Supporting Information for

Investigation of vanadocene(IV) α-amino acids complexes: Synthesis, structure and behavior in physiological solutions, human plasma and blood.

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Measurements. IR spectra were recorded in the 4000-350 cm^{-1} region on a Perkin-Elmer 684 using nujol mulls between KBr windows. Raman spectra of solid samples were recorded on a Bruker IFS 55s with extension FRA 106 at 50-3500 cm^{-1}.

EPR spectra were measured on ERS 221 (ZWG Berlin) apparatus in microwave X-band (~ 9.5 GHz). The apparatus was calibrated with DPPH value (g = 2.0036 ± 2). Liquid samples were measured in flat quartz cuvettes (width 0.3 mm) at room temperature whereas solids were measured in quartz capillaries (width 0.5 mm) at liquid nitrogen temperature. The EPR spectra obtained were computer-simulated using EPR simulation software SimFonia v.1.2 (Bruker). A second-order perturbation theory for interaction of unpaired electronic spin with vanadium nuclear spin, anisotropic line widths and mixed Lorentzian/Gaussian lineshapes were used.

Positive- and negative-ion electrospray ionization (ESI) mass spectra were measured on an Esquire 3000 ion trap analyzer (Bruker Daltonics, Bremen, Germany) in the range m/z 50 - 1000. The samples were dissolved in methanol and analyzed by direct infusion at a flow rate 1 µl/min. The selected precursor ions were further analyzed by MS/MS analyses under the following conditions: the isolation width m/z = 4, the collision amplitude 0.9 V, the ion source temperature 300°C, the flow rate and the pressure of nitrogen 4 l/min and 10 psi, respectively.

The study of behavior of complexes **1**, **2a**-**9a** at physiological conditions was made using EPR spectroscopy. The pH adjustments of aqueous solutions were made with carbonate-free NaOH solution (c = 0.5 $mol.l^{-1}$) and with concentrated $HClO_4$. The pH measurements were performed with a MV-870 Digital pH-meter using a glass electrode Radelkis OP-0808P.

The samples of complexes **1**, **2a**-**9a** were prepared by dissolution of 5μmol of the studied vanadocene compound in 5 ml appropriate medium (i.e. NaCl solution, Krebs-Ringer solution, human plasma or blood).

Compounds **2a**-**4a** and **2b**-**4b** were prepared according the literature procedure.[1]

[Cp_2V(gly)]Cl (2a). Positive-ion MS: m/z 545 $[2M\text{-}Cl]^+$, 255 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 255: m/z 181 $[Cp_2V]^+$ (100%).

[Cp_2V(ala)]Cl (3a). Positive-ion MS: m/z 573 $[2M\text{-}Cl]^+$, 269 $[M\text{-}Cl]^+$ (100%), 181 $[Cp_2V]^+$. Positive-ion MS/MS of 269: m/z 181 $[Cp_2V]^+$ (100%).

[Cp_2V(val)]Cl (4a). Positive-ion MS: m/z 297 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 297: m/z 231 $[M\text{-}Cl\text{-}CpH]^+$, 203 $[M\text{-}Cl\text{-}CpH\text{-}CO]^+$, 181 $[Cp_2V]^+$ (100%).

[Cp_2V(gly)]PF_6 (2b). Positive-ion MS: m/z 255 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

[Cp_2V(ala)]PF_6 (3b). Positive-ion MS: m/z 269 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

[Cp_2V(val)]PF_6 (4b). Positive-ion MS: m/z 297 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

Synthesis of [Cp_2V(leu)]Cl (5a). After dissolving of compound **1** (0.5g, 1.98 mmol) in 20 ml of water, L-leucine (0.26 g, 1.98 mmol) was added to the solution. Then the reaction mixture was neutralized by 3.96 ml of carbonate free NaOH (c = 0.5 $mol.l^{-1}$), solvent was removed *in vacuo* and the solid residue was crystallized from the acetone-methanol mixture. The green powder was then washed with 10 ml acetone and dried *in vacuo*. Yield: 0.57g (1.64 mmol, 83 %). Calc. for $C_{16}H_{22}ClNO_2V$ (MW 346.74): C, 55.4; H, 6.4; N, 4.0; Cl, 10.2 Anal.Found: C, 55.1; H, 6.3; N, 3.9; Cl, 10.4 EPR (CH_3OH solution): $A_{iso}= 62.7 \times 10^{-4}$ cm^{-1}, $g_{iso}= 1.989$; EPR (frozen CH_3OH solution) $A_x= 76.6 \times 10^{-4}$ cm^{-1}, $A_y= 102.5 \times 10^{-4}$ cm^{-1} $g_x=$

[1] Vinklárek, J.; Paláčková, H.; Honzíček, J. *Collect. Czech. Chem. Commun.* **2004**, *69*, 811-821.

