass spectra: Varian MAT CH 5.

1,3-Bis-(4'-methoxyphenyl)-2-propen-1-one (**3a**)

To a stirred mixture of NaOH (5.07 g, 0.1265 mole) in H_2O (45 ml) and EtOH (29 ml) at 15°C were added 4-methoxyacetophenone (15.02 g, 0.1 mole) and 4-methoxybenzaldehyde (13.62 g, 0.1 mole). The mixture was stirred for 12 h at room temp. and filtered. The filter cake was washed with EtOH/H_2O (1:1, v/v; 20 ml) and dried to afford **3a** as a light yellow solid. Yield 25.5 g (95%). - m.p. 101-102°C, Lit.[8]: m.p. 101-102°C. - IR (KBr, cm^{-1}): 1600 (C=C); 1665 (C=O). - ^{1}H-NMR ($CDCl_3$): δ (ppm) = 3.80 (s; 3H, $-OCH_3$), 3.84 (s; 3H, $-OCH_3$), 6.83-8.13 (m; 10H, 8 Ar-H and 2 olefinic H).

1,3-Bis-(3',4'-dimethoxyphenyl)-2-propen-1-one (**3b**)

3b was prepared as described for **3a**. Yield 94%. - m.p. 116-118°C, Lit.[9]: m.p. 116-118°C. - IR (KBr, cm^{-1}): 1605 (C=C); 1660 (C=O). - ^{1}H-NMR ($CDCl_3$): δ (ppm) = 3.91, 3.94 (2s; 12H, $-OCH_3$), 6.87-7.88 (m; 8H, 6 Ar-H and 2 olefinic H).

1,3-Bis-(4'-methoxyphenyl)-3-hydroxyamino-1-hydroxyiminopropane (**4a**)

To a stirred solution of **3a** (26.83 g, 0.1 mole) in EtOH (240 ml) at 50°C were added $NH_2OH{\cdot}HCl$ (18.3 g, 0.263 mole) in H_2O (40 ml) and KOH (24 g, 0.42 mole) in H_2O (40 ml). The resulting solution was refluxed for 20 min and cooled to room temp. H_2O (1.5 l) was added and the mixture was stirred at 0-5°C for 1 h. The solid was filtered, stirred in CH_2Cl_2 (100 ml) for 20 min and filtered again. Crystallization from MeOH (220 ml) afforded **4a** as white crystals. Yield 14.0 g (44%). - m.p. 133-134°C. - IR (KBr, cm^{-1}): 1610 (C=N); 2800-3500 (broad, NH and OH). - ^{1}H-NMR ($CDCl_3$ + DMSO-d_6): δ (ppm) = 2.83-3.50 (m; 2H, $-CH_2-$), 3.73 (s; 3H, $-OCH_3$), 3.77 (s; 3H, $-OCH_3$), 4.20 (t; J = 7.5 Hz, 1H, -CH-), 5.33 (broad s; 1H, D_2O-exchange), 6.67-7.60 (m; 8H, Ar-H), 7.20 (broad s; 1H, D_2O-exchange), 10.77 (broad s; 1H, D_2O-exchange). - EI-MS: m/z = 316 (7%, $M^{+\cdot}$), 298 (7, $(M-H_2O)^{+\cdot}$), 165 (23, $(M - {}^{\cdot}C_8H_9NO_2)^+$, *McLafferty*), 152 (100, $(M - {}^{\cdot}C_9H_{10}NO_2)^+$, benzyl- and β-cleavage). - $C_{17}H_{20}N_2O_4$ (316.4) Calc. C 64.5 H 6.37 N 8.9 Found C 64.4 H 6.40 N 8.8.

1,3-Bis-(3',4'-dimethoxyphenyl)-3-hydroxyamino-1-hydroxyiminopropane (**4b**) *and 1,3-Bis-(3',4'-dimethoxyphenyl)-propane-1,3-dioxime*

4b was prepared analogously to **4a**; but a mixture of **4b** and the formal dehydrogenation product (bisoxime, no number) was obtained. Crystallization from EtOH (99%) afforded the pure dioxime, whilst crystallization from toluene led to pure **4b**. In these crystallization procedures the respective other component of the mixture remained in the mother liquors in each case. Yield 21.2 g of the mixture.

