Electronic Supplementary Information for

Towards the elaboration of new gold-based optical theranostics

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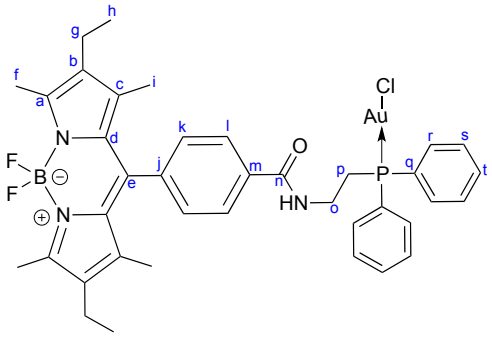
GENERAL INFORMATION

All reactions were carried out under an atmosphere of purified argon using schlenk technics. All solvents used were analytical grade and when specified taken from sps machine or dried and distilled under argon atmosphere. BODIPY–acid **A** derivative was synthesized as reported by Tomasulo *et al.*. The precursor [AuCl(tht)] has been synthesized according to literature procedure (Uson R. *et al*, Inorg Synth. 1989, 26, 85-91). All other reagents were commercially available and used as received. The analyses were performed at the "Plateforme d'Analyses Chimiques et de Synthèse Moléculaire de l'Université de Bourgogne". The identity and purity (≥95%) of the complexes were unambiguously established using multinuclear NMR spectroscopy, high-resolution mass spectrometry and elemental analysis. ^{1}H (300.13, 500.13 or 600.23 MHz), ^{13}C (125.77 MHz), ^{19}F (470.55 MHz) and ^{31}P (121.50, 202.45 or 242.90 MHz) NMR spectra were recorded on Bruker 300 Avance III, Bruker 500 Avance III, or Bruker 600 Avance II spectrometers. Chemical shifts are quoted in parts per million (δ) relative to tetramethylsilane, TMS (^{1}H and ^{13}C), using the residual protonated solvent (^{1}H) or the deuterated solvent (^{13}C) as an internal standard. Alternatively, 85% H_3PO_4 (^{31}P) and $CFCl_3$ (^{19}F) were used as external standards. The coupling constants are reported in Hertz. The exact mass of the complexes was obtained on a Thermo LTQ Orbitrap XL ESI-MS. Infrared spectra were recorded on a Bruker Vertex 70v FT-IR spectrophotometer (ATR Diamant). The elemental analyses were performed using a Thermo Electron Flash EA 1112 Series CHNS/O elemental analyser instrument.

CHARACTERIZATION AND NMR SPECTRA

BODI-Au-1



^{1}H NMR (500.13 MHz, DMSO-d$_6$): δ (ppm) 0.94 (t, 6H$_h$, ^{3}J = 7.6 Hz), 1.24 (s, 6H$_i$), 2.29 (q, 4H$_g$, ^{3}J = 7.6 Hz), 2.44 (s, 6H$_f$), 3.12 (dt, 2H$_p$, ^{2}J = 11.6 Hz, ^{3}J = 7.1 Hz), 3.60 (m, 2H$_o$), 7.43 (d, 2H$_k$, ^{3}J = 8.2 Hz), 7.56 (m, 6H, 4H$_s$ & 2H$_t$), 7.81 (m, 4H$_r$), 7.92 (d, 2H$_l$, ^{3}J = 8.4 Hz), 8.89 (t, NH, ^{3}J = 5.5 Hz). **^{13}C{1H} NMR (125.77 MHz, DMSO-d$_6$):** δ (ppm) 11.5 (s, 2C$_i$), 12.2 (s, 2C$_f$), 14.5 (s, 2C$_h$), 16.4 (s, 2C$_g$), 26.4 (d, C$_p$, $^{1}J_{C–P}$ = 38.7 Hz), 36.0 (d, C$_o$, $^{2}J_{C–P}$ = 5.8 Hz), 128.0 (s, 2C$_k$ & 2C$_l$), 129.1 (s, C$_d$), 129.3 (d, 4C$_s$, $^{3}J_{C–P}$ = 11.7 Hz), 129.6 (d, 2C$_q$, $^{1}J_{C–P}$ = 11.4 Hz), 132.0 (s, 2C$_t$), 132.7 (s, 2C$_b$), 133.1 (d, 4C$_r$, $^{2}J_{C–P}$ = 13.1 Hz), 134.2 (s, C$_e$), 137.6 (s, C$_m$), 138.0 (s, 2C$_c$), 139.6 (s, C$_j$), 153.4 (s, 2C$_a$), 165.5 (s, C$_n$). **^{19}F{1H} NMR (470.55 MHz, DMSO-d$_6$):** δ (ppm) -143.0 (q, $^{1}J_{F–B}$ = 31.8 Hz). **^{31}P{1H} NMR (202.45 MHz, DMSO-d$_6$):** δ (ppm) 25.7 (s, P-Au-Cl). **HR-MS (ESI):** m/z calcd for $C_{38}H_{41}AuBClF_2N_3OP + Na^+$: 890.23012 [M+Na]$^+$. Found: 890.23383. **IR:** υ (cm^{-1}) 319, 479, 533, 691, 1538, 1654, 3335. **Anal. Calcd** for $C_{38}H_{41}AuBClF_2N_3OP + H_2O$: C, 51.52, H, 4.89, N, 4.74%. Found: C, 51.54, H, 4.69, N, 4.91%.

