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Investigation on Optical and Biological Properties of 2-(4-Dimethylaminophenyl)benzothiazole Based Cycloplatinated Complexes

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Supporting Information

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1.- Experimental Section

General comments. All reactions were carried out under an atmosphere of dry nitrogen, using standard Schlenk techniques. Solvents were obtained from a solvent purification system (M-BRAUN MB SPS-800). Elemental analyses were carried out with a Carlo Erba EA1110 CHNS-O microanalyzer. Mass spectra were recorded on a HP-5989B mass spectrometer (ES). IR spectra were obtained on a Perkin Elmer Spectrum Two FT-IR Spectrometer. NMR spectra were recorded on a Bruker Advance 400 spectrometer at 293 K. Chemical shifts are reported in parts per million (ppm) relative to external standards (SiMe₄, CFCl₃ and H₃PO₄), and all coupling constants are given in hertz (Hz). The starting compounds [Pt(Me₂N-pbt-κN)₂(C₆F₅)₂], [Pt(C^N)(µ-Cl)]₂, O(CH₂CH₂OCOC₆H₄PPh₂)₂ (PR₄P) and O[(CH₂CH₂O)₃COC₆H₄PPh₂]₂ (PR₁₂P) have been synthesized following similar procedures to those previously established for related complexes. Other commercially available reagents were used as received.

Photophysical properties. The UV−vis absorption spectra were measured with a Hewlett-Packard 8453 spectrophotometer. Excitation and emission spectra were obtained in a Shimadzu RF-6000 spectrofluorometer. The lifetime measurements were performed with a Jobin Yvon Horiba Fluorolog 3-11 Tau 3 spectrofluorometer operating in the phosphorimeter mode (with an F1-1029 lifetime emission PMT assembly, using a 450 W Xe lamp) or with a Datastation HUB-B with a nanoLED controller and software DAS6. The nanoLED employed for lifetime measurements was of 390 nm with pulse length of 1.4 ns. Quantum yields were measured using a F-3018 Integrating Sphere mounted on a Fluorolog 3-11 Tau-3 spectrofluorometer. The lifetime data have been fitted using the Jobin-Yvon software package. The oxygen singlet signal was measured for CH₂Cl₂ solutions (10⁻² M) of 2 and 4 on an Edinburgh FLS 1000 fluorescence spectrometer with a Xe2 continuous Xenon Lamp with excitation at 455 nm and a filter at 645 nm, configured with a NIR-PMT-1700 in cooling housing (77 K).

X-ray crystallography. Crystals of the complex 2 were obtained by slow diffusion of ¹PrOH into a solution in dichloromethane, by diffusion of n-hexane into a solution of 3 with excess of phosphine in MeOH to obtain 7, or by evaporation of a solution of 4 in CDCl₃ at room temperature The diffraction data were collected using a Bruker APEX-II diffractometer at a temperature of 145 (2, 7) or 140 (4) K using the APEX-II software. The structures were solved by intrinsic phasing using SHELXT[4] program with the WinGX graphical user interface.[5] Multi-scan absorption corrections were applied to all the data sets and refined by full-matrix least squares on F² with SHELXL.[6] All hydrogen atoms were positioned geometrically, with isotropic parameters Uiso = 1.2 Ueq (parent atom) for aromatic hydrogens and CH₂ and Uiso = 1.5 Ueq (parent atom) for methyl groups
except for the 'PrOH hydrogen in 2 or all the MeOH hydrogens in 7 which were found in the electron density map. The hydrogens of the carboxy groups has been found only for compound 7. The structures show some residual peaks greater than 1 eÅ⁻³, but with no chemical meaning.

**Computational details.** Calculations were carried out with the Gaussian 16 package,[7] using the functional B3LYP.[8] The results were visualized with GaussView 6. Overlap populations between molecular fragments were calculated using the GaussSum 3.0 software.[9] The basis set used for the metal atoms was the LanL2DZ effective core potential and 6-31G(d,p) for the ligand atoms.[10] No negative frequency was found in the vibrational frequency analysis of the final equilibrium geometries. The effect of the solvent in the ground state and in triplet state calculations (DFT, TD-DFT) was considered using the polarized continuum model approach (PCM) [11] implemented in the Gaussian 16 software. The emission energies were calculated as the difference between the optimized T₁ state and the S₀ state in the optimized T₁ geometry (adiabatic electronic transition).

**Determination of ¹O₂ generation quantum yields.** Singlet Oxygen quantum yields (φΔPC) were determined for [Ru(bpy)₃]Cl₂ in acetonitrile according to a relative procedure adapted from the literature,[12] which is based on monitoring by UV-Vis spectroscopy the oxidation of 1,3-diphenylisobenzofuran (DPBF, yellow) to 1,2-dibenzoylbenzene (colorless) photosensitized by the Pt(II) derivative.

![Reaction Scheme](image)

DPBF was selected as the ¹O₂ scavenger due to its fast reaction with ¹O₂. Air-equilibrated acetonitrile solutions containing DPBF were prepared (~8 x 10⁻⁵ M) in a cuvette and their absorbance adjusted to around 1.0 at 410 nm. Then, the photosensitizer ([Ru(bpy)₃]Cl₂, 10⁻⁵ M, corresponding to absorbance around 0.2) was introduced in the cuvette. Low dye concentrations were used to minimize quenching of ¹O₂ by the dyes. The mixture was irradiated with a blue LED strip (λirr = 460 nm) at room temperature for 1 second irradiation intervals during a total exposure period of 20 seconds and absorption UV-Vis spectra were recorded after every irradiation interval. The decrease in the absorption band at 410 nm was plotted vs. the irradiation time and the experimental data were fitted to a straight line. An acetonitrile solution of DPBF without the Pt(II) complex was examined to confirm its photostability under identical irradiation conditions (20 s). The φΔPC were
calculated by a relative method using equation (1), and [Ru(bpy)₃]Cl₂ as the reference for
¹O₂ photosensitization in acetonitrile (φ₅S = 0.56).[13]

\[ \phi_{5}^{PC} = \phi_{5}^{S} \times \left( \frac{S^{PC} \times F^S}{S^S \times F^{PC}} \right) \quad \text{eq} \ (1) \]

Where S, is the slope of a linear fit for the change in absorbance of DPBF (at 410 nm)
with the irradiation time, and F, is the absorption correction factor, which is given by F =
1×10⁻⁰⁶ₐ₃D (where OD is the optical density at the irradiation wavelength). The superscripts
PC and S stand for the Pt(II) photocatalyst and the standard sensitizer, respectively.

Cell Lines and Culture Conditions. A549 (tumor adenocarcinomic alveolar basal
epithelial cells) and HeLa (tumor epithelioid cervix carcinoma cells) human cell lines, as
well as immortalized mouse embryonic fibroblasts (3T3) obtained from lungs (LMEFs)
were cultured following the American Type Culture Collection (www.atcc.org)
recommendations and standard methods, as previously described.[1, 14] A549, HeLa and
184B5 human cells, and murine LMEFs were maintained in an RPMI 1640 medium and
DMEM (Dulbecco’s Modified Eagle’s Medium), respectively, supplemented with 10%
fetal bovine serum (FBS) and 2.0 mM L-glutamine. Penicillin (100 U mL⁻¹) and
streptomycin (100 μg mL⁻¹) were added to all media. Cultures were maintained under a
humidified atmosphere of 95% air/5% CO₂ at 37 °C and subcultured before they became
confluent using a 0.25% trypsin/EDTA solution.

