Supporting Information

Efficient one-pot synthesis of trans-Pt(II)(salicylaldimine)(4-picoline)Cl complexes: Effective agents for enhanced expression of p53 tumor suppressor genes

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Synthesis and characterization of ligands L1–8

General procedure for the synthesis of ligands L1–8

1 mmol of amine/aniline, particular salicylaldehyde and anhyd. Na₂SO₄ (200 mg) were taken in 20 mL of CH₂Cl₂. The mixture was stirred under reflux for 4h (checked by TLC). On completion it is cooled to room temperature and filtered to remove undissolved solid which is further washed with CH₂Cl₂. The filtrate was vacuum evaporated to get L1 to L8 which was dried and used in the next step without further purification.

Characterization of ligand L1.

Yellow liquid, ¹H NMR (400 MHz, CDCl₃) δ 13.45 (s, 1H), 8.26 (s, 1H), 7.11 (d, J = 8.3 Hz, 1H), 7.05 (s, 1H), 6.87 (d, J = 8.3 Hz, 1H), 3.41 (d, J = 7.5 Hz, 2H), 2.29 (s, 3H), 2.02–1.92 (m, 1H), 0.98 (d, J = 6.7 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 164.7, 159.1, 132.9, 131.2, 127.4, 118.5, 116.8, 67.6, 29.6, 20.5, 20.4.

Characterization of ligand L2.

Orange solid, ¹H NMR (400 MHz, CDCl₃) δ 13.01 (s, 1H), 8.56 (s, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.27 (t, J = 7.6 Hz, 3H), 7.18 (d, J = 7.0 Hz, 2H), 6.93 (d, J = 8.6 Hz, 1H), 2.31 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 162.7, 159.0, 148.7, 134.1, 132.3, 129.4, 128.2, 126.8, 121.2, 118.9, 117.0, 20.4.
Light yellow solid, $^1$H NMR (400 MHz, CDCl$_3$) δ 12.85 (s, 1H), 8.54 (s, 1H), 7.28–7.22 (m, 2H), 7.22–7.16 (m, 2H), 7.15–7.07 (m, 2H), 6.94 (d, $J = 8.1$ Hz, 1H), 2.32 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ –116.17. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.5, 161.6 (d, $J_{C-F} = 247.45$ Hz), 158.9, 144.8, 134.2, 132.3, 128.2, 122.58 (d, $J_{C-F} = 8.3$ Hz), 118.7, 117.0, 116.2 (d, $J_{C-F} = 22.7$ Hz), 20.4.

**Characterization of ligand L4.$^1$**

Light yellow solid, $^1$H NMR (400 MHz, CDCl$_3$) δ 13.27 (s, 1H), 8.64 (s, 1H), 7.48–7.36 (m, 4H), 7.34–7.27 (m, 3H), 7.04 (d, $J = 8.1$ Hz, 1H), 6.96 (t, $J = 7.5$ Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.7, 161.2, 148.5, 133.2, 132.3, 129.4, 126.9, 121.2, 119.2, 119.1, 117.3.

**Characterization of ligand L5.$^2$**

Light yellow solid, $^1$H NMR (400 MHz, CDCl$_3$) δ 13.10 (s, 1H), 8.57 (s, 1H), 7.42–7.33 (m, 2H), 7.26 (dd, $J = 5.1$, 3.0 Hz, 1H), 7.23 (dd, $J = 5.0$, 3.0 Hz, 1H), 7.15–7.06 (m, 2H), 7.02 (d, $J = 8.8$ Hz, 1H), 6.94 (t, $J = 7.5$ Hz, 1H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ –115.93. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.5, 161.7 (d, $J_{C-F} = 247.45$ Hz), 161.1, 160.4, 144.7, 133.2, 132.3, 122.6 (d, $J_{C-F} = 8.3$ Hz), 119.2, 117.3, 116.2 (d, $J_{C-F} = 22.7$ Hz).

**Characterization of ligand L6.**

Yellow liquid, $^1$H NMR (400 MHz, CDCl$_3$) δ 13.41 (s, 1H), 8.25 (s, 1H), 7.06–6.98 (m, 1H), 6.95 (dd, $J = 8.4$, 3.1 Hz, 1H), 6.90 (dd, $J = 9.0$, 4.5 Hz, 1H), 3.43 (d, $J = 6.5$ Hz, 2H), 2.03–1.93 (m, 1H), 0.98 (d, $J = 6.7$ Hz, 6H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ –
126.64. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.7, 157.4, 155.3 (d, $J_{C-F} = 236.2$ Hz), 119.0 (d, $J_{C-F} = 23.2$ Hz), 118.5 (d, $J_{C-F} = 7.2$ Hz), 118.0 (d, $J_{C-F} = 7.4$ Hz), 116.2 (d, $J_{C-F} = 23.1$ Hz), 67.6, 29.6, 20.4.