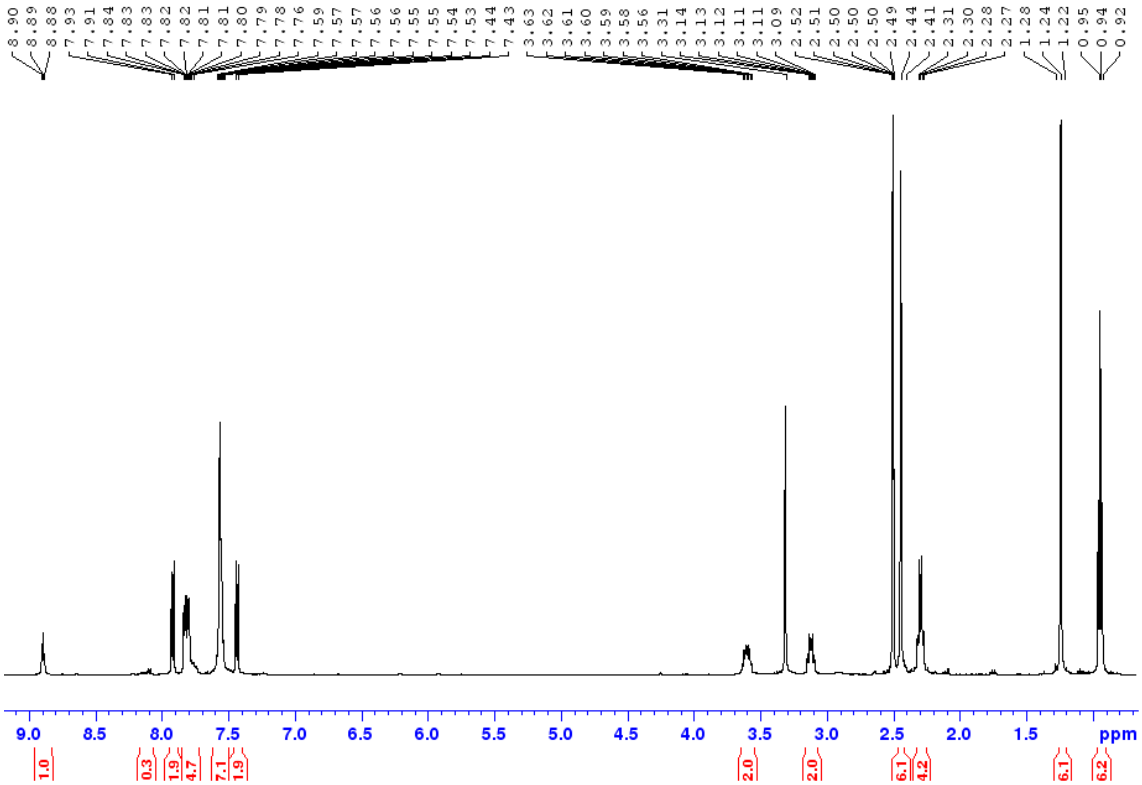


Figure S1: ^{1}H NMR spectrum of BODI-Au-1 in DMSO-d_6

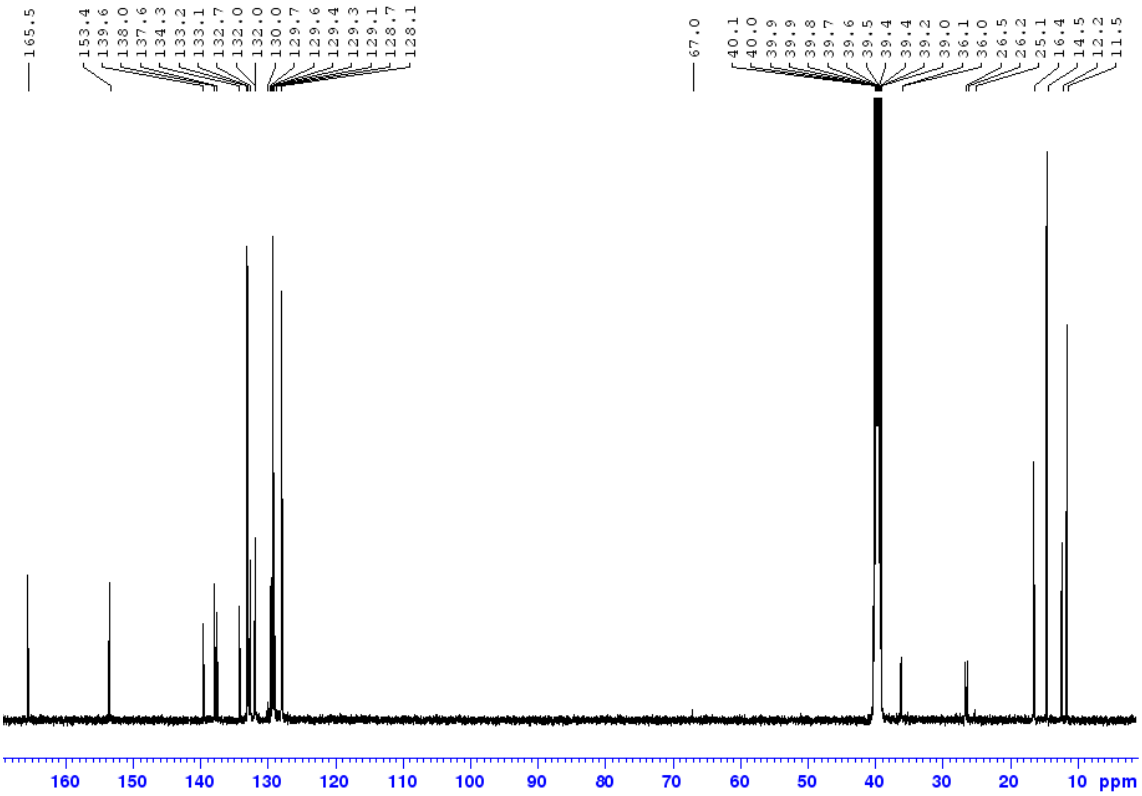
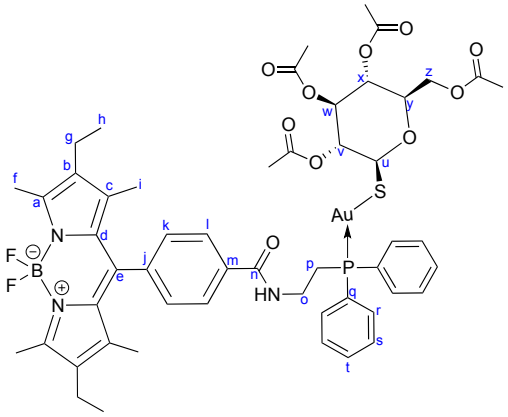


