New Selectivity in Peptide Hydrolysis by Metal Complexes. Platinum(II) Complexes Promote Cleavage of Peptides Next to the Tryptophan Residue.

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SUPPORTING INFORMATION

Proton and Carbon-13 NMR Spectra of the Reactants

Indole-3-acetamide

Proton NMR data (δ in ppm) in acetone-d_6: N(1)H 10.32 br s; C(2)H 7.28 s; C(4)H 7.59 d, C(5)H 7.01 t, C(6)H 7.08 t, C(7)H 7.38 d, C(8)H 3.60 s, amide NH_2 6.63 br s and 6.30 br s. Carbon-13 chemical shifts (in ppm) in acetone-d_6: C(2) 124.5, C(3) 110.0, C(4a) 128.2, C(4) 119.5, C(5) 119.5, C(6) 122.0, C(7) 112.0, C(7a) 137.3, C(8) 33.5, C=O 174.0.

N-(3-indolylacetyl)-L-alanine

Proton NMR data (δ in ppm) in acetone-d_6: N(1)H 10.10 br s; C(2)H 7.40 s; C(4)H 7.60 d, C(5)H 7.02 t, C(6)H 7.10 t, C(7)H 7.48 d, C(8)H 3.66 s, amide NH 7.22 br s, CH 4.52 q, CH_3 1.45 d. Carbon-13 chemical shifts (in ppm) in acetone-d_6: C(2) 124.8, C(3) 109.5, C(4a) 128.3, C(4) 119.5, C(5) 119.6, C(6) 122.0, C(7) 112.0, C(7a) 137.5, C(8) 33.5, C=O 172.0, CH 58.0, CH_3 18.0, C(O)OH 174.1.

N-(3-indolylacetyl)-L-valine

Proton NMR data (δ in ppm) in acetone-d_6: N(1)H 10.15 br s; C(2)H 7.50 s; C(4)H 7.60 d, C(5)H 7.03 t, C(6)H 7.15 t, C(7)H 7.45 d, C(8)H 3.93 s and 3.91 s, amide NH 7.20 br s, CH 4.46 d, CH 2.10, CH_3 0.94 m.

Indole-3-acetic acid

Proton NMR data (δ in ppm) in acetone: N(1)H 10.32 br s; C(2)H 7.30 s; C(4)H 7.58 d, C(5)H 7.01 t, C(6)H 7.09 t, C(7)H 7.39 d, C(8)H 3.73 s, amide NH_2 6.63 br s and 6.30 br s.

Indole-3-acetic acid ethyl ester

Proton NMR data (δ in ppm) in acetone: N(1)H 10.32 br s; C(2)H 7.27 s; C(4)H 7.54 d, C(5)H 7.00 t, C(6)H 7.08 t, C(7)H 7.38 d, C(8)H 3.71 s, CH_2 4.08 q, CH_3 1.16 t, amide NH_2 6.63 br s and 6.30 br s.

N-acetyl-5-hydroxy-tryptamine

Proton NMR data (δ in ppm) in acetone: N(1)H 10.30 br s; C(2)H 7.05 s; C(4)H 6.97 d, C(6)H 6.70 m, C(7)H 7.20 d, C(8)H 3.56 t, CH_2 2.54 t, amide NH 6.63 br s and 6.30 br s, CH_3 2.10 s.

AcTrp

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.21 s; C(4)H 7.55 d, C(5)H 7.05 t, C(6)H 7.12 t, C(7)H 7.40 d, C(8)H 3.30 m, amide NH 7.80 br s, α-CH 4.75 t, CH_3 1.99 s. Carbon-13 chemical shifts (in ppm) in acetone-d_6: : C(2) 124.3, C(3) 111.0, C(4a) 128.8, C(4) 119.3, C(5) 119.0, C(6) 122.0, C(7) 112.0, C(7a) 137.4, C(8) 23.0, α-C 54.0, C(O)OH 174.0, CH_3 28.8, $C(O)NH_2$ 170.0.