**Characterization of ligand L7.**

![L7](image)

Orange solid, $^1$H NMR (400 MHz, CDCl$_3$) δ 13.02 (s, 1H), 8.56 (s, 1H), 7.49–7.38 (m, 2H), 7.36–7.26 (m, 3H), 7.16–7.05 (m, 2H), 7.02–6.94 (m, 1H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ −125.82. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 161.5, 157.3, 155.6 (d, $J_{C-F} = 237.5$ Hz), 148.1, 129.5, 127.3, 121.2, 120.3 (d, $J_{C-F} = 23.3$ Hz), 118.9 (d, $J_{C-F} = 6.8$ Hz), 118.4 (d, $J_{C-F} = 7.3$ Hz), 117.1 (d, $J_{C-F} = 23.2$ Hz).

**Characterization of ligand L8.$^3$**

![L8](image)

Orange solid, $^1$H NMR (400 MHz, CDCl$_3$) δ 12.87 (s, 1H), 8.53 (s, 1H), 7.33–7.22 (m, 2H), 7.18–7.05 (m, 4H), 6.98 (dd, $J = 8.7, 4.5$ Hz, 1H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ −115.27, −125.68. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 161.9 (d, $J_{C-F} = 248.5$ Hz), 161.2, 157.2, 155.6 (d, $J_{C-F} = 237.4$ Hz), 144.3, 122.7 (d, $J_{C-F} = 8.4$ Hz), 120.35 (d, $J_{C-F} = 23.3$ Hz), 118.8 (d, $J_{C-F} = 5.7$ Hz), 118.4 (d, $J_{C-F} = 7.4$ Hz), 117.1 (d, $J_{C-F} = 23.1$ Hz), 116.4 (d, $J_{C-F} = 22.8$ Hz).

**References:**

$^{1}H$, $^{13}C$ and $^{19}F$ NMR Spectra of Ligands

**Fig. S1** $^{1}H$ NMR of $L_1$ in CDCl$_3$ at 25°C

**Fig. S2** $^{13}C$ NMR of $L_1$ in CDCl$_3$ at 25°C
Fig. S3 $^1$H NMR of L2 in CDCl$_3$ at 25°C

Fig. S4 $^{13}$C NMR of L2 in CDCl$_3$ at 25°C
Fig. S5 $^1$H NMR of L3 in CDCl$_3$ at 25°C

Fig. S6 $^{13}$C NMR of L3 in CDCl$_3$ at 25°C
Fig. S7 $^{19}$F NMR of L3 in CDCl$_3$ at 25°C

Fig. S8 $^1$H NMR of L4 in CDCl$_3$ at 25°C
Fig. S9 $^{13}$C NMR of L4 in CDCl$_3$ at 25°C

Fig. S10 $^1$H NMR of L5 in CDCl$_3$ at 25°C
Fig. S11 $^{13}$C NMR of L5 in CDCl$_3$ at 25°C

Fig. S12 $^{19}$F NMR of L5 in CDCl$_3$ at 25°C
Fig. S13 $^1$H NMR of L6 in CDCl$_3$ at 25°C

Fig. S14 $^{13}$C NMR of L6 in CDCl$_3$ at 25°C
Fig. S15 $^{19}$F NMR of L6 in CDCl$_3$ at 25°C

Fig. S16 $^1$H NMR of L7 in CDCl$_3$ at 25°C
**Fig. S17** $^{13}$C NMR of L7 in CDCl$_3$ at 25°C

**Fig. S18** $^{19}$F NMR of L7 in CDCl$_3$ at 25°C
Fig. S19 $^1$H NMR of L8 in CDCl$_3$ at 25°C

Fig. S20 $^{13}$C NMR of L8 in CDCl$_3$ at 25°C
Fig. S21 $^{19}$F NMR of L8 in CDCl$_3$ at 25°C
$^1$H, $^{13}$C and $^{19}$F NMR Spectra of platinum complexes

**Fig. S22** $^1$H NMR of C1 in CDCl$_3$ at 25°C

**Fig. S23** $^{13}$C NMR of C1 in CDCl$_3$ at 25°C
Fig. S24 $^1$H NMR of C2 in CDCl$_3$ at 25°C

Fig. S25 $^{13}$C NMR of C2 in CDCl$_3$ at 25°C
Fig. S26 $^1$H NMR of C3 in CDCl$_3$ at 25°C

Fig. S27 $^{13}$C NMR of C3 in CDCl$_3$ at 25°C
Fig. S28 $^{19}$F NMR of C3 in CDCl$_3$ at 25°C

