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Supporting Information

Phosporescent Iridium-containing nanomicelle: synthesis, characterization and preliminary applications in nanomedicine imaging.

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- ***Synthesis of ligand 12.***

Azide **7** was prepared as previously described.[1]

*Synthesis of 11-((2-bromopyridin-3-yl)oxy)undecan-1-ol **3**.*

To a solution of 2-bromo-3-hydroxy pyridine **1** (0.79 g, 4.55 mmol) in acetone (10 ml), K_2CO_3 (1.26 g, 9.10 mmol), 11-bromoundecan-1-ol **2** (1.49 g, 5.91 mmol) and a catalytic amount of NaI were added. The mixture was left to stir at reflux overnight. Water (10 ml) was then added to the cooled reaction and the mixture was extracted with DCM (2 x 20 ml). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated. The crude was purified by silica gel flash chromatography using a mixture of hexane/EtOAc (2:1) to give **3** in 95%yields (1.49 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (dd, J_1 = 4.6 Hz, J_2 = 1.6 Hz, 1H), 7.10 (dd, J_1 = 8.0 Hz, J_2 = 4.6 Hz, 1H), 7.04 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 3,93 (t, J = 6.5 Hz, 2H), 3.53 (t, J = 6.8 Hz, 2H), 2.69 (bs, 1H) 1.78-1.70 (m, 2H), 1.51-1.36 (m, 4H), 1.30-1.17 (m, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.3 (C), 140.6 (CH), 132.7 (C), 123.2 (CH), 119.4 (CH), 69.1 (CH_2), 62.4 (CH_2), 32.5 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.6 (CH_2), 25.6 (CH_2), 25.5 (CH_2).

*Synthesis of 3-((2-((trimethylsilyl)ethynyl)pyridin-3-yl)oxy)undecan-1-ol **4**.*

To a solution of 11-((2-bromopyridin-3-yl)oxy)undecan-1-ol **3** (1.49 g, 4.33 mmol) in THF (30 ml), ethynyltrimethylsilane (0.85 g, 8.66 mmol), Et_3N (7 ml) and CuI (0.041 g, 8.05 mmol) were added. After stirring 15 min at room temperature, $PdCl_2(PPh_3)_2$ (0.46 g, 0.65 mmol) was added and the mixture was left to stir overnight. After solvent evaporation, water (15 ml) was added to the crude and the product was extracted with DCM (2x20 ml) The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated. The crude was purified by silica gel flash chromatography using a mixture of hexane/EtOAc (2:1) to give **4** in 78%yields (1.23 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15 (dd, J_1 = 4.1 Hz, J_2 = 1.9 Hz, 1H), 7,16-7,08 (m, 2H), 3.96 (t, J = 6.0 Hz, 2H), 3,58 (t, J = 6.8 Hz, 2H), 2.14 (bs, 1H), 1.82-1.74 (m, 2H), 1.55-1.44 (m, 4H), 1.35-1.20 (m, 12H), 0.27 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.8 (C), 141.3 (CH), 133.3 (C), 123.7 (CH), 118.8 (CH), 100.2 (C), 99.4 (C), 68.6 (CH_2), 62.7 (CH_2), 32.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 25.8 (CH_2), 25.6 (CH_2), -0.4 ($3CH_3$).