4b: m.p. 175-178°C. - IR (KBr, cm^{-1}): 1610 (C=N), 3600-3100 (broad, NH and OH). - ^{1}H-NMR ($CDCl_3$ + DMSO-d_6): δ (ppm) = 2.93-3.27 (m; 2H, $-CH_2-$), 3.70, 3.75 (2s; 12H, $-OCH_3$), 4.15 (t; J = 7.5 Hz, 1H, -CH-), 5.55 (broad s; 1H, D_2O-exchange), 6.75-7.02 (m; 6H, Ar-H), 7.18 (s; 1H, D_2O-exchange), 10.89 (s; 1H, D_2O-exchange). - EI-MS: m/z = 376 (10%, $M^{+\cdot}$), 358 (7, $(M-H_2O)^{+\cdot}$), 195 (100, $(M - {}^{\cdot}C_9H_{11}NO_3)^+$, *McLafferty*), 181 (83, $(M - {}^{\cdot}C_{10}H_{13}NO_3)^+$, *McLafferty*). - $C_{19}H_{24}N_2O_6$ (376.4) Calc. C 60.6 H 6.43 N 7.4 Found C 60.6 H 6.21 N 7.1.

1,3-Bis-(3',4'-dimethoxyphenyl)-propane-1,3-dioxime · 0.5 C_2H_5OH

M.p. 187-189°C. - IR (KBr, cm^{-1}): 1610 (C=N); 3400 (OH). - ^{1}H-NMR ($CDCl_3$ + DMSO-d_6): δ (ppm) = 1.10 (t; J = 7.5 Hz, 1.5H, 0.5 CH_3-), 2.50 (s; 0.5H, 0.5-OH, D_2O-exchange), 3.50 (q; J = 7 Hz, 1H, 0.5-CH_2-), 3.72, 3.74 (2s; 12H, $-OCH_3$), 4.32 (s; 2H, $-CH_2-$), 6.75-7.20 (m; 6H, Ar-H), 11.33 (s; 2H, -OH, D_2O-exchange). - NI-FAB-MS (glycerol/DMSO): m/z = 374 (23%), 373 (100, $(M-H)^-$). - $C_{19}H_{22}O_6N_2{\cdot}0.5\ C_2H_5OH$ (397.4) Calc. C 60.4 H 6.34 N 7.0 Found C 60.1 H 6.24 N 6.7.

1,3-Bis-(4'-methoxyphenyl)-1,3-diacetaminopropane (**5a**)

To a stirred solution of $TiCl_4$ (33.7 ml, 0.307 mole) in dry 1,2-dimethoxyethane (370 ml) was added $NaBH_4$ (23.4 g, 0.613 mole) cautiously at 0°C under N_2. The resulting dark blue solution was stirred for 30 min at 0°C and **4a** (23.15 g, 0.073 mole) in dry 1,2-dimethoxyethane (350 ml) was added dropwise for 30 min. The mixture was stirred at room temp. for 20 h and cooled to 0°C. H_2O (300 ml) was added drop by drop and the resulting solution was neutralized with conc. aqueous NH_3 (180 ml). To the suspension were added EtOAc (1l) and H_2O (1l), and stirring was continued for 1 h. The mixture was filtered through celite and the upper layer was separated. The aqueous layer was further extracted with EtOAc (2 x 250 ml). The combined org. layers were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and evaporated in vacuo.

The residue was dissolved in CH_2Cl_2 (1.4 l) and cooled to 0°C. Pyridine (17.05 ml, 0.219 mole) and Ac_2O (20.44 ml, 0.219 mole) were added, the mixture was stirred for 2 h at room temp., washed with N-HCl (1 l), H_2O (1 l) and saturated NaCl solution (1 l) and dried over Na_2SO_4. After evaporating the solvent, the two diastereomeres were separated by CC ($CHCl_3$/MeOH (10/1; v/v)) and identified by HPLC on a chiral column (see below); the first crop was found to be the meso-isomer, the second one to be the racem.-isomer.