Cytotoxicity Assay. The 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-
(4-sulfophenyl)-2H-tetrazolium (MTS) hydrolysis method (MTS-based CellTiter 96,
AQueous Assay; Promega Corp., Madison, WI) was used to determine the cell viability
as an indicator of A549, HeLa and 184B5 cell sensitivity to the complexes as previously
reported.[1] Briefly, 50 μL of exponentially growing cells were seeded at densities of 1.5
× 10³ (A549 and HeLa) and 7.0 × 10³ (184B5) cells per well, in a 96-well flat-bottomed
microplate in growing media with 5% (A549) and 10% (HeLa and 184B5) FBS. 24 h
later, they were incubated for 72 h with the compounds. The complexes were dissolved
in DMSO at 16 mM (3) or 8 mM (Me₂N-pbtlH, 1, 2, 4, 5 and 6). Cisplatin (Alfa Aesar,
Karlsruhe, Germany) as a reference was dissolved at 6.4 mM in a saline solution.[2] These
stock solutions were kept frozen until they were dissolved in a test medium as nine 1:1.5
serial dilutions for the three cell lines except complex 2 for 184B5 cells that was serially
diluted 1:2. A total of 50 μL of each dilution or medium alone was added to growing cells
in the 96-well plate designed as previously recommended.[15] Available at
http://www.oecd.org/env/testguidelines). Final concentrations in sextuplicates ranged
from: 200 to 7.80 μM (Me₂N-Hpbt, 1, 4 and 5), from 50 to 1.95 μM (2 and 6), and from
100 to 3.90 μM (3) for A549 cells, from 100 to 3.90 μM (2, 3 and 6) for HeLa cells, and
from 200 to 0.78 μM (2), from 100 to 3.90 μM (3), and from 50 to 1.95 μM (6) for 184B5 cells. In the case of cisplatin, serial dilutions were 1:1.5 ranging from 40 to 1.56 μM for A549 cells and 1:2 ranging from 200 to 0.78 μM for HeLa cells,\cite{1,2} and from 100 to 0.39 μM for 184B5 cells. After 72 h at 37 °C, 20 μL of MTS was added and plates were incubated for 1 h at 37 °C. Finally, the optical density was measured at 490 nm using a 96-well multiscanner autoreader (POLARstar Omega; BMG Labtech, Offenburg, Germany). Each experiment was repeated three times. Appropriate solvent controls were run along with samples to discard the DMSO cytotoxic effect. The IC₅₀ (drug concentration that produced 50% inhibition of cell proliferation) was calculated by plotting the percentage of growing inhibition versus log of the drug concentration using the GraphPad Prism 6 (La Jolla, CA) software.\cite{2}

**Selectivity index.** The selectivity index (SI) was calculated according to the following equation: SI = IC₅₀ non-tumor cell (184B5)/IC₅₀ tumor cells (A549 or HeLa), as previously reported.\cite{14a}

**Lipophilicity Determinations.** Relative Lipophilicity measurements by RP-UPLC were performed using a Waters Acquity UPLC system (Waters, Milford, MA, USA), which was interfaced to quadrupole, high resolution, TOF mass spectrometer (micrOTOF-Q Bruker, Bremen, Germany), using an ESI interface operating in positive ion mode. The UPLC separation was performed using an Acquity UPLC BEH C18 1.7 μm particle size analytical column 100 mm × 2.1 mm (Waters) at a flow rate of 0.35 mL/min. The mobile phases used were A = H₂O with 0.1% HCOOH and B = acetonitrile with 0.1% HCOOH. The percentage of organic modifier (B) was changed linearly as follows: 0 min, 50%; 9.5 min, 99%; 11.5 min, 99%; 12 min, 20%; 12.5 min, 20%. Nitrogen (from a nitrogen generator) was used as the drying gas and nebulizing gas (2 Bar). The column temperature was set to 30°C. MS data were acquired over an m/z range of 50–3300. A capillary voltage of 4.5 kV, set end plate offset -500 V, dry gass of 7.0 L/min and set dry heater of 190º were used. Calibrations were conducted from m/z 50 to 3300 with a HCOONa solution (15 mg) in 100 mL (90:10 H₂O:MeOH). MS data were acquired in centroid mode and were processed by the DataAnalysis application manager (within Compass Data Analysis 4.2 SR2; Bruker Corporation). Samples were dissolved in 10% v/v methanol in water, ∼10 μM.

**In vitro Photocytotoxicity Testing.** Induction of phototoxicity in cultured cells was performed following previous reports, with modifications.\cite{16} Cells, (A549 and HeLa) were seeded in 96-well plates as described above for the MTS assay. 24 h after later, cells were washed with HBSS (Hank’s Balanced Salt Solution) (with Ca²⁺, Mg²⁺ and 1 g/L glucose, without phenol red and pyruvate; Cat No. 14025 Thermo Fisher; Waltham, MA) and incubated in 50 μL sextuplicates of HBSS alone or in 1:2 nine serial dilutions of non-
toxic compound 4 ranging from 20 to 0.078 μM in HBSS for 1 h at 37 °C in a 5% CO2 atmosphere. After 1 h of exposure to the compound, plates were removed from the incubator, laid 91 mm under a LED lamp (λ_{max} 396 nm; Onforu 15W IP66) and irradiated for 1 min (“photoinduced” plate) under room normoxic atmosphere. Meanwhile, an equivalent control non-irradiated plate was manipulated in the same way (“non-photoinduced” plate). Cells were washed with HBSS, added 100 μL of cell type specific complete medium and further incubated for 72 h at 37 °C in a 5% CO2 atmosphere. Plates incubated in HBSS alone and irradiated up to 30 min with the same lamp were also used as control to determine irradiation effects on cell viability. Finally, 20 μL of MTS was added to each well, plates were incubated for 1 h at 37 °C and the optical density was measured at 490 nm using a 96-well multi-scanner auto reader. Each experiment was repeated three times. The IC_{50} was calculated as described above under the Cytotoxicity Assay section.

Interaction of Complexes with DNA. The interaction between complexes and cisplatin with pBR322 plasmid DNA was studied by gel electrophoresis (mobility shift assay) as we have previously described.[14a] The amount of DNA was kept constant (200 ng), while the concentrations of the compounds were varied to obtain increasing molar ratios with respect to plasmid DNA base pairs (0.00:1, 0.25:1, 0.5:1, 1:1, 2:1, and 4:1). Aliquots of 2 μL of pBR322 plasmid DNA were mixed either alone or with 0.25, 0.5, 1, 2, or 4 μL of each compound solution (300 μM), respectively, in a 10 μL final volume of interaction buffer (50 mM NaClO4, 5 mM Tris-HCl, pH 7.5). Mixtures were incubated at 37 °C for 20 h in the dark and, after the addition of 2 μL of loading dye, were loaded onto 1% (w/v) agarose gels made in Trisacetate/ethylenediaminetetraacetic acid (EDTA) buffer (TAE) and separated by electrophoresis for 4 h at 70 V in TAE. Finally, gels were dyed for 30 min by immersion in a 3X solution of GelRed nucleic acid gel stain (Biotium Inc., Fremont, CA) diluted in 100 mM NaCl and images registered using a Gel-Doc System with the help of Quantity One software (BioRad, Hercules, CA).