1.989, g_y= 1.965. IR (KBr, nujol mull): 3391m ($\nu_a(NH_2)$aa), 3091w (ν(C-H)Cp), 2728w, 1636s (ν_a(COO)aa), 1339w, 1210w, 1153m, 1077m, 1025m (δ(C-H)Cp), 950w, 922w, 850m (γ(CH)Cp), 802m, 665w, 604w, 570w, 448w. Raman: 3110 (6) (ν(C-H)Cp), 2921 (3), 2871 (3), 1132 (8) (ν_s(C-C)Cp), 738 (1), 488 (1), 390 (1), 360 (1), 283 (10) (κ(Cp)), 115 (3). Positive-ion MS: m/z 311 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 311: m/z 245 $[M\text{-}Cl\text{-}CpH]^+$, 217 $[M\text{-}Cl\text{-}CpH\text{-}CO]^+$, 198 $[Cp_2VOH]^+$, 181 $[Cp_2V]^+$ (100%).

Synthesis of $[Cp_2V(ile)]Cl$ (6a). The reaction was carried out as described above, but with 0.26 g (1.98 mmol) L-isoleucine. Yield: 0.54g (1,54 mmol, 78%) Calc. for $C_{16}H_{22}ClNO_2V$ (MW 346,74): C, 55.4; H, 6.4; N, 4.0; Cl, 10.2. Anal. Found: C, 55.4; H, 6.4; N, 4.1; Cl, 10.0. EPR (CH_3OH solution): $A_{iso}= 62.5 \times 10^{-4}$ cm^{-1}, g_{iso}= 1.987; EPR (frozen CH_3OH solution): $A_x= 76.9 \times 10^{-4}$ cm^{-1}, $A_y= 102.4 \times 10^{-4}$ cm^{-1}, g_x= 1.981, g_y= 1.965. IR (KBr, nujol mull): 3218 m ($\nu_s(NH_2)$aa), 3099m (ν(C-H)Cp), 1646vs (ν_a(COO)aa),1516m, 1345w, 1327w, 1206m, 1154w, 1130m (ν_s(C-C)Cp), 1086m, 1012m, 968m, 850s (γ(CH)Cp), 801m, 666m, 569m, 483w, 449w, 403w. Raman: 3108 (5) (ν(C-H)Cp), 2892 (5), 1131 (10) (ν_s(C-C)Cp), 604 (1), 435 (3), 286 (8) (κ(Cp)), 170 (2), 128 (1), 111 (1). Positive-ion MS: m/z 311 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 311: m/z 245 $[M\text{-}Cl\text{-}CpH]^+$, 217 $[M\text{-}Cl\text{-}CpH\text{-}CO]^+$, 198 $[Cp_2VOH]^+$, 181 $[Cp_2V]^+$ (100%).

Synthesis of $[Cp_2V(phe)]Cl$ (7a). The reaction was carried out as described above, but with 0.33 g (1.98 mmol) L-phenylalanine. Yield: 0.51g (1.34 mmol, 68%) Calc. for $C_{19}H_{20}ClNO_2V$ (MW 380,75): C, 59.9; H, 5.3; N, 3.7; Cl, 9.3. Anal. Found: C, 59.7; H, 5.3; N, 3.7; Cl, 8.9. EPR (CH_3OH solution): $A_{iso}= 62.7 \times 10^{-4}$ cm^{-1}, g_{iso}= 1.986; EPR (frozen CH_3OH solution): $A_x= 77.7 \times 10^{-4}$ cm^{-1}, $A_y= 102.5 \times 10^{-4}$ cm^{-1}, g_x= 1.986, g_y= 1.964. IR (KBr, nujol mull): 3311m ($\nu_a(NH_2)$aa), 3174w ($\nu_s(NH_2)$aa), 3096m (ν(C-H)Cp), 1651vs (ν_a(COO)aa), 1575m, 1494w, 1361m, 1317m, 1260m, 1213m, 1082m, 1030m (δ(C-H)Cp),