Figure S2: ^{13}C NMR spectrum of BODI-Au-1 in DMSO-d_6

BODI-Au-2



^{1}H NMR (600.23 MHz, DMSO-d$_6$): δ (ppm) 0.94 (t, 6H$_h$, ^{3}J = 7.6 Hz), 1.23 (s, 6H$_i$), 1.84, 1.90, 1.97, 1.98 (s, 12H, 4C**H**$_3$CO), 2.29 (q, 4H$_g$, ^{3}J = 7.5 Hz), 2.44 (s, 6H$_f$), 3.08 (m, 2H$_p$), 3.60 (m, 2H$_o$), 4.00 (m, 1H$_z$ & H$_y$), 4.09 (dd, 1H$_z$, ^{2}J = 12.9 Hz & ^{3}J = 5.7 Hz), 4.88 (t, H$_v$, $^{3}J_{a\text{-}a}$ = 9.3 Hz), 4.93 (t, H$_x$, $^{3}J_{a\text{-}a}$ = 9.7 Hz), 5.18 (t, H$_w$, $^{3}J_{a\text{-}a}$ = 9.5 Hz), 5.32 (d, H$_u$, $^{3}J_{a\text{-}a}$ = 9.4 Hz), 7.44 (d, 2H$_k$, ^{3}J = 8.2 Hz), 7.56 (m, 6H, 4H$_s$ & 2H$_t$), 7.89 (m, 4H$_r$ & 2H$_l$), 8.86 (t, NH, ^{3}J = 5.5 Hz). **^{13}C{1H} NMR (125.77 MHz, DMSO-d$_6$):** δ (ppm) 11.5 (s, 2C$_i$), 12.3 (s, 2C$_f$), 14.5 (s, 2C$_h$), 16.4 (s, 2C$_g$), 20.4 to 20.8 (s, 4**C**H$_3$CO), 26.5 (d, C$_p$, $^{1}J_{C\text{–}P}$ = 34.1 Hz), 36.1 (d, C$_o$, $^{2}J_{C\text{–}P}$ = 7.7 Hz), 62.5 (s, C$_z$), 68.6 (s, C$_x$), 73.3 (s, C$_w$), 74.3 (s, C$_y$), 77.3 (s, C$_v$), 81.7 (s, C$_u$), 128.1 (pseudo-d, 2C$_k$ & 2C$_l$), 129.3 (d, 4C$_s$, $^{3}J_{C\text{–}P}$ = 10.9 Hz), 129.7 (s, 2C$_d$), 130.2 (d, 1C$_q$, $^{1}J_{C\text{–}P}$ = 35.0 Hz), 130.6 (d, 1C$_q$, $^{1}J_{C\text{–}P}$ = 32.2 Hz), 131.8 (s, 2C$_t$), 132.8 (s, 2C$_b$), 133.3 (t, 4C$_r$, $^{2}J_{C\text{–}P}$ = 12.2 Hz), 134.4 (s, C$_e$), 137.6 (s, C$_m$), 138.0 (s, 2C$_c$), 139.6 (s, C$_j$), 153.5 (s, 2C$_a$), 165.5 (s, C$_n$), 169.1, 169.4, 169.6, 170.0 (s, 4**C**H$_3$**C**O). **^{19}F{1H} NMR (470.55 MHz, DMSO-d$_6$):** δ (ppm) -143.0 (q, $^{1}J_{F\text{–}B}$ = 34.7 Hz). **^{31}P{1H} NMR (202.45 MHz, DMSO-d$_6$):** δ (ppm) 30.8 (s, P-Au-S). **HR-MS (ESI):** m/z calcd for $C_{52}H_{60}AuBF_2N_3O_{10}PS$ + Na^+: 1218.33647 $[M+Na]^+$. Found: 1218.33910. **IR:** υ (cm^{-1}) 311, 373, 481, 532, 599, 1538, 1654, 3335. **Anal. Calcd** for $C_{52}H_{60}AuBF_2N_3O_{10}PS$ + H_2O: C, 51.45, H, 5.15, N, 3.46, S, 2.64%. Found: C, 51.30, H, 5.82, N, 3.51, S, 2.16%.