Fig. S29 $^{1}$H NMR of C4 in CDCl$_3$ at 25°C
**Fig. S30** $^{13}$C NMR of C4 in CDCl$_3$ at 25°C

**Fig. S31** $^1$H NMR of C5 in CDCl$_3$ at 25°C
Fig. S32 $^{13}$C NMR of C5 in CDCl$_3$ at 25°C

Fig. S33 $^{19}$F NMR of C5 in CDCl$_3$ at 25°C
Fig. S34 $^1$H NMR of C6 in CDCl$_3$ at 25°C

Fig. S35 $^{13}$C NMR of C6 in CDCl$_3$ at 25°C
Fig. S36 $^{19}$F NMR of C6 in CDCl$_3$ at 25°C

Fig. S37 $^1$H NMR of C7 in CDCl$_3$ at 25°C
Fig. S38 $^{13}$C NMR of C7 in CDCl$_3$ at 25°C

Fig. S39 $^{19}$F NMR of C7 in CDCl$_3$ at 25°C
Fig. S40 $^1$H NMR of C8 in CDCl$_3$ at 25°C

Fig. S41 $^{13}$C NMR of C8 in CDCl$_3$ at 25°C
Fig. S42 $^{19}$F NMR of C8 in CDCl$_3$ at 25°C
Mass Spectra of all platinum complexes

**Fig. S43** Mass Spectrum of C1

**Fig. S44** Mass Spectrum of C2
Fig. S45 Mass Spectrum of C3

Fig. S46 Mass Spectrum of C4
Fig. S47 Mass Spectrum of C5

Fig. S48 Mass Spectrum of C6
Fig. S49 Mass Spectrum of C7

Fig. S50 Mass Spectrum of C8
Stability study

Stability of metal complex studied for cytotoxic analysis is always important. Therefore we performed stability analysis experiments for C2, C3 and C5 as model complexes using $^1$H NMR spectroscopy in 10–15% D$_2$O–DMSO-d$_6$ mixture under room temperature at 0, 24, 48, and 72 h. No changes were observed in $^1$H chemical shifts and also in peak number (Fig. S51 for C2, Fig. S52 for C3 and Fig. S53 for C5 below). It is concluded that C2, C3 and C5 are highly stable under these conditions.

Fig. S51 Stability analysis of C2 using $^1$H NMR, taken in 15% D$_2$O–DMSO-d$_6$ at room temperature during (bottom to top) 0, 24, 48 and 72 h.
**Fig. S52** Stability analysis of C3 using $^1$H NMR, taken in 10% D$_2$O–DMSO-$d_6$ at room temperature during (bottom to top) 0, 24, 48 and 72 h.

**Fig. S53** Stability analysis of C5 using $^1$H NMR, taken in 10% D$_2$O–DMSO-$d_6$ at room temperature during (bottom to top) 0, 24, 48 and 72 h.
Single crystal structure study and refinement data of C1, C2 and C3

Table S1 data and structure refinement of the complex C1, C2 and C3

<table>
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<th>Empirical formula</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
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<td>293(2)</td>
<td>233(2)</td>
<td>293(2)</td>
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<td>Unit cell dimensions</td>
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<td>14.219(7)</td>
<td>13.766(2)</td>
<td>7.961(3)</td>
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<td>1869.1(6)</td>
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<td>Theta range for data collection (°)</td>
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<td>12631</td>
<td>4009</td>
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<td>Independent reflections</td>
<td>3582 [R(int) = 0.1028]</td>
<td>4228 [R(int) = 0.0493]</td>
<td>3327 [R(int) = 0.0484]</td>
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<td>99.4</td>
<td>99.5</td>
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<td>Semi-empirical from equivalents</td>
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<td>4228 / 0 / 228</td>
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<td>R1[a] = 0.0580, wR2[b] = 0.1699</td>
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<td>R1[a] = 0.0655, wR2[b] = 0.1736</td>
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<td>Extinction coefficient</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
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<td>Largest diff. peak and hole</td>
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<td>1.763 and –2.859 e.Å⁻³</td>
<td>2.342 and –3.095 e.Å⁻³</td>
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</tbody>
</table>

[a] R1 = Σ all reflections | F0 - Fc | Σ all reflections | F0 | [b] wR2 = [Σ w(F0² - Fc²)² / Σ w(F0²)²]₁/².
Packing plot of C1

Fig. S54 1D array made by intermolecular bond between chloride attached to Pt center and H of the next molecule in C1

Packing plot of C2

Fig. S55 3D arrangement of molecules in crystal packing; made by intermolecular bonds between chloride attached to Pt center and H of the next molecule (blue bonds) in C2
Packing plot of C3

**Fig. S56** 3D arrangement of molecules in crystal packing; made by intermolecular bonds between chloride attached to Pt center and H of the neighbor molecule in C3