Effects on Microtubule Polymerization: Cell Treatment, Immunocytochemistry, and Confocal Microscopy. A549 cells were cultured over 1-cm-diameter poly(L-lysine) (Sigma-Aldrich)-coated coverslips into a 24-well plate in 0.5 mL of a supplemented culture medium per well for 48 h, as reported. Then, 0.5 mL of a medium containing either 100 μM of compounds 2 and 6, or 10 μM nocodazole (Sigma-Aldrich) was added to cells. Cells were incubated at 37 °C for 6 h with compounds or for 2h with nocodazole, the medium was removed, and the cells were washed twice with HBSS (pH 7.2) and fixed in 4% paraformaldehyde in PBS. Nocodazole was used to induce microtubule depolymerization as reported.[2, 14a] For immunocytochemical fluorescent staining, the cells were permeabilized with 0.5% IGEPAL (Sigma-Aldrich) and 100 mM glycine in PBS (pH 7.4), washed with PBS, blocked with 5% FBS in PBS, and exposed to a mouse
monoclonal anti-β tubulin primary antibody (clone TUB 2.1; Sigma-Aldrich; 1:1000 dilution in a blocking solution) overnight at 4 °C to specifically label microtubules. The following day, after three washes in 0.02% Tween-20 (Sigma-Aldrich) in PBS, Cy3 goat antimouse IgGs (Jackson Immuno Research; 1:400 dilution in a blocking solution), which bind antitubulin IgGs, was added to the cells for 2 h. Finally, after three PBS washes, coverslips were placed on glass slides using a ProLong Gold Antifade Reagent (Molecular Probes) containing 4',6-diamidino-2-phenylindole (DAPI; Molecular Probes) as a nuclear counterstain. Slides were examined under a confocal microscope (TCS SP5; Leica Microsystems, Mannheim, Germany) and documented using a 63× oil immersion objective and an additional digital zoom with the help of LAS AF Lite microscopy software (Leica Microsystems). Images were projected into a single layer, and the resulting 2D data set was merged using the Fiji/ImageJ Open Source image processing software package.[2]

Cytolocalization by Confocal Microscopy. Cytolocalization of compounds in living cells was analyzed as described by Wiranowska et al.[17] with modifications. A549 and LMEF cells were seeded onto poly-D-lysine-coated glass-bottomed culture dishes (MatTek Corporation, Ashland, MA) and let then grow up to 50-70 % confluency for 24-48 h. Next, the growth medium was removed and cells were either non-treated or treated with 10 μM of compounds NMe2-pbtH, 1, 2, 4 and 6 in growth medium at 37°C in 5% CO₂ up to 22 h. To determine cytolocalization of compounds in nuclei, mitochondria, lysosomes or Golgi-complex, cells were co-stained with corresponding trackers: Hoechst 33342 (Sigma-Aldrich), Mito-Tracker® Deep Red FM, Lyso-Tracker® Red DND-99 or BODIPY® TR C5-Ceremide-BSA (Thermo Fisher). To label mitochondria and lysosomes following treatments with compounds, media were removed and substituted with fresh media containing compounds and 3.2 μM Hoechst, 100 nM Mito-Tracker-Red and/or 100 nM LysoTracker and incubated for 30 min at 37°C in 5% CO₂, in order to obtain either single or multiple fluorescent labelings. To stain the Golgi complex, growth medium was removed and plates were washed 3 times with HBSS and moved to ice in the last wash. After adding 500 μL of 5 μM BODIPY TR C5-ceremide sphingolipids complex to BSA in HBSS cells were incubated for 30 min at 4°C. Next, the BODIPY TR C5-ceremide-BSA solution was removed and cells were rinsed three times with ice-cold medium, followed by addition of room-temperature medium. The plates were placed in 37°C in 5% CO₂ incubator for 30 min. and fluorescence immediately evaluated by confocal microscopy.

Micrographs of living cells were taken at different incubation times with the compounds alone or combined with trackers using a Leica TCS SP5 laser scanning confocal microscope and analyzed as described above. All images were taken at 37°C and 5% CO₂ and using immersion oil. 405 Diode, Argon, and HeliumNeon (HeNe) laser lines were
applied to excite the samples and tunable filters were used to minimize crosstalk between fluorochromes. Gain, offset, and pinhole settings were identical for all samples within each experiment. The non-treated cells were used to establish the gain and offset settings to exclude non-specific and auto fluorescence. Images were documented with the help of LAS AF Lite microscopy software and projected into a single layer, or merged in one multilayered data set using the Fiji/ImageJ Open Source image processing software package as above mentioned.

Synthesis

**Preparation of [Pt(Me2N-pbt)(C6F5)(Me2N-pbtH)] 1**

[Pt(Me2N-pbtH)2(C6F5)2] (0.423 g, 0.41 mmol) was refluxed in toluene (15 mL) for 10 h under argon atmosphere. Then, the yellow solution obtained was evaporated to dryness and treated with n-hexane (~50 mL) to yield 1 as an orange solid (0.348 g, 98 %). IR (cm⁻¹): ν(C-F, C6F5) 1060 (m), 955 (s); ν(C6F5)X-sens 790 (s). ESI (+): m/z (%) 616 [M-L+H]+ (100), 870 [M+H]+ (80). Anal. Found (calcd for C 36H27F5N4PtS2): C, 49.61 (49.71); H, 3.65 (3.13); N, 6.46 (6.44). 1H NMR (400 MHz, CDCl3, 20º C, δ): 9.15 (d, 1H, J = 8, H7'), 8.73 (d, 2H, J = 9, H8'), 7.78 (d, 1H, J = 8, H4'), 7.68 (d, 1H, J = 8, H4), 7.48 (d, 1H, J = 8, H8), 7.38 (t, 1H, J = 7, H5'), 7.34 (t, 1H, J = 7, H5), 7.06 (t, 1H, J = 8, H5), 6.85 (t, 1H, J = 8, H6), 6.64 (d, 2H, J = 9, H9'), 6.55 (d, 1H, J = 8, H7), 6.42 (dd, 1H, J = 8, JH-H = 2.5, H9), 6.04 (d, 1H, JH-H = 2.4, JPt-H = 77, H11), 2.99 (s, 6H, Me2N), 2.84 (s, 6H, Me2N). 13C{1H} NMR (100.6 MHz, CDCl3, 20º C, δ): 181.4 (C2), 172.1 (C2'), 153.6 (C7a'), 152.6 (C 10/10'), 152.5 (C 10/10'), 151.2 (C 7a), 141.0 (C12), 131.3 (C3a/3a'), 130.5 (C5'), 129.0 (C13), 127.3 (C8), 126.9 (C6), 126.4 (C6'), 125.5 (C5'), 125.0 (C7'), 123.4 (C5), 122.2 (C4), 120.9 (C4'), 119.1 (C13'), 118.8 (C11), 117.7 (C7), 111.4 (C9'), 107.2 (C9), 40.0-39.9 (Me2N/Me2'N). 19F{1H} NMR (376.5 MHz, CDCl3, 20º C, δ): 115.4 (m, JPt-oF = 487, o-F), -116.8 (m, JPt-oF = 508, o-F), -164.2 (t, p-F), -165.4 (m, m-F), -165.6 (m, m-F).