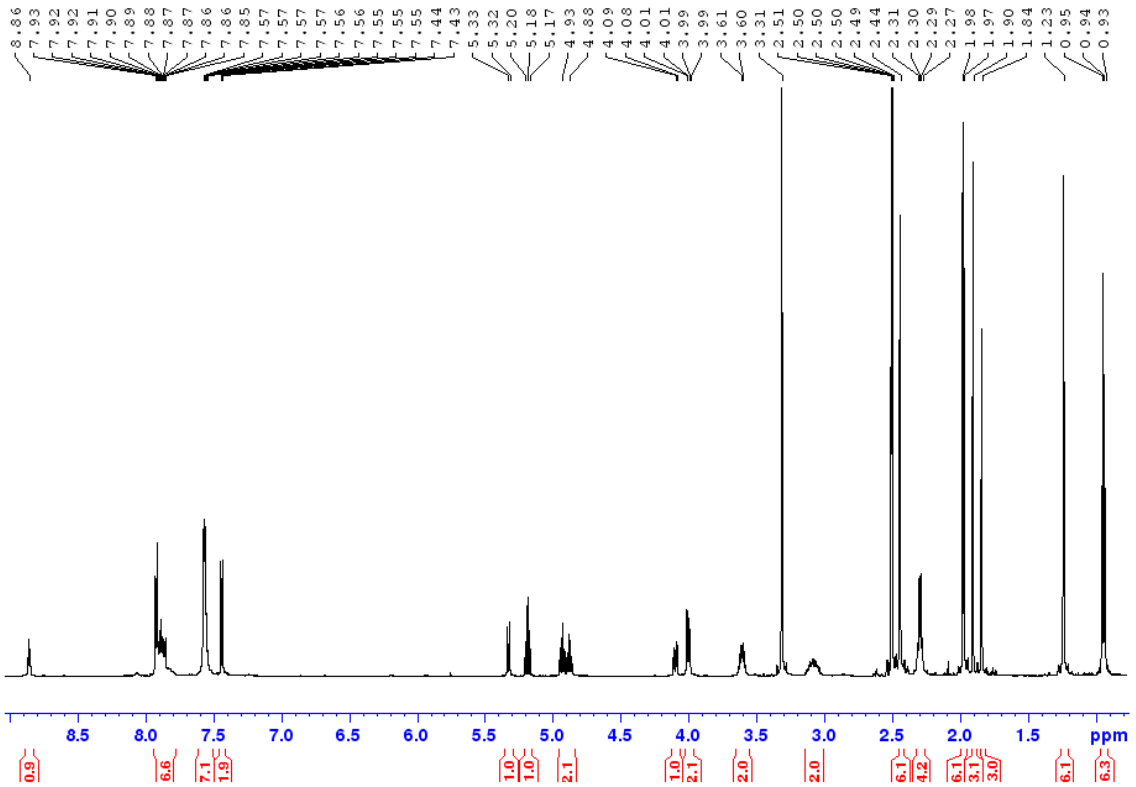


Figure S3: ^{1}H NMR spectrum of BODI-Au-2 in DMSO-d_6

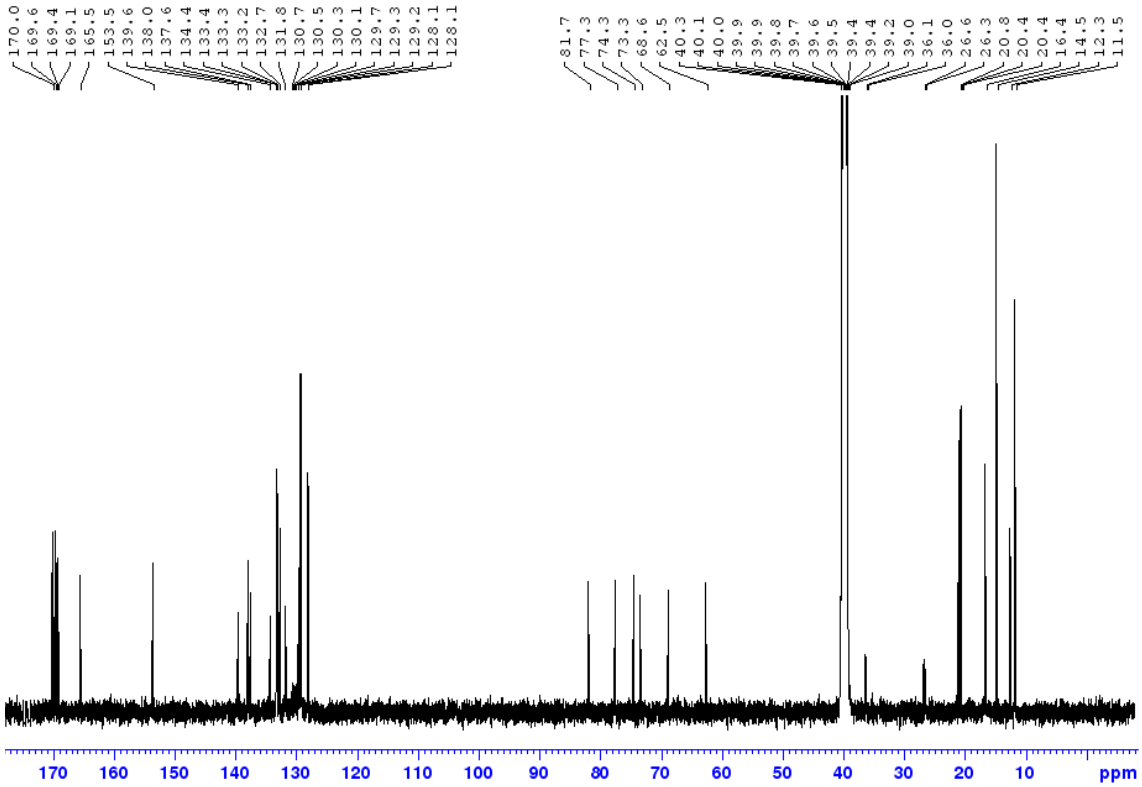
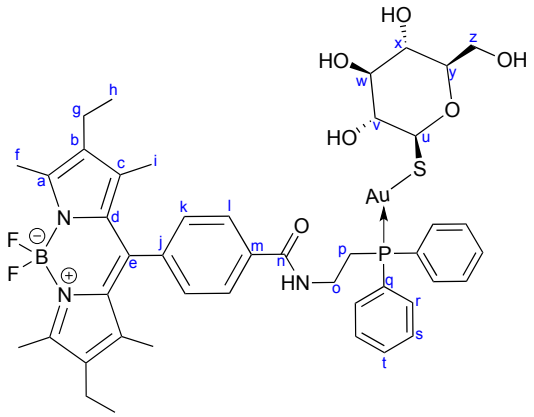