N-acetyl-L-tryptophanamide

Proton NMR data (δ in ppm) in acetone: N(1)H 10.08 br s; C(2)H 7.15 s; C(4)H 7.64 d, C(5)H 7.00 t, C(6)H 7.08 t, C(7)H 7.35 d, C(8)H 3.18 m, amide NH 6.90 br s, 6.35 br s, and 7.12 br s, α-CH 4.65 m, CH_3 1.85 s. Carbon-13 chemical shifts (in ppm) in acetone-d_6: C(2) 124.2, C(3) 111.6, C(4a) 128.8, C(4) 119.3, C(5) 119.3, C(6) 122.0, C(7) 112.0, C(7a) 137.2, C(8) 23.0, α-C 54.3, C(O) 174.0, CH_3 29.0, $C(O)NH_2$ 170.0.

N-acetyl-L-tryptophan ethyl ester

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.20 s; C(4)H 7.55 d, C(5)H 7.02 t, C(6)H 7.08 t, C(7)H 7.38 d, C(8)H 3.25 m, amide NH 7.30 br s, α-CH 4.80 t, CH_3 1.90 s, CH_2(Et)4.10 q, CH_3 (Et) 1.15 t.

L-tryptophan methyl ester

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.25 s; C(4)H 7.50 d, C(5)H 7.02 t, C(6)H 7.08 t, C(7)H 7.35 d, C(8)H 3.35 m, amide NH 7.30 br s, α-CH 4.30 t, CH_3 3.70 s.

AcTrp-Gly

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.20 s; C(4)H 7.62 d, C(5)H 7.00 t, C(6)H 7.08 t, C(7)H 7.35 d, C(8)H 3.20 m, amide NH 7.80 br s and 7.85 br s, CH 4.73 q, CH_2 3.93 m, CH_3 1.90 s.

AcTrp-Ala

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.27 s; C(4)H 7.64 d, C(5)H 7.00 t, C(6)H 7.09 t, C(7)H 7.39 d, C(8)H 3.20 m, amide NH 8.12 br s and 7.90 br s, α-CH 4.75 q, α-CH 4.40 q, CH_3 1.90 s; CH_3 (Ala) 1.32 d.

AcTrp-Val

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.24 s; C(4)H 7.58 d, C(5)H 6.99 t, C(6)H 7.07 t, C(7)H 7.38 d, C(8)H 3.30 m, amide NH 7.85 br s and 7.80 br s, α-CH 4.80 m, α-CH 4.40 d, CH_3 1.90 s; CH_3 (Val) 0.93 m, CH (Val) 2.10 m.

AcTrp-ValOMe

Proton NMR data (δ in ppm) in acetone: N(1)H 10.10 br s; C(2)H 7.37 s; C(4)H 7.62 d, C(5)H 7.00 t, C(6)H 7.10 t, C(7)H 7.41 d, C(8)H 3.50 m, amide NH 7.95 br s and 7.90 br s, α-CH 4.72 m, α-CH 4.43 m, CH_3 1.90 s; CH_3 (Val) 0.90 m, CH (Val) 2.10 m, CH_3 (Me) 3.67 s.

Table S1. Temperature Dependence of ^{195}Pt Chemical Shifts

complex	$\Delta\delta$, ppm/K
K_2PtCl_4 [a]	0.977 ± 0.023
cis-[Pt(en)(sol)$_2$](ClO$_4$)$_2$ [b]	1.21 ± 0.20
cis-[Pt(en)(indole-3-acetamide)](ClO$_4$)$_2$ [b] **(6)**	0.29 ± 0.10
cis-[Pt(en)(*N*-acetyl-L-tryptophanamide)](ClO$_4$)$_2$ [c] **(7)**	0.73 ± 0.04

[a] In 1.0 M solution of NaCl in D_2O

[b] From ref. 42.

[c] In acetone-d_6.

Table S2. Platinum-195 Chemical Shifts for the Platinum(II) Complexes

complex	chemical shift, ppm
$K_2[PtCl_4]$[a]	-1628
$[Pt(acac)_2]$	-408
$[Pt(en)(O^3\text{-HAsc})_2]$[b]	-1780
$[Pt(en)(O^2,O^3\text{-Asc})]$[b]	-1712
$[Pt(en)(C^2,O^5\text{-Asc})]$[b]	-2634
$[Pt(en)(C^2\text{-HAsc})(O^3\text{-HAsc})]$[b]	-2663
$[Pt(NH_2CH_2C(O)NR)_2]$[c]	-2483
cis-$[Pt(en)(sol)_2](ClO_4)_2$[d]	-1890
cis-[Pt(en)(indole-3-acetamide)]$(ClO_4)_2$ (6)[d]	-2332
cis-[Pt(en)(*N*-(3-indolylacetyl)-L-alanine)]$(ClO_4)_2$ (6)[d]	-2340
cis-[Pt(en)(*N*-acetyl-L-tryptophanamide)]$(ClO_4)_2$ (7)[e]	-2301
cis-[Pt(en)(AcTrp-Ala)]$(ClO_4)_2$ (7)	-2338[f], -2301[g]