1009w, 921w, 884w, 851s (γ(CH)Cp), 823w, 751m, 724w, 702s, 666w, 637m, 579w, 550m, 483w, 386w. Raman: 3479 (2), 3282 (3), 3067 (5) (ν(C-H)Cp), 3053 (6), 2923 (3), 2651 (3), 1131 (9) (ν_s(C-C)Cp), 1002 (6), 277 (10) (κ(Cp)), 118 (5). Positive-ion MS: m/z 345 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 345: m/z 279 $[M\text{-}Cl\text{-}CpH]^+$, 251 $[M\text{-}Cl\text{-}CpH\text{-}CO]^+$, 224, 198 $[Cp_2VOH]^+$, 181 $[Cp_2V]^+$ (100%), 120.

Synthesis of [Cp_2V(his)]Cl (8a). The reaction was carried out as described above, but with 0.31 g (1.98 mmol) L-histidine. Yield: 0.39g (1.07 mmol, 54%) Calc. for $C_{16}H_{18}ClN_3O_2V$ (MW 370.72): C, 51.8; H, 4.9; N, 11.3; Cl, 9.6. Anal. Found: C, 51.8; H, 4.8; N, 11.1; Cl, 9.6. EPR (CH_3OH solution): $A_{iso}= 62.6 \times 10^{-4}$ cm^{-1}, $g_{iso}= 1.985$; EPR (frozen CH_3OH solution): $A_x= 77.7 \times 10^{-4}$ cm^{-1}, $A_y= 102.6 \times 10^{-4}$ cm^{-1}, $g_x= 1.988$, $g_y= 1.966$. IR (KBr, nujol mull): 3209w ($\nu_s(NH_2)$aa), 3096s (ν(C-H)Cp), 1642vs (ν_a(COO)aa), 1490m, 1339w, 1319w, 1261m, 1172m, 1104m, 1019m (δ(C-H)Cp), 963m, 850s (γ(CH)Cp), 655w, 623m, 555m, 483w. Raman: 3119 (4) (ν(C-H)Cp), 2925 (2), 1574 (<1), 1491 (<1), 1434 (2), 1368 (1), 1267 (1), 1132 (9) (ν_s(C-C)Cp), 1070 (1), 1018 (<1) (δ(C-H)Cp), 961 (1), 887 (<1), 857 (1) (γ(CH)Cp), 837 (<1), 594 (<1), 471 (<1), 439 (2), 419 (2), 282 (10) (κ(Cp)), 190 (1), 119 (3). Positive-ion MS: m/z 335 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 335: m/z 270 $[M\text{-}Cl\text{-}Cp]^+$, 242 $[M\text{-}Cl\text{-}Cp\text{-}CO]^+$, 226 $[M\text{-}Cl\text{-}Cp\text{-}CO_2]^+$ (100%), 181 $[Cp_2V]^+$, 111.

Synthesis of [Cp_2V(trp)]Cl (9a). The reaction was carried out as described above, but with 0.4 g (1.98 mmol) L- tryptophane. Yield: 0.44g (1.05 mmol, 53%) Calc. for $C_{21}H_{21}ClN_2O_2V$ (MW 419,79): C, 60.1; H, 5.0; N, 6.7; Cl, 8.4. Anal. Found: C, 60.1; H, 4.8; N, 6.7; Cl, 8.5. EPR (CH_3OH solution): $A_{iso}= 62.6 \times 10^{-4}$ cm^{-1}, $g_{iso}= 1.986$; EPR (frozen CH_3OH solution): $A_x= 77.7 \times 10^{-4}$ cm^{-1}, $A_y= 102.6 \times 10^{-4}$ cm^{-1}, $g_x= 1.991$, $g_y= 1.966$. IR (KBr, nujol mull): 3194m ($\nu_s(NH_2)$aa), 3094m (ν(C-H)Cp), 1700m, 1640vs (ν_a(COO)aa), 1343w, 1320w (ν_s(C-C)Cp), 1266m, 1228m, 1168w, 1130w, 1099m, 1011m, 967m, 843s (γ(CH)Cp), 745s, 655w, 603w, 557m, 462w, 429m, 388w. Raman: 3113 (1) (ν(C-H)Cp), 3053 (2) (ν(C-H)Cp), 2922