*HPLC-resolution of racem.-***5a**

Conditions: Column: Bakerbond Covalent Chiral, 5 (250 mm x 4.6 mm). - Eluent: hexane/2-propanol/MeOH = 85/10/5 (v/v/v; plus 4 drops of conc. NH_3/100 ml of eluent). - Flow rate: 0.8 ml/min. - Detector: UV (254 nm).

meso-**5a**: Yield 4.36 g (16%). - m.p. 250-251°C (EtOH 99%). - IR (KBr, cm^{-1}): 1660 (C=O); 3310 (NH). - ^{1}H-NMR ($CDCl_3$ + DMSO-d_6): δ (ppm) = 1.81 (s; 6H, $-COCH_3$), 1.87-2.12 (m; 2H, $-CH_2-$), 3.72 (s; 6H, $-OCH_3$), 4.48-4.57 (m; 2H, -CH-), 6.96 (m; AA'BB', 8H, Ar-H), 8.30 (d; J = 8.4 Hz, 2H, -NH-). - EI-MS: m/z = 370 (6%, $M^{+\cdot}$), 311 (11, $(M - CH_3CONH_2)^{+\cdot}$, *McLafferty*), 268 (15, (311 - CH_3CO), 192 (74, (M - Ar-CH-NHAc)$^+$), 178 (36, (Ar-CH=NH-Ac)$^+$), 150 (42, (192 - CH_2=C=O), 136 (100, (Ar-CH=NH_2)$^+$). - $C_{21}H_{26}N_2O_4$ (370.4) Calc. C 68.1 H 7.07 N 7.6 Found C 67.7 H 7.41 N 7.2.

racem.-**5a**: Yield 7.60 g (28%). - m.p. 228-229°C (EtOH 99%). - IR (KBr, cm^{-1}): 1645 (C=O); 3260 (NH). - ^{1}H-NMR (DMSO-d_6): δ (ppm) = 1.70 (s; 6H, $-COCH_3$), 1.96 (t; J = 7.7 Hz, 2H, $-CH_2-$), 3.72 (s; 6H, $-OCH_3$), 4.67-4.76 (m; 2H, -CH-), 7.01 (m; AA'BB', 8H, Ar-H), 8.22 (d; J = 8.3 Hz, 2H, -NH-). - EI-MS: m/z = 370 (16, $M^{+\cdot}$), 311 (26, $(M - CH_3CONH_2)^{+\cdot}$, *McLafferty*), 268 (33, (311 - CH_3CO), 192 (94, (M - Ar-CH-NHAc)$^+$), 178 (47, (Ar-CH=NH-Ac)$^+$), 150 (51, (192 - CH_2=C=O), 136 (100, (Ar-CH=NH_2)$^+$). - $C_{21}H_{26}N_2O_4$ (370.4) Calc. C 68.1 H 7.07 N 7.6 Found C 67.8 H 7.17 N 7.6.

1,3-Bis-(3',4'-dimethoxyphenyl)-1,3-diacetaminopropane (**5b**)

5b was prepared in the same way as **5a**, but the mixture was extracted with CH_2Cl_2 instead of EtOAc and the eluent for CC was acetone/CH_2Cl_2 (1/1; v/v).

meso-**5b**: Yield 6%. - m.p. 187-188°C (toluene/EtOAc (1/4; v/v)). - IR (KBr, cm^{-1}): 1650 (C=O); 3260 (NH). - ^{1}H-NMR ($CDCl_3$): δ (ppm) = 1.99 (s; 6H, $-COCH_3$), 2.12-2.47 (m; 2H, $-CH_2-$), 3.84, 3.85 (2s; 12H, $-OCH_3$), 4.78-4.86 (m; 2H, -CH-), 6.32 (d; J = 7.4 Hz, 2H, -NH-), 6.77-6.81 (m; 6H, Ar-H). - EI-MS: m/z = 430 (13, $M^{+\cdot}$), 387 (4, $(M - COCH_3)^+$), 371 (14, $(M - CH_3CONH_2)^{+\cdot}$, *McLafferty*), 328 (27, (371 - CH_3CO), 222 (100, (M - Ar-CH-NH-Ac)$^+$), 208 (28, (Ar-CH=NH-Ac)$^+$), 180 (57, (222 - CH_2=C=O), 166 (86, (Ar-CH=NH_2)$^+$). - $C_{23}H_{30}N_2O_6$ (430.5) Calc. C 64.2 H 7.02 N 6.5 Found C 63.8 H 6.82 N 6.4.

