Supplementary information

1. UV/Vis of the complexes:

- Ethisterone
- Quinoline
- Isoquinoline
- Pyridine
- Py.Pt-trans
- py.Pt-cis
2. Additional spectroscopy of Ligands:

2.1. ET-3-Py (1)

Figure 2.1.1 The $^1$H NMR spectrum of 1 in CDCl$_3$. 

$C_{26}H_{31}NO_2$
2.2. ET-4-Py (2)

C_{26}H_{31}NO_{2}
Figure 2.2.1 The $^1$H NMR of 2 in CD$_3$OD.

2.3. ET-3-Q (3)
Figure 2.3.1 The $^1$H NMR spectrum of 3 in CDCl$_3$.

Figure 2.3.2 The COSY spectrum of 3 in CDCl$_3$. 
Figure 2.3.3 The low field region in the $^1\text{H-}^{13}\text{C}$ HMQC spectrum of 3 in CDCl$_3$.

Figure 2.3.4 The $^{13}\text{C}$ DEPT NMR spectrum of 3 in CDCl$_3$. 
Figure 2.4.1 The $^1$H NMR spectrum of 4 in CDCl$_3$. 
Figure 2.4.2 The aromatic region in the COSY spectrum for 4 in CDCl₃

Figure 2.4.3 The low field $^1$H-$^{13}$C HMQC spectrum of 4 in CDCl₃
Figure 2.4.4 The aliphatic region in the $^1$H-$^{13}$C HMQC spectrum of 4 in CDCl$_3$.

Figure 2.4.5 The $^{13}$C NMR spectrum of 4 in CDCl$_3$. 
2.5. ET-6-Q (5)

\[ \text{C}_{30}\text{H}_{33}\text{NO}_2 \]

Figure 2.5.1 The $^1$H NMR spectrum of 5 in CD$_3$OD
3. Additional spectroscopy of trans complexes:

3.1. Py.Pt-trans

![Diagram](image)

\[
[C_5H_{11}ClN_3Pt][NO_3]
\]
Figure 3.1.1 Comparison of the chemical shifts of free pyridine and Py.Pt-trans

3.2. Qui.Pt-trans

[\text{[C}_9\text{H}_{13}\text{N}_3\text{Pt}[\text{NO}_3]]]

Figure 3.2.1 The $^1$H NMR spectrum of qui.Pt-trans in CD$_3$OD.
3.3. 1.Pt-trans

[\text{C}_{26}\text{H}_{37}\text{ClN}_3\text{O}_2\text{Pt}[\text{NO}_3]]

Figure 3.3.1 The $^1$H NMR spectrum of 1.Pt-trans in CD$_3$OD.
Figure 3.3.2 The COSY spectrum for 1.Pt-trans in CD$_3$OD

Figure 3.3.3 The aromatic region in $^1$H NMR spectra of 1 (top) and 1.Pt-trans(bottom) in CD$_3$OD
3.4. 2.Pt-trans

\[
[C_{26}H_{37}ClN_3O_2Pt][NO_3]
\]

Figure 3.4.1 The \(^1\)H NMR spectrum of 2.Pt-trans in CD\(_3\)OD.
Figure 3.4.2 The aromatic region of the $^1$H NMR spectrum of 2 and 2.Pt-trans in CD$_3$OD

3.5. 3.Pt-trans

$\text{[C}_{30}\text{H}_{39}\text{ClN}_3\text{O}_2\text{Pt}[\text{NO}_3]}$
Figure 3.5.1 The $^1$H NMR spectrum of 3.Pt-trans in CD$_3$OD.

Figure 3.5.2 The $^1$H NMR COSY spectrum of 3.Pt-trans
Figure 3.5.3 The $^1$H NMR spectrum of 3 (top) and 3.Pt-trans (bottom) in CD$_3$OD

3.6. 4.Pt-trans

$$\begin{align*}
&\begin{array}{c}
\text{OH} \\
\text{NH}_3 \\
\text{Pt}^+ \\
\text{Cl} \\
\text{H}_3N
\end{array} \\
&\text{[C}_{30}\text{H}_{39}\text{ClN}_3\text{O}_2\text{Pt}[\text{NO}_3]]
\end{align*}$$
Figure 3.6.1 The $^1$H NMR spectrum of 4.Pt-trans in CD$_3$OD.

Figure 3.6.2 Comparison of the aromatic region of the $^1$H NMR spectrum of crude (upper) and pure (lower) 4.Pt-trans.
Figure 3.6.3 The aromatic region of the $^1$H NMR spectrum of 4 (top) and 4.Pt-cis (bottom) in CD$_3$OD.