**Preparation of [Pt(Me2N-pbt)(C6F5)(p-dpbH)] 2**

4-(diphenylphosphino)benzoic acid (0.040 g, 0.14 mmol) was added to a solution of 1 (0.113 g, 0.14 mmol) in CH2Cl2 (20 mL) and the reaction was kept stirred for 5 h. The solution was then evaporated to small volume and the addition of n-hexane yielded 2 as an orange microcrystalline solid (0.112 g, 93 %). IR (cm⁻¹): ν(C=O) 1695 (s); ν(C-O)
1095 (m); ν(C-F, C6F5) 1060 (m), 958 (s); ν(C6F5)X-sens 789 (m). ESI (+): m/z (%) 922 [M+H]+ (100). Anal. Found (calcd for C40H28F5N2O2PPtS): C, 46.51 (47.02); H, 3.18 (3.06); N, 3.22 (3.04). 1H NMR (400 MHz, CDCl3, 20º C, δ): 7.93 (d, 2H, Ph), 7.86-7.66 (br, 6H, Ph), 7.59 (m, 2H, H8, H4), 7.38 (m, 2H, Ph), 7.30 (m, 4H, Ph), 6.92 (t, 1H, J = 8, H5), 6.84 (d, 1H, J = 8, H7), 6.45 (dd, 1H, J1 = 9, 4JH-H = 3, H9), 6.40 (t, 1H, J = 8, H6), 5.92 (dd, 1H, J = 7, 3JPt-H = 63, H11), 2.80 (s, 6H, Me2N). 13C{1H} NMR (100.6 MHz, CDCl3, 20º C, δ): 170.1 (CO), 152.8 (C10), 150.3 (C7a), 135.1 (d, JC-P = 11, Ph), 134.3 (d, JC-P = 11, Ph), 132.1 (d, JC-P = 45, Ph), 131.0-130.3 (Ph, C3a), 129.9 (s, C13), 129.3 (d, JC-P = 9, Ph), 128.4 (d, JC-P = 11, Ph), 127.5 (C8), 124.9 (C6), 123.4 (C5), 121.8 (C4), 120.9 (C3), 118.2 (C11), 108.5 (C9), 39.9 (Me2N). 19F{1H} NMR (376.5 MHz, CDCl3, 20º C, δ): -116.4 (d, JPt-oF = 498, o-F), -164.3 (m, p-F), -164.5 (m, m-F). 31P{1H} NMR (162.1 MHz, CDCl3, 20º C, δ): 23.7 (s, JP-Pt = 1975).

Preparation of [Pt(Me2N-pbt)(C6F5)(o-dpbH)] 3

2-(diphenylphosphino)benzoic acid (0.060 g, 0.19 mmol) was added to a solution of 1 (0.141 g, 0.16 mmol) in CH2Cl2 (15 mL) and the yellow solution was stirred for 6 h. The yellow solid precipitated was filtered and washed with n-hexane (0.125 g, 83%). IR (cm⁻¹): ν(C=O) 1703 (s), ν(C-O) 1092 (m); ν(C-F, C6F5) 1063 (m), 958 (s); ν(C6F5)X-sens 788 (m). ESI (+): m/z (%) 754 [M-C6F5]+ (26), 922 [M+H]+ (100). Anal. Found (calcd for C40H28F5N2O2PPtS): C, 50.92 (51.12); H, 3.17 (3.06); N, 3.50 (3.04). 1H NMR (400 MHz, CD3COCD3, 20º C, δ): 7.80 (m, 2H, Ph), 7.38 (m, 2H, Ph), 7.01 (t, 1H, J = 8, H5), 6.49 (dd, 1H, J = 9, 4JH-H = 3, H9), 6.41 (t, 1H, J = 8, H6), 5.89 (dd, 1H, J = 7, 3JPt-H = 65, H11), 2.78 (s, 6H, Me2N). 19F{1H} NMR (376.5 MHz, CD3COCD3, 20º C, δ): -112.5 (m, JPt-oF = 511, o-F), -115.3 (m, JPt-oF = 538, o-F), -166.9 (m, m-F), -167.4 (m, p-F). 31P{1H} NMR (162.1 MHz, CD3COCD3, 20º C, δ): 26.9 (s, JPt-Pt = 1956). Not soluble enough to be characterised by 13C{1H} NMR.

Preparation of [Pt(Me2N-pbt)(o-dpb)] 4

A suspension of [Pt(Me2N-pbt)(µ-Cl)]2 (0.08 g, 0.14 mmol) in acetonitrile (40 mL) was treated with 2-(diphenylphosphino)benzoic acid (0.044 g, 0.14 mmol) and Na2CO3 (0.5 g, 4.72 mmol). The suspension dissolves initially to immediately form a yellow solution and, subsequently, a new precipitated was formed. The mixture was stirred for 30 min and then the solvent was evaporated to dryness. The residue was treated with CH2Cl2 (50 mL)
and washed with water (3x20 mL). The organic phase was dried with MgSO₄, filtered through celite and the filtrate evaporated to dryness to give 4 as an orange solid which was filtered and washed with n-hexane (0.09 g, 85 %). IR (cm⁻¹): ν(C=O) 1615 (m); ν(C-O) 1098 (m). ESI (+): m/z (%) 754 [M+H]⁺ (100). Anal. Found (calcd for C₃₄H₂₇N₂O₂PtS): C, 52.61 (53.08); H, 3.77 (3.61); N, 4.27 (3.81). ¹H NMR (400 MHz, CDCl₃, 20° C, δ): 9.36 (d, 1H, J = 8, H⁷), 8.50 (dd, 1H, J = 8, J₆₋₇ = 3, H⁴'), 7.78 (d, 1H, J = 8, H⁵), 7.75-7.68 (m, 4H, Ph), 7.61 (m, 2H, H⁶, H³), 7.55 (m, 2H, Ph), 7.47 (m, 4H, Ph), 7.41-7.32 (m, 3H, H₈, H⁵, H²'), 6.67 (dd, 1H, J = 8, J₈₋₉ = 12, H¹'), 6.35 (d, 1H, J = 8, H⁹), 5.94 (t, 1H, J₆₋₇ = 3, J₈₋₉ = 3, J₃₋₅ = 65, H¹₁), 2.50 (s, 6H, Me₂N). ³¹P{¹H} NMR (162.1 MHz, CDCl₃, 20° C, δ): 8.81 (s, J₉₋₁₀ = 4398 Hz). Not soluble enough to be characterised by ¹³C{¹H} NMR.

Evolution of [Pt(Me₂N-pbt)(C₆F₅)(p-dpb)] 3 in DMSO. 3 evolves slowly in warm DMSO solution (38°C, ~ 6 days) by a relatively easy OH activation and release of HC₆F₅ as confirmed by ¹⁹F{¹H} NMR. Monitoring of the evolution by ³¹P{¹H} NMR spectroscopy indicates that after 38 h, 3 is still the major component, but the signals due to 4 (δ 8.8; J₉₋₁₀ = 4398 Hz) and oxidized phosphine (o-dpbHO, δ 28.8) are visible. After 62 h, the signal of 4 gradually grows, while that of 3 decreases and a new complex [Pt(o-dpb)(C₆F₅)(o-dpbH)] 7, characterized by AB system (δA₂ 11.6, δB 21.1 J₋₋₄₉ = 438 Hz), starts to be formed. 7 is clearly visible upon 6 days. The formation of 4 takes place with concomitant formation of HC₆F₅ as confirmed by ¹⁹F{¹H} NMR.