racem.-**5b**: Yield 10%. - m.p. 189-190°C (toluene/EtOAc (1/4; v/v)). - IR (KBr, cm^{-1}): 1645 (C=O); 3260 (NH). - ^{1}H-NMR ($CDCl_3$): δ (ppm) = 1.93 (s; 6H, $-COCH_3$), 2.47 (t; J = 7.2 Hz, 2H, $-CH_2-$), 3.83, 3.85 (2s; 12H, $-OCH_3$), 4.67-4.76 (m; 2H, -CH-), 5.97 (d; J = 7.5 Hz, 2H, -NH-), 6.73-6.82 (m; 6H, Ar-H). - EI-MS: m/z = 430 (11, $M^{+\cdot}$), 387 (6, $(M - COCH_3)^+$); 371 (16, $(M - CH_3CONH_2)^{+\cdot}$, *McLafferty*), 328 (27, (371 - CH_3CO), 222 (100, (M - Ar-CH-NH-Ac)$^+$), 208 (25, (Ar-CH=NH-Ac)$^+$), 180 (65, (222 - CH_2=C=O), 166 (92, (Ar-CH=NH_2)$^+$). - $C_{23}H_{30}N_2O_6$ (430.5) Calc. C 64.2 H 7.02 N 6.5 Found C 63.9 H 6.83 N 6.3

1,3-Bis-(4'-methoxyphenyl)-1,3-diaminopropane dihydrochloride (**6a**)

meso-**6a**: The stirred mixture of meso-**5a** (1.2 g, 3.24 mmole) in 2N-HCl (60 ml) and dioxane (30 ml) was refluxed for 12 h and cooled to room temp. The solvents were evaporated in vacuo and the residue was stirred in acetone (30 ml), filtered and crystallized from AcOH/H_2O (10/1; v/v). The crystals were filtered, washed with acetone (10 ml), and dried to afford meso-**6a**·2HCl as white crystals. Yield 0.73 g (63%). - m.p. 277-282°C (dec.). - IR (KBr, cm^{-1}): 1620 (aromatic C=C); 2600-3400 (NH). - ^{1}H-NMR (D_2O): δ (ppm) = 2.60-2.93 (m; 2H, $-CH_2-$), 3.70 (s; 6H, $-OCH_3$), 4.27-4.50 (m; 2H, -CH-), 6.83 (m; AA'BB', 8H, Ar-H). - $C_{17}H_{22}N_2O_2$·2HCl (359.3) Calc. C 56.8 H 6.73 N 7.8 Found C 56.6 H 6.74 N 7.7.

racem.-**6a**: Same reaction as described for meso-**6a** using racem.-**5a** (2.3 g, 6.2 mmole) in 2N-HCl (110 ml) and dioxane (55 ml). Yield 1.35 g (61%). - m.p. 255-260°C (dec., glacial AcOH). - IR (KBr, cm^{-1}): 1620 (aromatic C=C); 2600-3400 (NH). - ^{1}H-NMR (D_2O): δ(ppm) = 2.60-2.80 (m; 2H, $-CH_2-$), 3.70-3.90 (m; 2H, -CH-), 3.75 (s; 6H, $-OCH_3$), 7.10 (m; AA'BB', 8H, Ar-H). - $C_{17}H_{22}N_2O_2$·2HCl (359.3) Calc. C 56.8 H 6.73 N 7.8 Found C 56.6 H 6.88 N 7.5.

1,3-Bis-(3',4'-dimethoxyphenyl)-1,3-diaminopropane dipicrate (**6b**)

The dihydrochlorides of **6b** were prepared analogously to those of **6a**. As it was not possible to purify them, the dipicrates were analyzed.

meso-**6b**-dipicrate: Yield 58%. - m.p. 193-198°C (dec., glacial AcOH/H_2O (1/10; v/v)). - IR (KBr, cm^{-1}): 2800-3600 (broad, NH). - ^{1}H-NMR (DMSO-d_6): δ(ppm) = 2.51 (broad s; 2H, $-CH_2-$), 3.65 (s; 6H, $-OCH_3$), 3.72 (s; 6H, $-OCH_3$), 4.13 (broad s; 2H, -CH-), 6.78-6.88 (m; 6H, Ar-H), 8.24 (braod s; 6H, $-NH_3^+$, D_2O-exchange), 8.60 (s; 4H, Ar-H). - $C_{19}H_{26}N_2O_4$·$2C_6H_3N_3O_7$·H_2O (822.7) Calc. C 45.3 H 4.17 N 13.6 Found C 45.4 H 4.24 N 13.2.