(3), 1545 (2), 1433 (2), 1132 (9) (ν_s(C-C)Cp), 1076 (1), 1012 (3), 878 (<1), 757 (2), 435 (1), 279 (10) (κ(Cp)), 121 (3). Positive-ion MS: m/z 384 $[M\text{-}Cl]^+$ (100%). Positive-ion MS/MS of 384: m/z 367 $[M\text{-}Cl\text{-}NH_3]^+$, 318, 274, 198 $[Cp_2VOH]^+$, 181 $[Cp_2V]^+$, 159 (100%), 132.

Synthesis of $[Cp_2V(leu)]PF_6$ (5b). After dissolving of complex **5a** (0.2 g, 0.58 mmol) in 2 ml of water, the 1 ml of saturated solution of KPF_6 was added. The mixture was stirred for 10 min. Then the precipitated was filtered on the frit, washed with 2 ml of cold water and dried *in vacuo*. Yield: 0.15 g (0.33 mmol, 57 %). Calc. for $C_{16}H_{22}F_6NO_2PV$ (MW 456,26): C, 42.1; H, 4.9; N, 3.1. Anal. Found: C, 42.0; H, 4.7; N, 3.0. EPR (CH_3OH solution): $A_{iso}= 62.7 \times 10^{-4}$ cm^{-1}, $g_{iso}= 1.983$; EPR (frozen CH_3OH solution): $A_x= 76.7 \times 10^{-4}$ cm^{-1}, $A_y= 102.7 \times 10^{-4}$ cm^{-1}, $g_x= 1.982$, $g_y= 1.969$. IR (KBr, nujol mull): 3314w ($\nu_a(NH_2)$aa), 3117w, 2728w, 1652m (ν_a(COO)aa), 1309w, 1261w, 1168w, 1084w, 1014w, 837vs (δ(CH)Cp; ν(P-F)PF_6), 722m, 560s (ν(P-F)PF_6), 447w. Raman: 3221(7), 2886(5), 1956(6), 1627(5), 1268(5), 1133 (10) (ν_s(C-C)Cp), 744(6), 280 (7) (κ(Cp)), 118(7). Positive-ion MS: m/z 311 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

Synthesis of $[Cp_2V(ile)]PF_6$ (6b). The reaction was carried out as described above, but with complex **6a** (0.2 g, 0.58 mmol). Single crystals suitable for X-ray diffraction analysis were obtained by cooling of saturated aqueous solution of **6b** from 20°C on 4°C. Yield: 0.11 g (0.24 mmol, 42 %). Calc. for $C_{16}H_{22}F_6NO_2PV$ (MW 456,26): C, 42.1; H, 4.9; N, 3.1. Anal. Found: C, 42.1; H, 4.9; N, 3.4. EPR (CH_3OH solution): $A_{iso}= 62.7 \times 10^{-4}$ cm^{-1}, $g_{iso}= 1.985$; EPR (frozen CH_3OH solution): $A_x= 77.1 \times 10^{-4}$ cm^{-1}, $A_y= 102.7 \times 10^{-4}$ cm^{-1}, $g_x= 1.980$, $g_y= 1.964$. IR (KBr, nujol mull): 3356w, 3187w (ν_a(C-H)Cp), 3091w, 1615s (ν_a(COO)aa), 1494w, 1339w, 1179m, 1088w, 971s, 841vs (δ(CH)Cp; ν(P-F)PF_6), 664w, 561s (ν(P-F)PF_6), 448w. Raman: 3113 (2), 2750 (<1), 2720 (<1), 1919 (<1), 1132 (10) (ν_s(C-C)Cp), 740 (4), 600 (<1),

500 (<1), 435 (1), 279 (10) (κ(Cp)), 209 (2), 119 (<1). Positive-ion MS: m/z 311 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