Preparation of [{Pt(Me₂N-pbt)(C₆F₅)}₂(μ-PR₄P)] 5

The diphosphine ligand O(CH₂CH₂OCOC₆H₄PPh₂)₂ (PR₄P) (0.057 g, 0.084 mmol) was added to a yellow solution of 1 (0.146 g, 0.167 mmol) in CH₂Cl₂ (20 mL) and the mixture stirred for 10 h. Then the solvent was evaporated to dryness and the final yellow oil obtained was treated with EtOH to give 5 a yellow solid which was filtered and washed with n-hexane (0.057 g, 35 %). IR (cm⁻¹): ν(C=O) 1723 (s), ν(C-O-C) 1085 (s); ν(C-F, C₆F₅) 1060 (s), 955 (s); ν(C₆F₅)X-sens 789 (m). ESI (+): m/z (%) 1914 [M+H]⁺ (25), 958 [M+2H]²⁺ (100). Anal. Found (calcd for C₈₄H₆₂F₁₀N₄O₅P₂Pt₂S₂): C, 53.51 (52.72); H, 3.63 (3.27); N, 4.40 (3.93). ¹H NMR (100.6 MHz, CDCl₃, 20° C, δ): 7.87 (d, 2H, Ph), 7.75 (br, 6H, Ph), 7.57 (m, 2H, H⁶, H³), 7.34 (2H, Ph), 7.29 (4H, Ph), 6.90 (t, J = 8, H⁵), 6.84 (d, J = 8, H⁷), 6.43 (d, J = 9, H⁹), 6.37 (t, J = 8, H⁸), 5.92 (d, J₉₋₁₀ = 6, J₈₋₉ = 59, H¹₁), 4.45 (t, 2H, COOCH₂), 3.83 (t, 2H, CH₂O), 2.80 (s, 6H, Me₂N). ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 20° C, δ): 185.0 (d, J₉₋₁₀ = 8, C²),

S10
165.7 (s, COO), 160.1 (d, J_{C,P} = 113, C^{12}), 152.8 (d, J_{C,P} = 7, C^{10}), 150.3 (s, C^{7a}), 139.1 (d, J_{C,P} = 43, Ph), 135.0 (d, J_{C,P} = 10, Ph), 134.1 (d, J_{C,P} = 12, Ph), 132.2 (d, J_{C,P} = 46, Ph), 130.7 (Ph, C^{3a}), 129.9 (s, C^{13}), 128.9 (d, J_{C,P} = 10, Ph), 128.3 (d, J_{C,P} = 10, Ph), 127.6 (d, J_{C,P} = 5, C^8), 124.9 (C^6), 123.4 (C^2), 121.8 (C^4), 121.0 (d, J_{C,P} = 4, C^7), 111.7 (C^{11}), 108.4 (C^9), 69.2 (s, CH_2O), 64.5 (s, COOCH_2), 39.9 (s, Me_2N).

19F{1H} NMR (376.5 MHz, CDCl_3, 20º C, δ): -116.3 (d, J_{Pt-oF} = 503, o-F), -164.6 (m, p-F, m-F).

31P{1H} NMR (162.1 MHz, CDCl_3, 20º C, δ): 23.5 (s, J_{P-Pt} = 1975).

Preparation of [{Pt(Me_2N-pbt)(C_6F_5)}_2(μ-PR_{12}P)]_6

The diphosphi ne ligand O[(CH_2CH_2O)_3COC_6H_4PPh_2]_2 (PR_{12}P) (0.050 g, 0.061 mmol) was added to a solution of 1 (0.106 g, 0.122 mmol) in CH_2Cl_2 (20 mL) and the mixture was stirred at room temperature for 9 h. Then evaporation of the solvent and addition of iPrOH the final yellow oil/residue gives a yellow solid which is washed with n-hexane (0.079 g, 62 %). IR (cm^{-1}): ν(C=O) 1724 (w), ν(C-O-C) 1095 (s); ν(C-F, C_6F_5) 1060 (m), 957 (s); ν(C_6F_5)X-sens 790 (m). ESI (+): m/z (%) 2091 [M+H]^+ (19), 1046 [M+2H]^{2+} (100). Anal. Found (calcd for C_{92}H_{78}F_{10}N_{4}O_{9}P_{2}Pt_{2}S_{2}): C, 50.90 (51.47); H, 3.60 (3.76); N, 3.19 (2.98).

1H NMR (400 MHz, CDCl_3, 20º C, δ): 7.90 (d, 2H, Ph), 7.76 (br, 6H, Ph), 7.57 (m, 2H, H^8,H^4), 7.39 (t, J = 9, 2H, Ph), 7.26 (m, 4H, Ph), 6.91 (t, 1H, J = 8, H^5), 6.85 (d, 1H, J = 9, H^7), 6.43 (dd, 1H, J = 9, ^4J_{H,H} = 2, H^2), 6.39 (t, 1H, J = 8, H^6), 5.92 (dd, 1H, ^4J_{H,H} = 2, ^4J_{P,H} = 7, ^3J_{Pt,H} = 60, H^{11}), 4.44 (m, 2H, COOC_2H_2), 3.79 (m, 2H, COOCH_2CH_2), 3.69-3.58 (m, 8H, OC_2HCH_2O), 2.80 (s, 6H, Me_2N).

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2.- NMR Spectra

a)

b)
Figure S1. a) $^1$H, b) $^{13}$C{$^1$H} and c) $^{19}$F{$^1$H} NMR spectra in CDCl$_3$ of 1.
Figure S2. a) $^1$H, b) $^{13}$C$\{^1$H$\}$, c) $^{19}$F$\{^1$H$\}$ and d) $^{31}$P$\{^1$H$\}$ NMR spectra in CDCl$_3$ of 2.
Figure S3. a) $^1$H, b) $^{19}$F-$^1$H and c) $^{31}$P-$^1$H NMR spectra in CDCl$_3$ of 3.
**Figure S4.** a) $^1$H and b) $^{31}$P–$^1$H NMR spectra in CDCl$_3$ of 4.
Figure S5. $^{19}\text{F}^1\text{H}$ NMR spectra of the evolution of 3 in DMSO-$d_6$ after 6 days at 38°C.

Figure S6. Monitoring of the $^{31}\text{P}^1\text{H}$ NMR spectra of the evolution of 3 in DMSO-$d_6$ at 311 K.
Figure S7. Comparison of the $^{31}$P($^1$H) NMR spectra of 3 and 4 in CDCl$_3$. 

a)
Figure S8. a) $^1$H, b) $^{13}$C{H$^1$}, c) $^{19}$F{1H} and d) $^{31}$P{1H} NMR spectra in CDCl$_3$ of 5 (* oxidized phosphine).
b) 

\begin{center}
\includegraphics[width=\textwidth]{image1}
\end{center}

c) 

\begin{center}
\includegraphics[width=\textwidth]{image2}
\end{center}
**Figure S9.** a) $^1$H, b) $^{13}$C$^{('}{^1}$H), c) $^{19}$F$^{('}{^1}$H) and d) $^{31}$P$^{('}{^1}$H) NMR spectra in CDCl$_3$ of 6 (* oxidized phosphine).
3.- Crystal Structures

Table S1. X-ray crystallographic data for complexes 2·iPrOH·CH₂Cl₂, 4·CHCl₃ and 7·2MeOH.