racem.-**6b**-dipicrate: Yield 63%. - m.p. 212-217°C (dec., glacial AcOH/H_2O 1/10 (v/v)). - IR (KBr, cm^{-1}): 2800-3600 (broad, NH). - ^{1}H-NMR (DMSO-d_6): δ(ppm) = 2.50-2.57 (m; 2H, $-CH_2-$), 3.61-3.66 (m; 2H, -CH-), 3.78, 3.79 (2s; 12H, $-OCH_3$), 6.83-7.07 (m; 6H, Ar-H), 8.18 (broad s; 6H, $-NH_3^+$, D_2O-exchange), 8.60 (s; 4H, Ar-H). - $C_{19}H_{26}N_2O_4$·$2C_6H_3N_3O_7$ (804.7) Calc. C 46.3 H 4.01 N 13.9 Found C 46.1 H 4.15 N 13.5.

Separation of the **6a***-diastereomers by fractional crystallization of their bis-hydrochlorides*

After reduction of **4a** and work-up to afford the mixture of **6a**-diastereomers, this mixture was freed from EtOAc in vacuo (oil pump), dissolved in absol. EtOH (300 ml) and converted to the bis-hydrochlorides by gaseous HCl under ice-cooling. After 48 h at -25°C the crystals were collected, washed with EtOH and dried in vacuo. meso-**6a**·2HCl so obtained is free from racem.-**6a** (tlc) and was recrystallized from AcOH/H_2O (see above).

The mother liquors were evaporated in vacuo, the residue was dried (oil pump), dissolved in acetone (200 ml), stirred for 30 min and filtered. After drying racem.-**6a**·2HCl, contaminated with meso-**6a**·2HCl, was obtained. This mixture was dissolved by boiling in glacial AcOH (80 ml). After 3 h at room temp. the crystals of contaminating meso-**6a**·2HCl were collected. A further crop of racem.-**6a**·2HCl separated from the filtrate during standing in the refrigerator for 24 h. Partial evaporation and addition of Et_2O afforded further racem.-**6a**·2HCl. Recrystallisation from glacial AcOH.

Yields: meso-**6a**·2HCl: 6.9 g (26%). - racem.-**6a**·2HCl: 6.6 g (25%).

1,3-Bis-(4'-hydroxyphenyl)-1,3-diaminopropane dihydrobromide (**7a**)

meso-**7a**: meso-**6a** (1.0 g, 2.8 mmole) was dissolved in H_2O (10 ml) and dropped into saturated $NaHCO_3$ solution (30 ml). After 30 min the crystals were filtered, washed with saturated NaCl solution (10 ml) and H_2O (10 ml) and dried in vacuo to afford the free diamine (meso-**6a**-base). To a stirred solution of meso-**6a**-base (0.5 g, 1.75 mmole) in dry $CHCl_3$ (50 ml) BBr_3 (1.3 ml, 14.0 mmole) in dry $CHCl_3$ (5 ml) was dropped at -5 - -10°C under N_2. The solution was refluxed for 6 h and stirred at room temp. for 12 h. To the ice-cooled solution dry CH_3OH (30 ml) was dropped for 30 min, then it was evaporated in vacuo. Acetone (20 ml) was added and the crystals formed were collected. Yield 0.40 g (55%). - m.p. 196-200°C (dec., after precipitation with Et_2O from ethanolic solution). - IR (KBr, cm^{-1}): 2600-3600 (broad, NH and OH). - ^{1}H-NMR (D_2O): δ(ppm) = 2.58-2.76 (m; 2H, $-CH_2-$), 4.26 (dd; J_1 = 10.0 Hz, J_2 = 4.4 Hz, 2H, -CH-), 6.74 (m; AA'BB', 8H, AR-H). - $C_{15}H_{18}N_2O_2$·2HBr (420.2) Calc. C 42.9 H 4.80 N 6.7 Found C 42.9 H 4.81 N 6.6. - If meso-**7a** is recrystallized from AcOH/H_2O (4/1; v/v), the crystals melt at 165-175°C (dec.) and contain AcOH: $C_{15}H_{18}N_2O_2$·2HBr·CH_3COOH (480.2) Calc. C 42.5 H 5.04 N 5.8 Found C 42.4 H 5.29 N 5.7.