*Synthesis of 3-((2-ethynylpyridin-3-yl)oxy) undecan-1-ol **5**.*

3-((2-((trimethylsilyl)ethynyl)pyridin-3-yl)oxy)undecan-1-ol **4** (1.23 g, 3.38 mmol) was dissolved in THF (20 ml) and H_2O (2ml) and cooled to 0°C with an ice-bath. Then TBAF (3.55 ml, 3.55 mmol), was added dropwise. After stirring 1 h at 0°C, the reaction was complete and H_2O (20 ml) was added and the product was extracted with DCM (2x 20 ml). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated. The crude was purified by silica gel flash chromatography using a mixture of hexane/EtOAc (1:1) to give **5** in 97%yields (0.95 g). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14 (dd, J_1 = 4.2 Hz, J_2 = 1.8 Hz, 1H), 7.23-7.14 (m, 2H), 4.01 (t, J = 6.7 Hz, 2H), 3,61 (t, J = 6.7 Hz, 2H), 3.35 (s, 1H), 1.87-1.75 (m, 3H), 1.59-1.44 (m, 4H), 1.39-1.22 (m, 12H).^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.9 (C), 141.5 (CH), 132.6 (C), 124.1 (CH), 118.9 (CH), 81.4 (C), 79.5 (CH), 68.9 (CH_2), 62.9 (CH_2), 32.7 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.8 (CH_2), 25.8 (CH_2), 25.7 (CH_2).

*Synthesis of ethyl 7-(4-(3-(11-hydroxy-undecanoxy)pyridin-2-yl)-1H-1,2,3-triazol-1-yl) heptanoanoate **8**.*

3-((2-Ethynylpyridin-3-yl)oxy) undecan-1-ol **5** (0.95 g, 3.30 mmol), Na-ascorbate (0.21 g, 0.99 mmol), $CuSO_4{\cdot}5H_2O$ (0.041 g, 0.17 mmol) were dissolved in a 1:1 mixture of tBuOH/H_2O (40ml) and ethyl 6-azidohexanoate **7** (0.678 g, 3.38 mmol) was added. After stirring 24 h at 40°C, the solvent was evaporated, DCM (20 ml) and aqueous NH_4OH (20 ml) were added and the mixture was vigorously stirred overnight. Then the layers were separated and the aqueous one was extracted twice with DCM (20 ml). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated. The crude was purified by silica gel flash chromatography using a mixture of DCM/MeOH (95:5) to give **8** in 71%yields (1.14 g). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.38 (dd, J_1 = 1.5 Hz, J_2 = 4.5 Hz, 1H), 8.12 (s, 1H), 7.27 (dd, J_1 = 1.5 Hz, J_2 = 8.3 Hz, 1H), 7.21 (dd, J_1 = 4.5 Hz, J_2 = 8.3 Hz, 1H), 4.43 (t, J = 7.7 Hz, 2H), 4.06-4.15 (m, 4H), 3.63 (t, J = 6.3 Hz, 2H), 2.28 (t, J = 8.4 Hz, 2H), 2.02-1.84 (m, 4H), 1.68-1.43 (m, 8H), 1.43-1.20 (m, 18H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.4 (C), 151.6 (C), 143.6 (C), 141.4 (CH), 139.0 (C), 124.0 (CH), 122.8 (CH), 118.6 (CH), 68.3 (CH_2), 62.6 (CH_2), 60.0 (CH_2), 49.9 (CH_2), 33.9 (CH_2), 33.5 (CH_2), 30.0 (CH_2), 29.34 ($2CH_2$), 29.26 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 28.3 (CH_2), 25.9 (CH_2), 25.6 (CH_2), 24.4 (CH_2), 14.0 (CH_3).

Synthesis of ethyl 3-(4-(3-(11-(tosyloxy)undecanoxy)pyridin-2-yl)-1H-1,2,3-triazol-1-yl)heptanoate **9**.

Alcohol **8** (0.74 g, 1.53 mmol) was dissolved in DCM (30 ml) and tosyl chloride (0.58 g, 3.05 mmol) and pyridine (0.23 ml, 2.90 mmol) were added at 0°C. The mixture was then stirred overnight at