Figure S4: ^{13}C NMR spectrum of BODI-Au-2 in DMSO-d_6

BODI-Au-3



^{1}H NMR (600.23 MHz, DMSO-d$_6$): δ (ppm) 0.94 (t, 6H$_h$, ^{3}J = 7.6 Hz), 1.24 (s, 6H$_i$), 2.29 (q, 4H$_g$, ^{3}J = 7.4 Hz), 2.44 (s, 6H$_f$), 3.03 (m, 3H, 2H$_p$ & H$_y$), 3.13 (m, 3H, H$_v$, H$_w$ & H$_x$), 3.43 (m, 1H$_z$), 3.60 (m, 2H$_o$), 3.70 (m, 1H$_z$), 4.49 (pseudo-t, 2H, OH), 4.74 (d, H$_u$, $^{3}J_{a\text{-}a}$ = 9.0 Hz), 4.85 (pseudo-dd, 2H, OH), 7.45 (d, 2H$_k$, ^{3}J = 8.2 Hz), 7.54 (m, 6H, 4H$_s$ & 2H$_t$), 7.87 (m, 4H$_r$), 7.94 (d, 2H$_l$, ^{3}J = 8.1 Hz), 8.87 (t, NH, ^{3}J = 5.5 Hz). **^{13}C{1H} NMR (125.77 MHz, DMSO-d$_6$):** δ (ppm) 11.5 (s, 2C$_i$), 12.3 (s, 2C$_f$), 14.5 (s, 2C$_h$), 16.4 (s, 2C$_g$), 26.7 (d, C$_p$, $^{1}J_{C\text{–}P}$ = 34.1 Hz), 36.2 (d, C$_o$, $^{2}J_{C\text{–}P}$ = 9.1 Hz), 61.5 (s, C$_z$), 70.6 (s, C$_w$), 77.6 (s, C$_x$), 80.7 (s, C$_y$), 81.2 (s, C$_v$), 85.4 (s, C$_u$), 128.2 (pseudo-d, 2C$_k$ & 2C$_l$), 129.3 (d, 4C$_s$, $^{3}J_{C\text{–}P}$ = 11.4 Hz), 129.7 (s, 2C$_d$), 130.3 (d, 1C$_q$, $^{1}J_{C\text{–}P}$ = 15.0 Hz), 130.8 (d, 1C$_q$, $^{1}J_{C\text{–}P}$ = 15.0 Hz), 131.7 (s, 2C$_t$), 132.8 (s, 2C$_b$), 133.3 (d, 4C$_r$, $^{2}J_{C\text{–}P}$ = 13.2 Hz), 134.4 (s, C$_e$), 137.6 (s, C$_m$), 138.1 (s, 2C$_c$), 139.6 (s, C$_j$), 153.5 (s, 2C$_a$), 165.6 (s, C$_n$). **^{19}F{1H} NMR (470.55 MHz, DMSO-d$_6$):** δ (ppm) -143.0 (q, $^{1}J_{F\text{–}B}$ = 31.8 Hz). **^{31}P{1H} NMR (202.45 MHz, DMSO-d$_6$):** δ (ppm) 30.2 (s, P-Au-S). **HR-MS (ESI):** m/z calcd for $C_{44}H_{52}AuBF_2N_3O_6PS + Na^+$: 1050.24909 [M+Na]$^+$. Found: 1050.29201. **IR:** υ (cm^{-1}) 307, 478, 531, 1538, 1654, 3335.