racem.-**7a**: racem.-**6a** (1.0 g, 2.8 mmole) was dissolved in water (10 ml). After addition of 3N-NaOH (5 ml) racem.-**6a**-base was extracted with EtOAc (3 x 30 ml). After work-up as usual, the free diamine was obtained in 95% yield as a colourless oil, which crystallizes after drying at room temp. and 0.1 torr. To a stirred solution of racem.-**6a**-base (0.5 g, 1.75 mmole) in dry $CHCl_3$ (50 ml) BBr_3 (1.3 ml, 14.0 mmole) in dry $CHCl_3$ (5 ml) was dropped at -5 - -10°C under N_2. The solution was refluxed for 6 h and stirred at room temp. for 12 h. Dry CH_3OH (30 ml) was dropped to the ice-cooled solution during 30 min, then it was evaporated completely in vacuo. Acetone (20 ml) was added and the crystals were collected. racem.-**7a**·2HBr was obtained as 0.5 acetone solvate after drying. Yield 0.43 g (55%). - m.p. 204-207°C (dec.). - IR (KBr, cm^{-1}): 1700 (C=O); 2700-3600 (broad, NH and OH). - ^{1}H-NMR (D_2O): δ (ppm) = 2.11 (s; 3H, $-CH_3$), 2.67 (dd; J_1 = 9.3 Hz, J_2 = 6.9 Hz, 2H, $-CH_2-$), 3.77 (dd; J_1 = 9.3 Hz, J_2 = 6.9 Hz, 2H, -CH-), 6.98 (m; AA'BB', 8H, Ar-H). - $C_{15}H_{18}N_2O_2$·2 HBr·0.5C_3H_6O (449.2) Calc. C 44.1 H 5.16 N 6.2 Found C 44.1 H 5.35 N 5.9.

1,3-Bis-(3',4'-dihydroxyphenyl)-1,3-diaminopropane dihydrobromide (**7b**)

meso- and racem.-**7b** were prepared as described for racem.-**7a**, but the free diamines were extracted with CH_2Cl_2 instead of EtOAc.

meso-**7b**: Yield 53%. - m.p. 178-183°C (dec., HBr 62%/H_2O (1/1; v/v)). - IR (KBr, cm^{-1}): 2600-3600 (broad, NH and OH). - ^{1}H-NMR (D_2O): δ (ppm) = 2.47-2.80 (m; 2H, $-CH_2-$), 4.28 (dd; J_1 = 10.0 Hz, J_2 = 4.5 Hz, 2H, -CH-), 6.48-6.71 (m; 6H, Ar-H). - $C_{15}H_{18}N_2O_4$·2HBr·H_2O (470.2) Calc. C 38.3 H 4.27 N 6.0 Found C 38.2 H 4.77 N 5.7.

racem.-**7b**: Yield 55%. - m.p. 179-183°C (dec., HBr 62%/H_2O (1/2; v/v)).- IR (KBr, cm^{-1}): 2600-3600 (broad, NH and OH). - ^{1}H-NMR (D_2O): δ (ppm) = 2.64 (dd; J_1 = 9.0 Hz, J_2 = 3.0 Hz, 2H, $-CH_2-$), 3.75 (dd; J_1 = 9.0 Hz, J_2 = 3.0 Hz, 2H, -CH-), 6.59-6.96 (m; 6H, Ar-H). - $C_{15}H_{18}N_2O_4$·2HBr (452.1) Calc. C 39.9 H 4.46 N 6.2 Found C 39.8 H 4.40 N 6.1.