room temperature. The reaction was quenched with H_2O (20 ml) and extracted with DCM (2x20ml). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$, dried over Na_2SO_4, filtered and the solvent was evaporated. The crude was purified by silica gel flash chromatography using a mixture of DCM/MeOH (98:2) to give **9** in 71%yields (0.70 g). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.37 (d, *J* = 4.2 Hz, 1H), 8.13 (s, 1H), 7.77 (d, *J* = 7.9 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.31-7.17 (m, 2H), 4.43 (t, *J* = 7.2 Hz, 2H), 4.16-4.06 (m, 4H), 4.01 (t, *J* = 6.5 Hz, 2H), 2.44 (s, 3H), 2.28 (t, *J* = 7.4 Hz, 2H), 2.05-1.85 (m, 4H), 1.70-1.55 (m, 4H), 1.55-1.15 (m, 21H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.3 (C), 151.6 (C), 144.5 (C), 143.6 (C), 141.5 (CH), 139.2 (C), 133.0 (C) 129.6 (CH), 127.6 (CH), 124.1 (CH), 122.8 (CH), 118.6 (CH) 70.5 (CH_2), 68.3 (CH_2), 50.0 (CH_2), 33.9 (CH_2), 33.0 (CH_2), 30.0 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 28.7 (CH_2), 28.6 (CH_2), 28.3 (CH_2), 25.9 (CH_2), 25.1 (CH_2), 24.5 (CH_2), 21.4 (CH_3), 14.0 (CH_3).

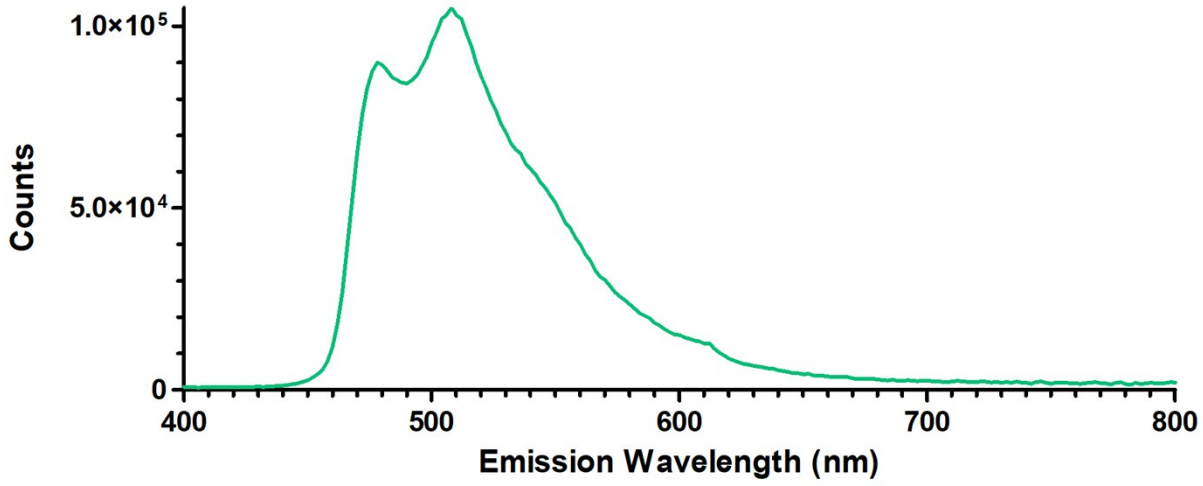
Synthesis of ethyl 3-(4-(3-(11-aminoundecanoxy)pyridin-2-yl)-1H-1,2,3-triazol-1-yl)heptanoate **11**.