3.7. 5.Pt-trans

$[\text{C}_{30}\text{H}_{39}\text{ClN}_{3}\text{O}_{2}\text{Pt}][\text{NO}_3]$
Figure 3.7.1 The $^1$H NMR spectrum of 5.Pt-trans in CD$_3$OD.

Figure 3.7.2 The comparison of the $^1$H NMR spectra of 5 and 5.Pt-trans

4. Additional spectroscopy of cis complexes:

4.1. Py.Pt-cis
Figure 4.1.1 The $^1$H NMR spectra of pyridine (upper) and Py.Pt-cis (lower) in CD$_3$OD

4.2. 1.Pt-cis

![Structural formula for Pt-cis]
Figure 4.2.1 The $^1$H NMR spectrum of 1.Pt-cis in CD$_3$OD.

Figure 4.2.2 The $^1$H NMR spectra of 1 (upper) and 1.Pt-cis (lower) in CD$_3$OD
4.3. 4.Pt-cis

[\text{C}_{30}\text{H}_{39}\text{ClN}_3\text{O}_2\text{Pt}[\text{NO}_3]]

Figure 4.3.1 The $^1$H NMR spectrum of 4.Pt.cis in CD$_3$OD
Figure 4.3.2 The $^1$H NMR spectra of 4.Pt-cis showing the crude (top) spectrum and purified (bottom) spectrum. Those signals marked double prime represent the disubstituted complex in CD$_3$OD.

Figure 4.3.3 The aromatic region in the COSY spectrum of 4.Pt-cis in CD$_3$OD.
Figure 4.3.4 The $^1$H NMR spectra of 4 and 4.Pt-cis in CD$_3$OD

4.4. 5.Pt-cis

$$[\text{C}_{30}\text{H}_{35}\text{ClN}_3\text{O}_2\text{Pt}][\text{NO}_3]$$
Figure 4.4.1 The $^1$H NMR spectrum of 5.Pt-cis in CD$_3$OD.

Figure 4.4.2 The $^1$H NMR spectra of 5 (upper) and 5.Pt.cis (bottom) in CD$_3$OD.
5. Geometry of trans and cis complexes:

5.1. Py.Pt-trans and Py.Pt-cis

Figure 5.1.1 Comparison of the $^1$H NMR spectra of Py.Pt-trans (upper) and Py.Pt-cis (lower) in CD$_3$OD.

5.2. 1.Pt-trans and 1.Pt-cis

Figure 5.2.1 Comparison of the aromatic fraction of the $^1$H NMR spectra of 1.Pt-trans (upper) and 1.Pt-cis (lower) in CD$_3$OD.
Figure 5.2.2 Comparison of the full $^1$H NMR spectra of 1.Pt-trans and 1.Pt-cis in CD$_3$OD, showing the difference between the ammine groups (around 4ppm).
5.3. 4.Pt-trans and 4.Pt-cis

**Figure 5.3.1** Comparison of the $^1$H NMR spectra of 4.Pt-trans (upper) and 4.Pt-cis (lower) in CD$_3$OD.

5.4. 5.Pt-trans and 5.Pt-cis

**Figure 5.4.1** Comparison of the $^1$H NMR spectra of 5.Pt-trans (upper) and 5.Pt-cis (lower) in CD$_3$OD.
### 6. Cytotoxicity