[a] External reference in all the experiments. Dissolved in a 1.0 M solution of NaCl in D_2O.

[b] From ref. 47.

[c] From ref. 45. The ligand atoms are highlighted.

[d] From ref. 42 at 296 K.

[e] In acetone-d_6 at 296 K

[f] At 233 K.

[g] Extrapolated to 296 K using the coefficient 0.73 ppm/K, from Table S1 in the Supporting Information.

Table S3. Proton Chemical Shifts (ppm) for the Two Products of Peptide Coordination to *cis*-$[PdL(sol)_2]^{2+}$ Complex.[a,b] Atom Numbering is Shown in Structure **4**

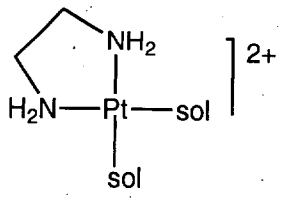
peptide	N(1)H	C(2)H	C(4)H	C(5)H	C(6)H	C(7)H	$C(8)H_2$	Amide-NH[c]	other
cis-[Pd(en)(*N*-acetyl-L-tryptophanamide)]$^{2+}$	10.40 br	7.57 s	7.70 d	7.17 t	7.13 t	7.55 d	3.70 m	8.95 s, 8.69 s, 8.00 br	5.03 m, 4.48 m, 1.90 s,
cis-[Pd(en)(AcTrp-Ala)]$^{2+}$	10.45 br	7.60 br	7.65 d	7.09 t	7.18 t	7.6 br	3.60 br	9.70 br, 7.80 br	7.40 br, 5.05 m, 4.45 m, 2.0 s, 1.51 d
cis-[Pd(dtco)(AcTrp-Ala)]$^{2+}$	10.50 br	7.63 br	7.64 d	7.10 t	7.16 t	7.57 d	3.65 d	9.80 br	7.42 br, 5.20 t, 4.45 m, 1.95 s, 1.50 d

[a] All in acetone-d_6 at 313 K. L is en or dtco.

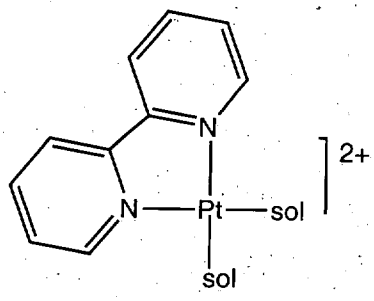
[b] From ref. 41.

[c] Amide group coordinated to the metal atom.

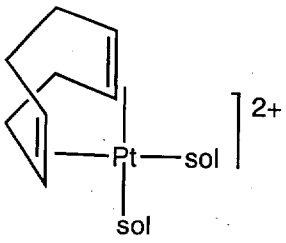
Chart S1. Promoters of Hydrolytic Cleavage of Peptides