|                  | 2·iPrOH·CH₂Cl₂ | 4·CHCl₃ | 7·2MeOH |
|------------------|----------------|---------|---------|
| **Empirical formula** | C₄₄H₃₇Cl₂F₅N₂O₃P₄ | C₂₈H₂₃ClN₂O₂P₂ | C₄₆H₃₇F₅O₆P₂Pt |
| **Molecular weight**  | 1065.77        | 873.06  | 1037.78 |
| **T (K)**          | 145(1)         | 140(1)  | 145(1)  |
| **Wavelength (Å)** | 0.71076        | 0.71076 | 0.71073 |
| **Crystal system**  | Monoclinic     | Triclinic| Monoclinic|
| **Space group**     | P₂₁/c          | P₁      | P₂₁/c   |
| **Crystal size (mm)** | 0.315 x 0.310 x 0.300 | 0.333 x 0.257 x 0.244 | 0.260 x 0.170 x 0.150 |
| **a (Å)**          | 14.9213(11)    | 9.2229(7)| 11.4050(11) |
| **b (Å)**          | 17.2893(14)    | 11.6763(9)| 21.859(2) |
| **c (Å)**          | 18.2087(15)    | 16.1952(12)| 17.3913(17) |
| **α (°)**          | 90             | 76.950(2) | 90      |
| **β (°)**          | 113.916(3)     | 75.692(2) | 109.069(3) |
| **γ (°)**          | 90             | 85.711(3)| 90      |
| **V (Å³)**         | 4294.16(6)     | 1646.0(2) | 4097.8(7) |
| **Z**              | 4              | 2       | 4       |
| **Density (calculated)** | 1.649          | 1.762   | 1.682   |
| **Absorption coefficient (mm⁻¹)** | 3.542          | 4.654   | 3.575   |
| **F(000)**         | 2108           | 856     | 2056    |
| **θ range for data collection (°)** | 2.790 to 26.023 | 2.869 to 27.889 | 3.058 to 27.960 |
| **Reflections collected** | 183229         | 103193  | 297311  |
| **Independent reflections** | 8454 [R(int) = 0.0353] | 7833 [R(int) = 0.1132] | 9825 [R(int) = 0.0452] |
| **Data / restraints / parameters** | 8454 / 0 / 536 | 7833 / 0 / 406 | 9825 / 0 / 577 |
| **Goodness-of-fit on F²** | 1.128          | 1.220   | 1.068   |
| **Final R indices [I>2σ(I)]** | R1 = 0.0244, | R1 = 0.0251, | R1 = 0.0163, |
|                  | wR2 = 0.0556   | wR2 = 0.0654 | wR2 = 0.0334 |
| **R indices (all data)** | R1 = 0.0280, | R1 = 0.0254, | R1 = 0.0204, |
|                  | wR2 = 0.0578   | wR2 = 0.0655 | wR2 = 0.0344 |
| **Largest diff. peak and hole** | 1.631 and -1.523 | 1.665 and -1.026 | 0.376 and -0.508 |
Table S2. Selected distances (Å) and angles (˚) for 2·iPrOH·CH$_2$Cl$_2$, 4·CHCl$_3$ and 7·2MeOH

| Distances (Å) | Angles (˚) |
|---------------|------------|
| Pt(1)-N(1)    | 2.144(3)   | N(1)-Pt(1)-P(1) | 101.42(7) |
| Pt(1)-P(1)    | 2.3178(8)  | P(1)-Pt(1)-C(16) | 88.56(9)  |
| Pt(1)-C(1)    | 2.053(3)   | C(1)-Pt(1)-C(16) | 89.78(12) |
| Pt(1)-C(16)   | 2.006(3)   | C(1)-Pt(1)-N(1)  | 80.45(11) |
| O(1)-C(28)    | 1.191(5)   |                   |           |
| O(2)-C(28)    | 1.312(5)   |                   |           |

| Distances (Å) | Angles (˚) |
|---------------|------------|
| Pt(1)-N(1)    | 2.106(2)   | N(1)-Pt(1)-C(1) | 81.28(10) |
| Pt(1)-P(1)    | 2.2054(7)  | C(1)-Pt(1)-P(1) | 99.63(8)  |
| Pt(1)-C(1)    | 2.004(3)   | P(1)-Pt(1)-O(1) | 87.96(6)  |
| Pt(1)-O(1)    | 2.0918(19) | O(1)-Pt(1)-N(1) | 91.63(8)  |
| O(1)-C(22)    | 1.286(3)   |                   |           |
| O(2)-C(22)    | 1.224(3)   |                   |           |

| Distances (Å) | Angles (˚) |
|---------------|------------|
| Pt(1)-C(1)    | 2.0057(16) | C(1)-Pt(1)-P(1) | 92.75(5)  |
| Pt(1)-P(1)    | 2.2534(5)  | C(1)-Pt(1)-P(2) | 91.96(5)  |
| Pt(1)-P(2)    | 2.3479(4)  | O(1)-Pt(1)-P(1) | 86.31(4)  |
| Pt(1)-O(1)    | 2.0784(12) | O(1)-Pt(1)-P(2) | 90.53(4)  |
| O(1)-C(13)    | 1.282(2)   |                   |           |
| O(2)-C(13)    | 1.238(2)   |                   |           |
| O(3)-C(32)    | 1.211(2)   |                   |           |
| O(4)-C(32)    | 1.325(2)   |                   |           |
Figure S10. a) Crystal packing of the unit cell of 2 showing weak π–π interactions (3.47 Å) between the cyclometalated ligands, b) hydrogen bonds between two molecules through the isopropanol crystallization molecules.

Figure S11. Crystal packing of 4 showing π–π interactions (3.50-3.54 Å) between the cyclometalated ligands of two molecules and weaker ones (3.57 Å) between pairs of molecules.
Figure S12. Supramolecular interactions in 7 through hydrogen bonds between two molecules through four methanol crystallization molecules.
4.- Photophysical Properties and Theoretical Calculations

| Compound  | λ_{abs}/nm (ε × 10^{-3} / M^{-1} cm^{-1}) |
|-----------|------------------------------------------|
| Me2N-pbtH | 233 (25.0), 264sh (8.8), 359 (46.6)      |
| 1         | 319 (19.2), 366sh (40.0), 395 (43.6), 436sh (28.4) |
| 2         | 319 (16.3), 339sh (12.5), 430 (31.7)     |
| 3         | 320 (13.6), 351 (11.7), 425 (25.4)       |
| 4         | 328 (18.1), 360 (13.8), 432 (30.3)       |
| 5         | 320 (26.4), 339 (22.2), 430 (53.9)       |
| 6         | 320 (23.9), 338sh (18.4), 430 (59.1)     |

Figure S13. Calculated stick absorption spectra of 1, 2 and 4 in CH$_2$Cl$_2$ compared with the experimental spectra.
Table S4. DFT optimized geometries for ground state and triplet state (in CH₂Cl₂) of species 1, 2 and 4.

|       | 1          | 2          | 4          |
|-------|------------|------------|------------|
|       | S₀  | T₁      | S₀  | T₁      | S₀  | T₁      |
| Pt(1)-N(1) | 2.183 | 2.141   | Pt(1)-N(1) | 2.247 | 2.181   | Pt(1)-N(1) | 2.146 | 2.112 |
| Pt(1)-N(2) | 2.256 | 2.259   | Pt(1)-P(1) | 2.450 | 2.454   | Pt(1)-P(1) | 2.273 | 2.280 |
| Pt(1)-C(1) | 2.014 | 2.008   | Pt(1)-C(1) | 2.057 | 2.050   | Pt(1)-C(1) | 2.023 | 2.013 |
| Pt(1)-C(16) | 2.028 | 2.036  | Pt(1)-C(16) | 2.016 | 2.027   | Pt(1)-O(1) | 2.155 | 2.161 |
| N(1)-Pt(1)-N(2) | 97.95 | 97.64   | N(1)-Pt(1)-P(1) | 102.50 | 101.83 | N(1)-Pt(1)-O(1) | 94.51 | 94.50 |
| N(2)-Pt(1)-C(16) | 88.89 | 88.44  | Pt(1)-Pt(1)-C(16) | 88.19 | 88.81 | Pt(1)-Pt(1)-O(1) | 81.98 | 81.13 |
| C(1)-Pt(1)-C(16) | 93.30 | 92.95  | C(1)-Pt(1)-C(16) | 90.17 | 89.72 | C(1)-Pt(1)-P(1) | 104.19 | 104.03 |
| C(1)-Pt(1)-N(1) | 80.17 | 81.28  | C(1)-Pt(1)-N(1) | 79.15 | 79.81 | C(1)-Pt(1)-N(1) | 80.20 | 81.03 |