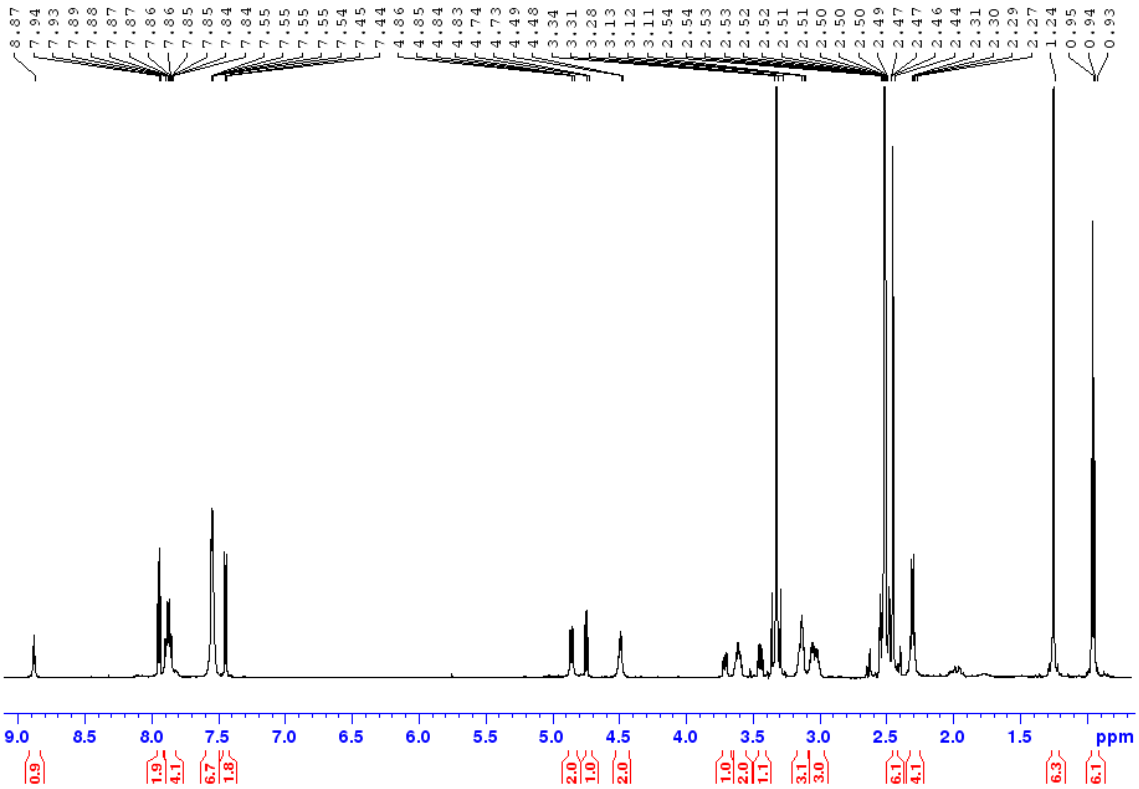


Figure S5: ^{1}H NMR spectrum of BODI-Au-3 in DMSO-d_6

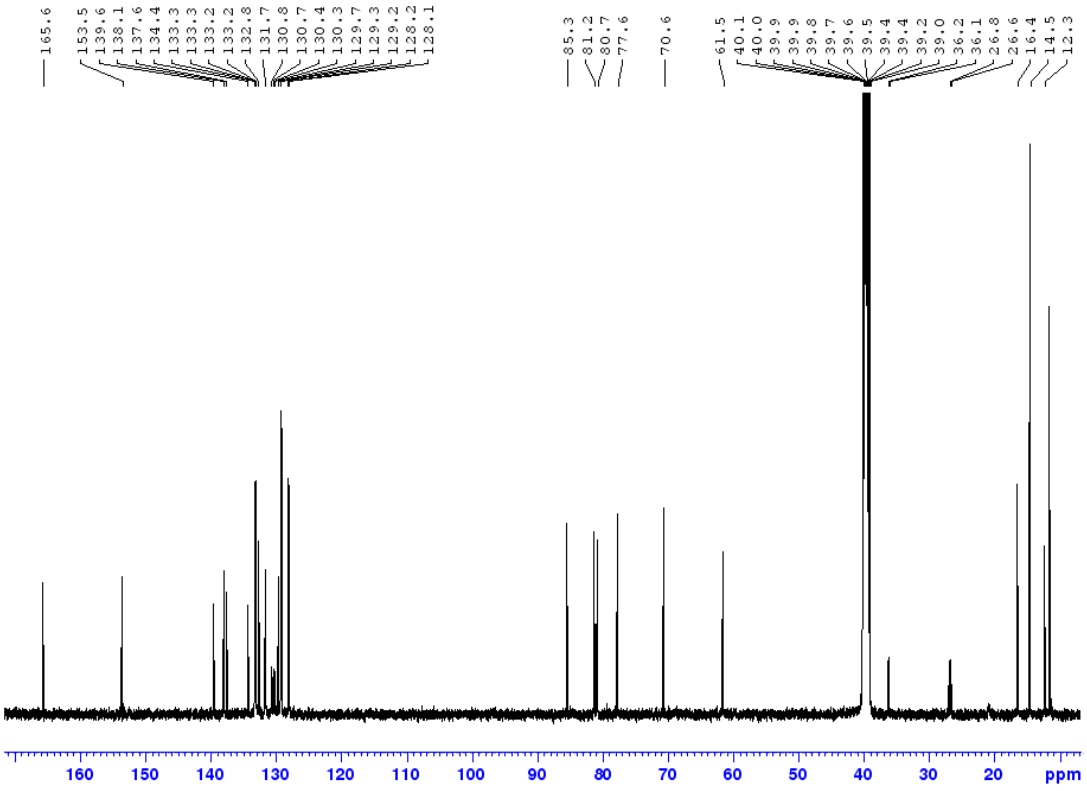
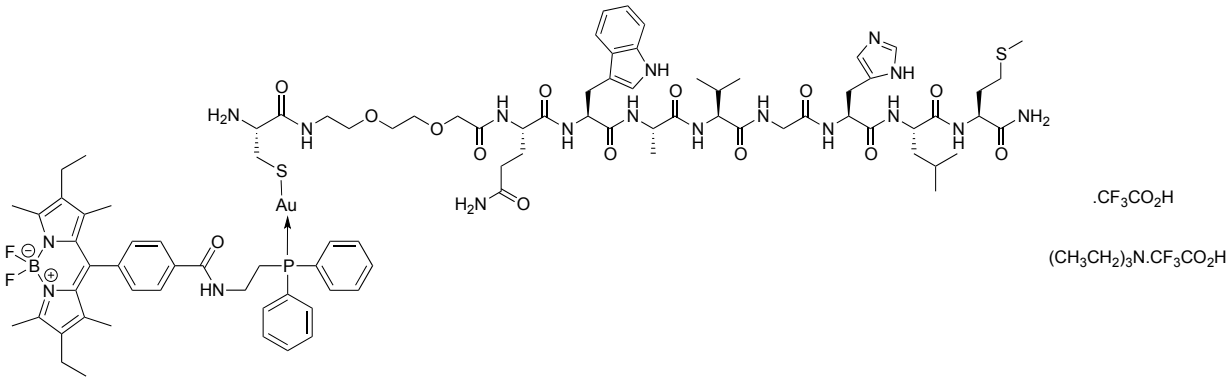


Figure S6: ^{13}C NMR spectrum of BODI-Au-3 in DMSO-d_6

BBN-SH:

HR-MS (ESI): m/z calcd for $C_{52}H_{81}N_{15}O_{13}S_2 + H^+$: 1188.56525 $[M+H]^+$. Found: 1188.56562.

BODI-Au-4



^{19}F{1H} NMR (470.55 MHz, MeOD): δ (ppm) -146.4 (q, $^{1}J_{F-B}$ = 32.3 Hz), -76.8 (s, CF_3CO_2H). **^{31}P{1H} NMR (202.45 MHz, MeOD):** δ (ppm) 29.4 (s, P-Au-S). **HR-MS (ESI):** m/z calcd for $C_{90}H_{121}AuBF_2N_{18}O_{14}PS_2 + H^+$: 2019.83020 $[M+H]^+$. Found: 2019.83759.