Synthesis of $[Cp_2V(phe)]PF_6$ (7b). The reaction was carried out as described above, but with complex **7a** (0.2 g, 0.53 mmol). Yield: 0.2 g (0.41 mmol, 77 %). Calc. for $C_{19}H_{20}F_6NO_2PV$ (MW 490.27): C, 46.5; H, 4.1; N, 2.9. Anal. Found: C, 46.4; H, 4.1; N, 2.8. EPR (CH_3OH solution): A_{iso}= 62.5 × 10^{-4} cm^{-1}, g_{iso}= 1.981; EPR (frozen CH_3OH solution): A_x= 76.4 × 10^{-4} cm^{-1}, A_y= 102.1 × 10^{-4} cm^{-1}, g_x= 1.979, g_y= 1.960. IR (KBr, nujol mull): 3329m ($\nu_a(NH_2)$aa), 3292m, 3130m ((C-H)Cp), 3092w, 2724w, 2529w, 2481w, 2356w, 1667s (ν_a(COO)aa), 1579m, 1317m, 1260m, 1217w, 1169m, 1088w, 1028w, 1013w, 971w, 842vs (δ(CH)Cp), 828vs (ν(P-F)PF_6), 756m, 704m, 637w, 559s (ν(P-F)PF_6), 483w. Raman: 1446 (6), 1130 (10) (ν_s(C-C)Cp), 497 (7), 319 (6), 272 (5), 116 (8). Positive-ion MS: m/z 345 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

Synthesis of $[Cp_2V(his)]PF_6$ (8b). The reaction was carried out as described above, but with complex **8a** (0.2 g, 0.54 mmol). Yield: 0.14 g (0.29 mmol, 54 %). Calc. for $C_{16}H_{18}F_6N_3O_2PV$ (MW 480.24): C, 40.0; H, 3.8; N, 8.8. Anal. Found: C, 39.8; H, 3.6; N, 8.9. EPR (CH_3OH solution): A_{iso}= 62.3 × 10^{-4} cm^{-1}, g_{iso}= 1.98; EPR (frozen CH_3OH solution): A_x= 77.3 × 10^{-4} cm^{-1}, A_y= 102.0 × 10^{-4} cm^{-1}, g_x= 1.975, g_y= 1.965. IR (KBr, nujol mull): 3362w ($\nu_a(NH_2)$aa), 3117w (ν_a(C-H)Cp), 2726w, 2677w, 2528w, 2482w, 1634s (ν_a(COO)aa), 1263w, 1170w, 1084m, 1020w, 970m, 838vs (δ(CH)Cp, ν(P-F)PF_6), 721m, 624w, 561s (ν(P-F)PF_6). Raman: 2494 (5), 1986 (5), 1126 (10) (ν_s(C-C)Cp), 748 (5), 279 (5). Positive-ion MS: m/z 335 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).

Synthesis of $[Cp_2V(trp)]PF_6$ (9b). The reaction was carried out as described above, but with complex **9a** (0.2 g, 0.48 mmol). Yield: 0.21 g (0.4 mmol, 83 %). Calc. for $C_{21}H_{21}F_6N_2O_2PV$ (MW 529.31): C, 47.6; H, 4.0; N, 5.3. Anal. Found: C, 47.4; H, 3.8; N, 5.3. EPR (CH_3OH solution): A_{iso}= 62.6 × 10^{-4} cm^{-1}, g_{iso}= 1.985; EPR (frozen CH_3OH solution): A_x=

76.9 × 10^{-4} cm^{-1}, A_y= 101.4 × 10^{-4} cm^{-1}, g_x= 1.97, g_y= 1.958. IR (KBr, nujol mull): 3630w, 3407w, 3235w, 3104w (ν_a(C-H)Cp), 2725w, 2531w, 2484w, 1640vs (ν_a(COO)aa), 1344w, 1323w, 1270m, 1231w, 1167w, 1130w (ν_s(C-C)Cp), 1099w, 1073w, 1011w, 970m, 844vs (δ(CH)Cp, ν(P-F)PF_6)), 748m, 723w, 560s (ν(P-F)PF_6), 460w, 427w. Raman: 1438 (5), 1130 (7) (ν_s(C-C)Cp), 876 (5), 280 (10) (κ(Cp)), 122 (5). Positive-ion MS: m/z 384 $[M\text{-}PF_6^-]^+$ (100%). Negative-ion MS: m/z 145 $[PF_6]^-$ (100%).