<table>
<thead>
<tr>
<th>Molecule</th>
<th>T47D</th>
<th>MDA-MB-231</th>
<th>SKOV-3</th>
<th>HBL-100</th>
<th>A2780</th>
<th>A2780cisR</th>
<th>Rx[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.Pt-cis</td>
<td>15.9 ± 0.5</td>
<td>29.2 ± 8.1</td>
<td>15.7 ± 0.5</td>
<td>7.4 ± 1</td>
<td>17.4 ± 3.1</td>
<td>33.3 ± 4.3</td>
<td>1.9</td>
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<tr>
<td>1.Pt-trans</td>
<td>63 ± 8</td>
<td>27.3 ± 4.7</td>
<td>30.1 ± 2</td>
<td>27.3 ± 1.9</td>
<td>35.3 ± 4.2</td>
<td>88 ± 2</td>
<td>2.5</td>
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<td>2.Pt-trans</td>
<td>19.2 ± 0.1</td>
<td>26.8 ± 1.8</td>
<td>12.1 ± 0.8</td>
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<tr>
<td>3.Pt-trans</td>
<td>51.4 ± 1.9</td>
<td>49.9 ± 4.5</td>
<td>24 ± 1.2</td>
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<tr>
<td>4.Pt-cis</td>
<td>32.8 ± 0.7</td>
<td>26.3 ± 0.3</td>
<td>27.7 ± 1</td>
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<tr>
<td>4.Pt-trans</td>
<td>51.4 ± 3.6</td>
<td>70.7 ± 2.7</td>
<td>28 ± 1.8</td>
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<tr>
<td>5.Pt-cis</td>
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<td>16.4 ± 0.7</td>
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<tr>
<td>5.Pt-trans</td>
<td>38.6 ± 2.4</td>
<td>45.4 ± 3.5</td>
<td>26.3 ± 2.8</td>
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<tr>
<td>py.Pt-cis</td>
<td>197 ± 17</td>
<td>186 ± 14</td>
<td>115 ± 5</td>
<td>210 ± 15</td>
<td>25.0 ± 1.2</td>
<td>105 ± 3</td>
<td>4.2</td>
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<tr>
<td>py.Pt-trans</td>
<td>181 ± 11</td>
<td>334 ± 54</td>
<td>98 ± 6</td>
<td>198± 10</td>
<td>72 ± 7</td>
<td>157 ± 2</td>
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<td>quin.Pt-trans</td>
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<td>243.3 ± 7.1</td>
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<td>1</td>
<td>&gt;200</td>
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<td>&gt;170</td>
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<td>5</td>
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<td>23.2</td>
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<tr>
<td>Cisplatin</td>
<td>32.0 ± 4.8</td>
<td>31.3 ± 4.7</td>
<td>6.0 ± 1.3</td>
<td>7.7 ± 0.5</td>
<td>3.0 ± 0.5</td>
<td>12.8 ± 1.4</td>
<td>4.3</td>
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[a] Rx is ratio of IC50 for a compound in A2780cisR compared to A2780. * indicate a oestradiol derivative.

### 7. Cellular uptake

<table>
<thead>
<tr>
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<th>SKOV-3</th>
<th>T47D</th>
<th>MDA-MB-231</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.Pt-cis</td>
<td>4.96</td>
<td>4.08</td>
<td>0.09</td>
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<td>1.Pt-trans</td>
<td>8.09</td>
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<tr>
<td>py.Pt-cis</td>
<td>114.04</td>
<td>9.1</td>
<td>15.89</td>
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<td>py.Pt-trans</td>
<td>57.49</td>
<td>37.02</td>
<td>5.93</td>
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<tr>
<td>Cisplatin</td>
<td>36.09</td>
<td>16.78</td>
<td>4.29</td>
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Table 7.1 pmoles of Pt in T47D, SKOV-3 and MDA-MB-231 per million cells after 3 hours of treatment with 30 µM of complexes.
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<tr>
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<th>SKOV-3</th>
<th>T47D</th>
<th>HBL-100</th>
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<tbody>
<tr>
<td>Pt added (μmol)</td>
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<tr>
<td>Pt in cells (nmol)</td>
<td>0.06</td>
<td>0.10</td>
<td>0.13</td>
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<tr>
<td>% Pt delivered</td>
<td>0.49</td>
<td>0.20</td>
<td>-</td>
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<tr>
<td>mol Pt/µmol DNA (bp)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pt added (μmol)</td>
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<td></td>
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<tr>
<td>Pt in cells (nmol)</td>
<td>0.05</td>
<td>0.03</td>
<td>0.08</td>
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<tr>
<td>% Pt delivered</td>
<td>0.08</td>
<td>0.04</td>
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<tr>
<td>mol Pt/µmol DNA (bp)</td>
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<tr>
<td>Pt added (μmol)</td>
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<td></td>
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<tr>
<td>Pt in cells (nmol)</td>
<td>0.12</td>
<td>0.14</td>
<td>0.10</td>
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<tr>
<td>% Pt delivered</td>
<td>0.13</td>
<td>0.14</td>
<td>0.10</td>
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<td>mol Pt/µmol DNA (bp)</td>
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<td>0.06</td>
<td>0.02</td>
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<td>Pt added (μmol)</td>
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<tr>
<td>Pt in cells (nmol)</td>
<td>0.12</td>
<td>0.22</td>
<td>0.16</td>
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<tr>
<td>% Pt delivered</td>
<td>0.14</td>
<td>0.14</td>
<td>0.16</td>
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<tr>
<td>mol Pt/µmol DNA (bp)</td>
<td>0.09</td>
<td>0.20</td>
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Table 7.2 nmoles of Pt in T47D, SKOV3 and HBL-100 per million cells after 72 hours of treatment with IC₅₀ µM of complexes.