Table S5. Composition (%) of Frontier MOs in terms of ligands and metals in the ground state for 1, 2 and 4 in CH₂Cl₂.

|       | MO       | eV   | bt | Ph | NMe₂ | bt’ | Ph’ | NMe₂’ | CyF₅ | Pt |
|-------|----------|------|----|----|------|-----|-----|-------|------|----|
| 1     | LUMO+5   | -0.09| 14 | 17 | 0    | 5   | 30  | 0     | 23   | 10  |
|       | LUMO+4   | -0.28| 84 | 1  | 0    | 9   | 4   | 0     | 1    | 1   |
|       | LUMO+3   | -0.39| 11 | 1  | 0    | 77  | 2   | 0     | 4    | 6   |
|       | LUMO+2   | -0.44| 6  | 9  | 0    | 24  | 33  | 0     | 13   | 16  |
|       | LUMO+1   | -1.58| 58 | 27 | 6    | 3   | 2   | 0     | 0    | 4   |
|       | LUMO     | -1.65| 3  | 1  | 0    | 65  | 24  | 5     | 0    | 1   |
|       | HOMO     | -5.08| 22 | 44 | 31   | 0   | 0   | 0     | 0    | 3   |
|       | HOMO-1   | -5.33| 0  | 1  | 0    | 16  | 44  | 37    | 0    | 2   |
|       | HOMO-2   | -5.90| 1  | 28 | 3    | 2   | 3   | 2     | 2    | 60  |
|       | HOMO-3   | -5.91| 1  | 20 | 3    | 1   | 1   | 0     | 2    | 70  |
|       | HOMO-4   | -6.06| 4  | 2  | 0    | 5   | 0   | 1     | 58   | 31  |
|       | HOMO-5   | -6.26| 40 | 3  | 1    | 9   | 0   | 0     | 5    | 41  |

|       | MO       | eV   | bt | Ph | NMe₂ | PCOOH | CyF₅ | Pt |
|-------|----------|------|----|----|------|-------|------|----|
| 2     | LUMO+5   | -0.46| 6  | 9  | 0    | 70    | 3    | 12 |
|       | LUMO+4   | -0.68| 4  | 2  | 0    | 89    | 3    | 2  |
|       | LUMO+3   | -0.73| 2  | 4  | 0    | 87    | 3    | 4  |
|       | LUMO+2   | -1.11| 2  | 0  | 0    | 97    | 0    | 0  |
|       | LUMO+1   | -1.64| 56 | 26 | 6    | 7     | 0    | 5  |
|       | LUMO     | -1.71| 3  | 3  | 0    | 91    | 1    | 3  |
|       | HOMO     | -5.11| 21 | 44 | 33   | 0     | 0    | 1  |
|       | HOMO-1   | -6.06| 1  | 7  | 0    | 2     | 8    | 82 |
|       | HOMO-2   | -6.10| 7  | 46 | 6    | 2     | 2    | 37 |
|       | HOMO-3   | -6.17| 2  | 4  | 0    | 3     | 63   | 28 |
|       | HOMO-4   | -6.40| 55 | 4  | 0    | 3     | 8    | 29 |
|       | HOMO-5   | -6.45| 0  | 0  | 0    | 2     | 96   | 1  |
Table S6. Selected vertical excitation energies singlets (S0) and first triplets computed by TDDFT/SCRF (CH2Cl2) with the orbitals involved for 1, 2 and 4.

| State | λ/nm  | f     | Transition (% Contribution)                                      |
|-------|-------|-------|-----------------------------------------------------------------|
| 1 T1  | 544.9 | -     | HOMO→L+1 (91%)                                                  |
| T2    | 498.5 | -     | H-1→LUMO (89%)                                                 |
| T3    | 415.0 | -     | HOMO→LUMO (94%)                                                |
| S1    | 415.0 | 0.0257| HOMO→LUMO (99%)                                                |
| S2    | 402.1 | 0.5715| HOMO→L+1 (91%)                                                 |
| S3    | 380.7 | 0.2994| H-1→LUMO (61%), H-1→L+1 (33%)                                  |
| S4    | 377.6 | 0.4267| H-1→LUMO (33%), H-1→L+1 (63%)                                  |
| S5    | 354.8 | 0.0733| H-3→LUMO (35%), H-3→L+1 (13%), H-2→LUMO (31%), H-2→L+1 (15%)    |
| S6    | 351.2 | 0.0162| H-3→LUMO (12%), H-3→L+1 (46%), H-2→LUMO (16%), H-2→L+1 (22%)    |
| S7    | 344.2 | 0.1157| H-3→LUMO (17%), H-3→L+1 (24%), H-2→L+1 (42%)                   |
| S8    | 339.2 | 0.0514| H-3→LUMO (32%), H-3→L+1 (11%), H-2→LUMO (39%), H-2→L+1 (13%)    |
| S9    | 327.7 | 0.0269| H-4→LUMO (90%)                                                 |
| S10   | 322.8 | 0.0198| H-4→L+1 (90%)                                                  |
| S11   | 310.9 | 0.0195| H-5→LUMO (92%)                                                 |
| S12   | 308.5 | 0.0798| H-5→L+1 (82%)                                                  |
| 2 T1  | 548.5 | -     | HOMO→L+1 (90%)                                                 |
| T2    | 406.7 | -     | HOMO→LUMO (93%)                                                |
| T3    | 375.7 | -     | H-4→L+1 (13%), H-2→L+1 (54%)                                   |
| S1    | 407.7 | 0.1531| HOMO→LUMO (91%)                                                |
| S2    | 402.3 | 0.4847| HOMO→L+1 (88%)                                                 |
| S3    | 345.5 | 0.0022| HOMO→L+2 (92%)                                                 |
| S4    | 344.9 | 0.0045| H-1→LUMO (10%), H-1→L+1 (79%)                                  |
| S5    | 333.8 | 0.1154| H-2→L+1 (77%)                                                  |
| S6    | 329.4 | 0.0003| H-1→LUMO (81%), H-1→L+1 (11%)                                  |
| S7    | 323.8 | 0.0010| H-3→LUMO (88%)                                                 |
| S8   | 317.5 | 0.0284 | H-3→L+1 (87%) |
|------|-------|--------|----------------|
| S9   | 317.3 | 0.0078 | H-2→LUMO (34%), HOMO→L+3 (44%) |
| S10  | 316.8 | 0.0123 | H-2→LUMO (42%), HOMO→L+3 (41%) |
| S11  | 307.7 | 0.0421 | HOMO→L+4 (85%) |
| S12  | 304.2 | 0.0517 | H-4→L+1 (56%), HOMO→L+5 (10%), HOMO→L+6 (12%) |