Tosylate **9** (0.70 g, 1.08 mmol) was dissolved in DMSO (20 ml) and solid NaN_3 (0.12 g, 1.85 mmol) was added. The mixture was left to stir at room temperature, and after 5 h it was complete by TLC analysis. After addition of H_2O (30 ml), the product was extracted with DCM (2x20ml). The combined organic layers were washed with a saturated aqueous solution of NaCl, dried over Na_2SO_4, filtered and the solvent was evaporated. The crude **10** was pure enough by NMR analysis to be employed in the next step without any further purification. It was dissolved in THF (40 ml) and water (0.5 ml) and PPh_3 (1.30 mmol, 0,34 g) was added to the solution that was stirred at room temperature for 48h. The solvent was evaporated and the crude was purified by column chromatography (EtOAc/DCM=6/4) to give pure **11** in 75% yield (0. 39 g, 0.81 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38 (dd, *J* = 1.4 Hz, *J* = 4.5 Hz, 1H), 8.12 (s, 1H), 7.28 (dd, *J* = 8.4 Hz, *J* = 1.4 Hz, 1H), 7.21 (dd, *J* = 8.4 Hz, *J* = 4.5 Hz, 1H), 4.43 (t, *J* = 7.0 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.11 (t, *J* = 6.5 Hz, 2H), 2.7 (bt, 2H), 2.28 (t, *J* = 7.4 Hz, 2H), 2.00-1.85 (m, 4H), 1.65-1.30 (m, 26H), 1.25 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.4 (C), 151.7 (C), 143.8 (C), 141.6 (CH), 139.2 (C), 124.1 (CH), 122.9 (CH), 118.7 (CH), 68.4 (CH_2), 60.1 (CH_2), 50.0 (CH_2), 42.1 (CH_2), 34.1 (CH_2), 33.8 ($2CH_2$), 30.2 (CH_2), 29.6 (CH_2), 29.5 ($2CH_2$), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.4 (CH_2), 26.8 (CH_2), 26.0 (CH_2), 24.6 (CH_2), 14.1 (CH_3).

Synthesis of 11-((2-(1-(6-carboxyhexyl)-1H-1,2,3-triazol-4-yl)pyridin-3-yl)oxy)undecan-1-aminium chloride **12**.

Ethyl ester **11** (0.20 g, 0.41 mmol) was dissolved in DCM (20 ml) and a solution of KOH (0.23 g, 4.12 mmol) in EtOH (10 ml) was added dropwise. The mixture was left to stir at room temperature, and

after 24 the solvent was evaporated. The crude was dissolved in DCM (20ml) and water (10 ml) and 1 M HCl was added to pH~6-7. The organic layer was separated, and the aqueous one washed with DCM (2x 20 ml). The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent evaporated. The crude was dissolved in DCM and HCl 1M in Et_2O was added (2 ml). The solvent was removed to give pure **12** (0.19 g, 0.38 mmol) in 92% yields. ^{1}H NMR (CD_3OD, 300 MHz) δ 8.76 (s, 1H), 8.41 (s, 1H), 8.38 (d, J = 2.1 Hz, 1H), 8.00-7.95 (m, 1H), 4.60 (t, J = 7.0 Hz, 2H), 4.47 (t, J = 6.4 Hz, 2H),3.63 (s, 1H), 2.9 (bt, 2H), 2.35-2.25 (m, 2H), 2.10-1.95 (m, 4H), 1.70-1.25 (m, 20H). ^{13}C NMR (CD_3OD, 100 MHz) δ 174.3 (C), 153.4 (C), 135.3 (C), 133.4 (C), 132.5 (CH), 128.8 (CH), 128.0 (CH), 126.1 (CH), 71.0 (CH_2), 50.3 (CH_2), 39.4 (CH_2), 33.2 (CH_2), 29.7 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.8 (CH_2), 28.3 (CH_2), 28.1 (CH_2), 27.1 (CH_2), 26.1 (CH_2), 25.7 ($2CH_2$), 24.4 (CH_2).



Supplementary Figure 1: Emission profile of PLGA-12/TPGS@PNPs-Ir dispersion in water after 2 months from synthesis. No variations in the emission spectrum are observed, thus confirming the stability over time of emission from iridium.

[1] M. Naddaka, E. Locatelli, D. Colecchia, L. Sambri, I. Monaco, A. Baschieri, F. Sasdelli, M. Chiariello, E. Matteucci, P. Zani, M. Comes Franchini. *RSC Adv*, 2015, **5**, 1091.