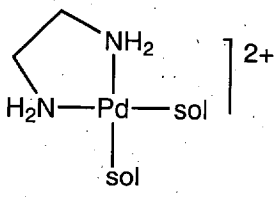
cis-[Pt(en)(sol)$_2$]$^{2+}$



cis-[Pt(bpy)(sol)$_2$]$^{2+}$



cis-[Pt(cod)(sol)$_2$]$^{2+}$



cis-[Pd(en)(sol)$_2$]$^{2+}$

sol is acetone or H_2O

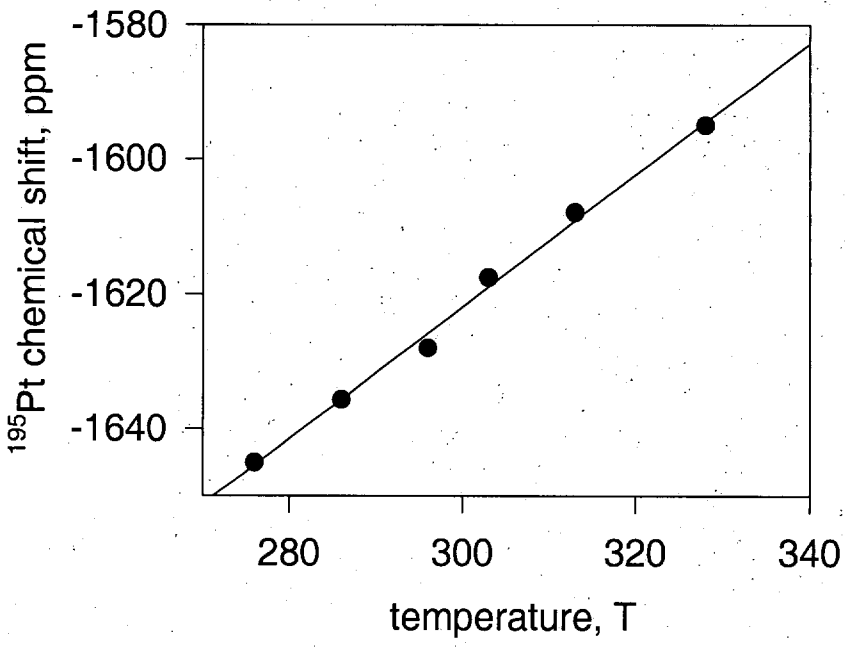


Figure S1. Dependence on temperature of the ^{195}Pt chemical shift for the complex *cis*-[Pt(en)(AcTrp-NH_2)]$^{2+}$. The initial concentrations of *cis*-[Pt(en)(sol)$_2$]$^{2+}$ and *N*-acetyl-L-tryptophanamide were 0.094 and 0.0094 M respectively, and the solvent was acetone-d_6.

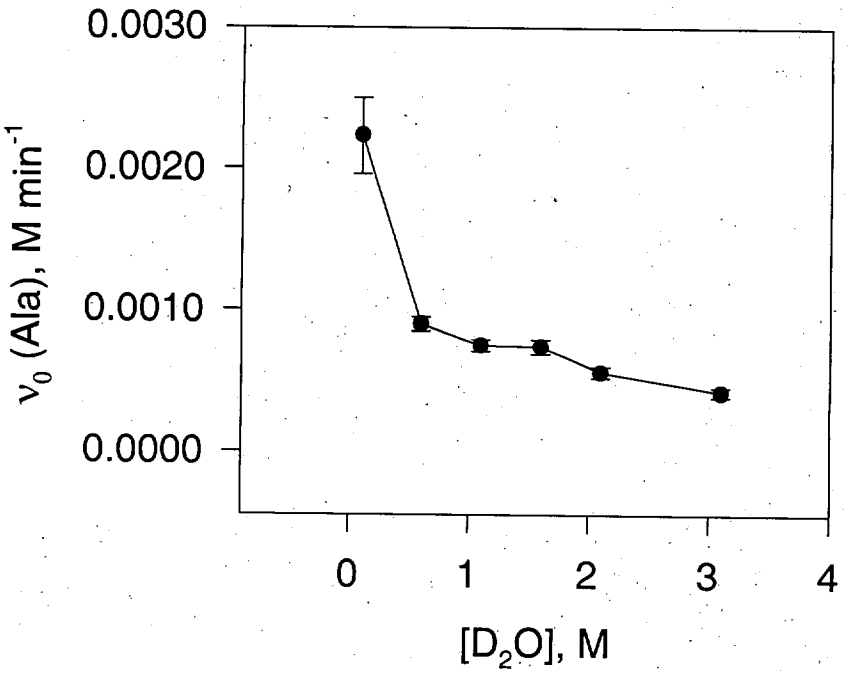


Figure S2. The initial rate for hydrolysis of AcTrp-Ala by *cis*-[Pt(en)(sol)$_2$]$^{2+}$ is somewhat inhibited by water. The initial rate was calculated from the appearance of free alanine. The initial concentrations of *cis*-[Pt(en)(sol)$_2$]$^{2+}$ and AcTrp-Ala were 0.094 and 0.0094 M, respectively, the solvent was acetone-d_6, and temperature was 313 K.