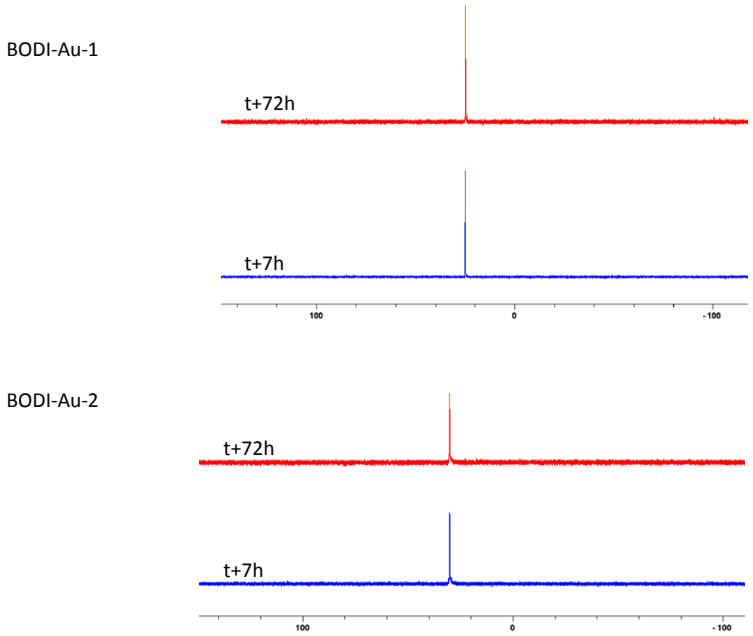
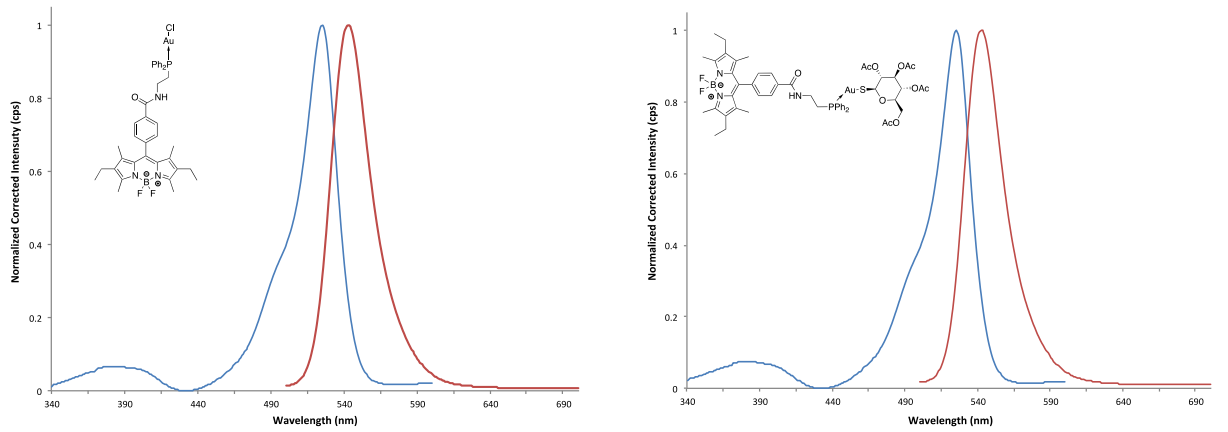


Figure S7: ^{1}H NMR stability studies of BODI-Au-1 and BODI-Au-2 in a mixture of DMEM: DMSO (1:4) at 7 et 72 h.

PHOTOPHYSICAL MEASUREMENTS

Absorption spectra were recorded on a JASCO V630BIO spectrometer. The steady-state fluorescence emission spectra were obtained by using a JASCO FP8560 spectrofluorometer instrument.

(a) (b)



(c) (d)

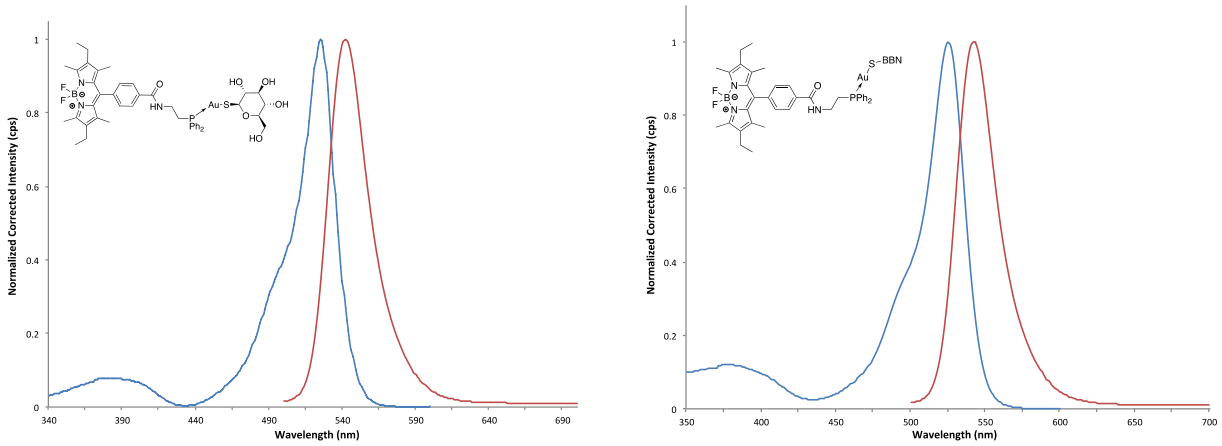


Figure S8: Absorption & emission spectra of BODI-Au-1 (a), BODI-Au-2 (b), BODI-Au-3 (c) and BODI-Au-4 (d) in DMSO at 298K

BIOLOGICAL EXPERIMENTS

Antiproliferative assay

Human MDA-MB-231 breast cancer cells and PC3 prostate cancer cells were obtained from the ATCC. These cells were maintained at 37°C in DMEM with 4.5 g/L glucose supplemented with 10% FBS and antibiotics (Dutscher, Brumath, France). DMSO at comparable concentrations did not show any effects on cell cytotoxicity.