Diiodo-1,3-bis-(4'-hydroxyphenyl)-1,3-diaminopropane-platinum(II) (**2a**)

meso-**2a**: K_2PtI_4 solution was prepared by stirring K_2PtCl_4 (0.104 g, 0.25 mmole) and KI (0.375 g) in H_2O (2.5 ml) for 30 min at room temp. - meso-**7a**·AcOH (0.12 g, 0.25 mmole) was dissolved in 12 ml of H_2O/tert. butanol (1/1; v/v), and the pH-value was adjusted to 6.0-6.5 by 0.1 N-NaOH. K_2PtI_4 solution was dropped to this solution during 30 min at 40°C. The mixture was stirred at 40°C and pH 6.0-6.5 for 4 h. After further 3 h at room temp. the yellow coloured product was filtered, washed with water and dried in vacuo. Yield 0.171 g (97%). - m.p. 199-201°C (dec.). - IR (KBr, cm^{-1}): 2800-3600 (broad, NH and OH). - ^{1}H-NMR (DMF-d_7): δ (ppm) = 2.02-2.18 (m; 1H, $-CH_2-$), 2.46-2.75 (m; 1H, $-CH_2-$), 4.32-4.52 (m; 2H, -CH-), 4.60-4.85 (m; 2H, $-NH_2$), 5.30-5.70 (m; 2H, $-NH_2$), 7.12 (m; AA'BB', 8H, Ar-H), 9.70 (s; 2H, Ar-OH). - PI-FAB-MS (glycerol/DMSO; ^{194}Pt): m/z = 657 (85%, (M - I + DMSO)$^+$). - $C_{15}H_{18}I_2N_2O_2Pt$ (707.2) Calc. C 25.5 H 2.57 N 4.0 Found C 25.2 H 2.68 N 3.7.

racem.-**2a**: same procedure as in the synthesis of meso-**2a** with racem.-**7a** (0.104 g, 0.25 mmole). Yield 0.163 g (92%). - m.p. 206-208°C. - IR (KBr, cm^{-1}): 2800-3600 (broad, NH and OH). - ^{1}H-NMR (DMF-d_7): δ (ppm) = 2.42-2.52 (m; 2H, $-CH_2-$), 4.10-4.27 (m; 2H, -CH-), 5.14-5.30 (m; 4H, $-NH_2$), 7.24 (m, AA'BB', 8H, Ar-H), 9.69 (s; 2H, Ar-OH). - PI-FAB-MS (glycerol/DMSO; ^{194}Pt): m/z = 657 (85%, (M - I + DMSO)$^+$). - $C_{15}H_{18}I_2N_2O_2Pt$ (707.2) Calc. C 25.5 H 2.57 N 4.0 Found C 25.2 H 2.57 N 3.8.

Diiodo-1,3-bis-(3',4'-dihydroxyphenyl)-1,3-diaminopropane-platinum(II) (**2b**)

meso-**2b** and racem.-**2b** were prepared as described for meso-**2a**.

meso-**2b**: Yield 0.073 g (39%). - m.p. 166-169°C (dec.). - IR (KBr, cm^{-1}): 2900-3600 (broad, NH and OH). - ^{1}H-NMR (DMF-d_7): δ(ppm) = 2.02-2.15 (m; 1H, $-CH_2-$), 2.48-2.66 (m; 1H, $-CH_2-$), 4.24-4.46 (m; 2H, -CH-), 4.50-4.66 (m; 2H, $-NH_2$), 5.32-5.66 (m; 2H, $-NH_2$), 6.78-7.10 (m; 6H, Ar-H), 9.12 (s; 4H, Ar-OH). - $C_{15}H_{18}I_2N_2O_4Pt$ (739.2) Calc. C 24.4 H 2.45 N 3.8 Found C 24.2 H 3.14 N 3.6.

racem.-**2b**: Yield 0.172 g (93%). - m.p. 170-172°C (dec.). - IR (KBr, cm^{-1}): 2900-3600 (broad, NH and OH). - ^{1}H-NMR (DMF-d_7): δ (ppm) = 2.34-2.48 (m; 2H, $-CH_2-$), 3.96-4.34 (m; 2H, -CH-), 4.90-5.40 (m; 4H, $-NH_2$), 6.78-7.22 (m; 6H, Ar-H), 9.05 (s; 4H, Ar-OH). - $C_{15}H_{18}I_2N_2O_4Pt$ (739.2) Calc. C 24.4 H 2.45 N 3.8 Found C 24.4 H 2.69 N 3.8.

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