| T1   | 550.3 | -      | HOMO→LUMO (93%) |
| T2   | 390.9 | -      | HOMO→L+1 (60%), H-1→LUMO (8%), H-1→L+1 (9%) |
| T3   | 384.0 | -      | H-1→LUMO (71%) |
| S1   | 410.2 | 0.4939 | HOMO→LUMO (92%) |
| S2   | 377.4 | 0.0627 | HOMO→L+1 (86%) |
| S3   | 351.3 | 0.0434 | H-1→LUMO (49%), HOMO→L+2 (42%) |
| S4   | 347.2 | 0.1389 | H-1→LUMO (39%), HOMO→L+2 (49%) |
| S5   | 332.8 | 0.0177 | H-2→LUMO (27%), H-1→L+1 (37%) |
| S6   | 330.2 | 0.0029 | H-2→LUMO (21%), HOMO→L+3 (72%) |
| S7   | 327.4 | 0.0130 | H-2→LUMO (35%), H-1→L+1 (33%), HOMO→L+3 (16%) |
| S8   | 317.1 | 0.0108 | H-2→L+1 (58%), H-3→L+1 (8%), H-2→L+2 (9%) |
| S9   | 311.6 | 0.0104 | HOMO→L+4 (92%) |
| S10  | 305.2 | 0.0254 | H-4→L+1 (13%), H-3→LUMO (53%) |
| S11  | 301.2 | 0.0500 | H-4→LUMO (11%), H-4→L+1 (14%), H-3→LUMO (22%), H-1→L+2 (22%) |
| S12  | 297.0 | 0.0365 | HOMO→L+5 (69%) |

**Figure S14.** Selected frontier Molecular Orbitals for 1 in the ground state.
Figure S15. Selected frontier Molecular Orbitals for 2 in the ground state.

Figure S16. Selected frontier Molecular Orbitals for 4 in the ground state
To further explain the photophysical properties of these derivatives, theoretical calculations by DFT/TD-DFT were carried out for complexes 1, 2, and 4. The NMe₂ group shows a planar conformation, which agrees with the X-ray data obtained for 2 and the photophysical properties shown by the derivatives. The compositions of the molecular orbitals from atomic orbital contributions are given in Table S5, while the properties of selected excited states are collected in Table S6. In 1, the HOMO is mainly located on the Me₂N-pbt cyclometalated ligand (bt 22%, Ph 44%, NMe₂ 31%), whereas the HOMO-1 is located in the Me₂N-pbtH pendant ligand (bt’ 16%, Ph’ 44%, NMe₂ 37%). The LUMO is mainly centered on the Me₂N-pbtH pendant ligand (bt’ 65%, Ph’ 24%, NMe₂ 5%), whereas the LUMO+1 in the cyclometalated ligand (bt 58%, Ph 27%, NMe₂ 6%).

In 2, the HOMO is delocalized over the Me₂N-pbt fragment (bt 21%, Ph 44%, NMe₂ 33%), whereas the LUMO is mainly centered on the phosphine ligand (91%) and the LUMO+1 on the Me₂N-pbt cyclometalated ligand (bt 56%, Ph 26%, NMe₂ 6%) and the phosphine auxiliary ligand (7%). For 4, the HOMO is delocalized over the Me₂N-pbt unit (bt 22%, Ph 41%, NMe₂ 31%), whereas the HOMO-1 is centered on the cyclometalated group (Ph 40%, NMe₂ 6%), the P^O chelating ligand (11%) and the Pt center (41%). The LUMO is mainly centered on the Me₂N-pbt ligand (bt 54%, Ph 27%, NMe₂ 6%) and the P^O ligand (8%), the L+1 is centered on the P^O ligand (79%) and in a lesser extension in the pbt group (12%) and Pt (9%) and L+2 similar to L+1 [P^O (88%), pbt group (6%), Pt (6%)].

**Table S7.** Calculated emission energies (nm) from the T₁ state and experimental data measured in CH₂Cl₂.

|       | 1   | 2   | 4   |
|-------|-----|-----|-----|
| E of emission (Calc.) | 616 | 624 | 623 |
| E of emission (Exp.)  | 562 | 568 | 564 |
Figure S17. Plots and composition (%) of the frontier MOs of the first triplet state for 1, 2 and 4 in CH₂Cl₂.
Figure S18. Emission spectra of 1-6 in CH$_2$Cl$_2$ (1x10^{-4} M) at 77 K ($\lambda_{exc}$ 420 nm).

Figure S19. Emission band of the singlet oxygen from a freshly solution of 2 in a) CH$_2$Cl$_2$ (10^{-2} M), b) DMSO.
Figure S20. Changes in the absorbance measurements at 410 nm of the $^1$O$_2$ scavenger DPBF in acetonitrile solution in the presence of a) 4, and b) the reference [Ru(bpy)$_3$]Cl$_2$ ($\lambda_{\text{irradiation}} = 460$ nm).
5.- Biological Studies

*Stability in DMSO-cellular medium*

**Figure S21.** UV-vis absorption spectra of a) 2, and b) 6 (5 x 10^{-5} M) recorded in DMSO (<1%)-cellular medium after been kept at room temperature since 0 h to 24 h (intervals in legends).
**Figure S22.** Dose-response curves for determination of the IC₅₀ cytotoxicity values of all compounds tested. **A**) IC₅₀ citotoxicity values of Me₂N-pbtH, 1 and 5, could not be determined in A549 cell line and they were considered as non-toxic compounds. **B**) IC₅₀ values of 2, 3 and 6 in A549 and HeLa tumor cell lines as well as in 184B5 non-tumor cells. The IC₅₀ values correspond to the dose required to inhibit 50% cellular growth after cellular exposure to compounds for 72 h.
**Lipophilicity Determinations**

Figure S23. RP-UPLC chromatograms with UV detection at 320 nm of ~10 μM 1-6 solutions in mobile phase, indicating the retention time for each. An Acquity UPLC BEH C18 1.7 μm particle size analytical column 100 mm × 2.1 mm (Waters) was used. The mobile phases used were A = H2O with 0.1% HCOOH and B = acetonitrile with 0.1% HCOOH. The percentage of organic modifier (B) was changed linearly as follows: 0 min, 50%; 9.5 min, 99%; 11.5 min, 99%; 12 min, 20%; 12.5 min, 20%. ESI(+) Mass Spectra for UPLC fractions are shown for all complexes (m/z 616 [M-Hpbt]+, 754 [M+H]+, 922 [M+H]+, 922 [M+H]+, 2090 [M+H]+, 1913 [M+H]+).

**Interaction with DNA by Gel Electrophoresis**

Figure S24. Electrophoresis mobility shift assay for cisplatin and compounds 1, 2 and 6. CisPt, cisplatin; MM, λHindIII DNA molecular marker; Numbers refer to complex/plasmid DNA (pBR322); base pairs (bp) increasing ratios; OC, open circular (relaxed) plasmid DNA form; CCC, covalently closed circular (supercoiled) plasmid DNA form (as described in Ref. [14]).
Cell colocalization in lung fibroblasts (LMEF)

Figure S25. Cell colocalization in lung fibroblasts (LMEF) of derivatives a) 4 and b) 6, at a concentration of 10 μM with the Lysotracker (lysosomes, red) and MitoTracker (mitochondria, magenta) markers at exposure times with compounds of 24 h.