Cells were grown at a density of $1x10^4$ cells per well in 96-well cell culture plates (Dutscher) the day before treatment with different concentrations of BODIPY complexes, compound C and auranofin, during 48 h. Thereafter, 10 µL of MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, Promega, Charbonnieres, France) was added in 200 µL of medium and absorbance at 490 nm was measured after 3h incubation at 37°C.

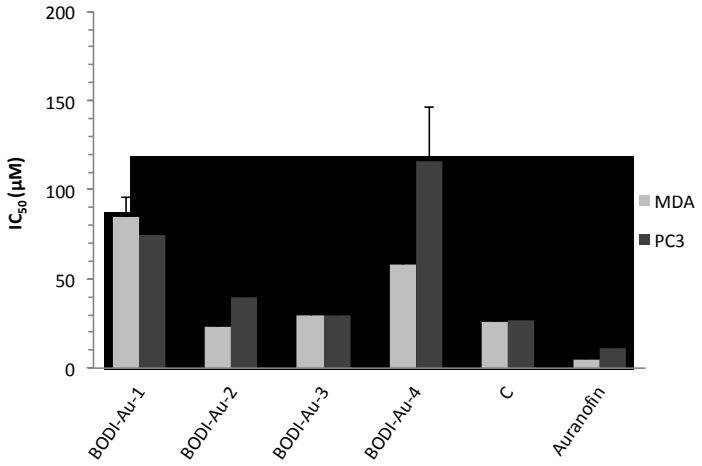


Figure S9: Determination of the IC_{50} values of BODIPY complexes on MDA-MB-231 cells (MDA) and PC3 cells by MTS assays at 48h

***In vitro* confocal fluorescence microscopy**

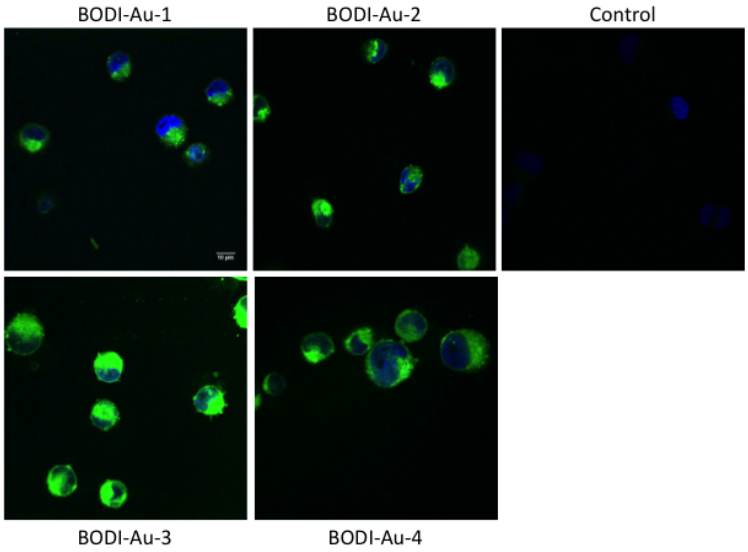


Figure S10: Confocal microscopy experiments of BODI-Au-1, -2, -3, and -4 in MDA cell line treated with 50 µM of metal complexes for 1

complexes for 1 h at 37 °C (exc. 405 nm, detection 503-568 nm range for BODIPY complexes and 408 488 nm for DAPI)

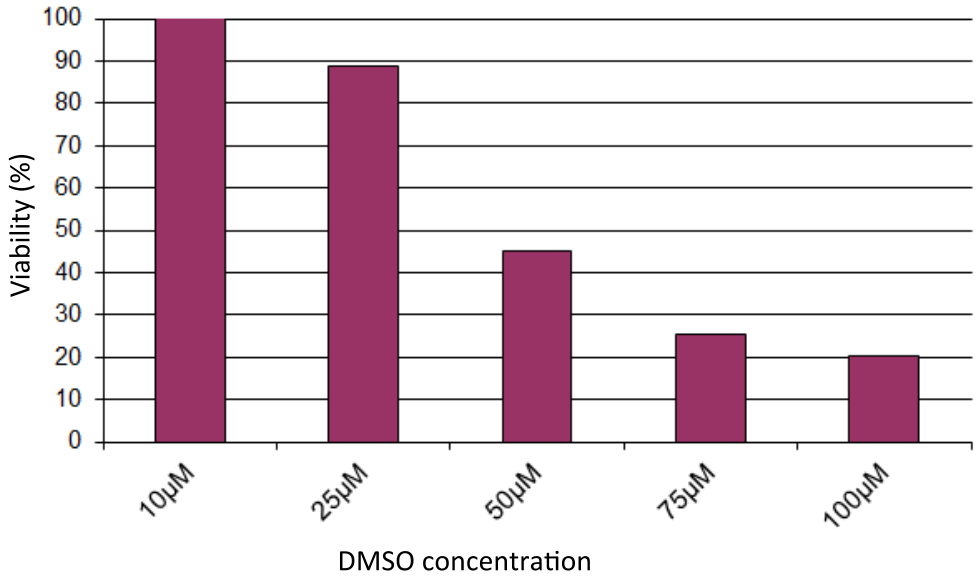


Figure S11: DMSO cytotoxicity on HMec cells