Direct functionalisation of group 10 N-heterocyclic carbene complexes for diversity enhancement

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General procedures
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General procedures
All reactions were performed under an inert atmosphere of argon or nitrogen using standard Schlenk line techniques. Solvents were purified and degassed by standard procedures. All other reagents were used without further purification. 5-(trimethylsilyl)ethynyl-1-methylimidazole and fluoride on Amberlyst® A-26 were purchased in Aldrich. ¹H and ¹³C Nuclear Magnetic Resonance (NMR) spectra were recorded on a Brucker AVANCE 300 spectrometer using the residual solvent peak as reference (CDCl₃: δ_H = 7.26 ppm; δ_C = 77.16 ppm) at 298K. MALDI analyses have been carried out on autoflexII, Bruker Daltonics and HRMS ESI analyses on microTOF, Bruker Daltonics. Polyethylene glycol derived azides,¹ lysine azide derivative² and oestrogen bromide derivative³ have been synthesized according to the procedures described in the literature.

1. Synthesis of the ligands

1-Methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-1H-imidazol-3-ium iodide 1. A mixture of 1-methylimidazole (0.50 g, 6.09 mmol), sodium iodide (1.82 g, 12.18 mmol) and 1-chloro-5-(trimethylsilyl)-4-pentyne (1.12 mL, 6.09 mmol) was suspended in dimethylether (8 mL) and the reaction was refluxed at 85°C overnight. The solvent was removed under vacuum. The obtained solid was dissolved in chloroform, filtered through a celite plug and concentrated in vacuo to yield the product 1 as a white solid (2.01 g, 95%). ¹H-NMR (CDCl₃, 300 MHz, 20°C): δ 0.10 (s, 9H, Si(CH₃)₃), 2.10 (m, 2H, CH₂), 2.30 (t, J = 6.5 Hz, 2H, CH₂), 4.06 (s, 3H, N-CH₃), 4.42 (t, J = 7.0 Hz, 2H, CH₂), 7.43 (s, 1H, CHylimidazol), 7.57 (s, 1H, CHylimidazol), 9.83 (s, 1H, N-CH=NH). ¹³C-NMR (CDCl₃, 125 MHz, 20°C): δ 0.08 (Si-(CH₃)₃), 16.8 (CH₃), 28.6 (CH₃), 37.3 (CH₃), 48.7 (N-CH₂), 87.3 (Calkyne), 103.8 (Calkyne), 122.5 (CHylimidazol), 123.8 (CHylimidazol), 136.8 (NCHlimidazol).
1-Methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-IH-imidazol-3-ium bromide. A mixture of 5-(trimethylsilyl)ethynyl-1-methylimidazole (1.04 g, 5.84 mmol) and bromobenzyle (0.69 mL, 5.84 mmol) was dissolved in acetonitrile (30 mL) and the reaction was refluxed at 75°C overnight. The solvent was removed under vacuum. The solid was washed with diethyl ether to yield the 1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-IH-imidazol-3-ium bromide as a white solid (1.93 g, 95%). 1H-NMR (CDCl3, 300 MHz, 20°C): δ 0.24 (s, 9H, Si(CH3)3), 3.98 (s, 3H, N-CH3), 5.60 (s, 2H, N-CH2), 7.20 (s, 1H, C=CH), 7.40-7.42 (br, 3H, Ar-H), 7.46 (m, 2H, Ar-H), 10.96 (br, 1H, N-CH=N). 13C-NMR (CDCl3, 125 MHz, 20°C): δ -0.68 (Si-(CH3)3), 34.8 (CH3), 53.8 (CH2), 86.5 (Calkyne), 108.7 (Calkyne), 119.0 (Cimidazole), 123.8 (CHimidazole), 129.3, 129.5, 129.6, 132.5 (C aromatic), 138.0 (NCHimidazolium).

2. Synthesis of the biscarbenic Pd(II) complexes

**Trans**-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II). The imidazolium 1 (125 mg, 0.359 mmol) was dissolved in THF (10 mL) and palladium (II) acetate (40 mg, 0.179 mmol) was added. The mixture was stirred for 2h at 75°C. The resulting suspension was filtered through a celite plug and concentrated in vacuo. The residue was purified by a silica gel chromatography with dichloromethane affording the complex **trans**-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II) (1:1 syn/anti) as a yellow powder (91 mg, 63%). 1H-NMR (CDCl3, 300 MHz, 20°C): δ 0.17 (s, 9H, Si-(CH3)3), 0.18 (s, 9H, Si-(CH3)3), 2.31 (br, 8H, 4CH2), 3.92 (s, 3H, N-CH3), 3.95 (s, 3H, N-CH3), 4.47 (br, 4H, 2N-CH2), 6.68 (br, 2H, 2CHimidazole), 6.96 (br, 2H, 2CHimidazole) The 1H NMR spectrum of complex **trans**-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II) shows a similar signal pattern to that of complexes reported in the literature.4-13C-NMR (CDCl3, 125 MHz, 20°C): δ 0.19 (2Si-(CH3)3), 17.0 (CH3), 17.1 (CH2), 28.3 (2CH2), 38.5 (CH2), 38.6 (CH), 49.3 (N-CH2), 49.5 (N-CH2), 86.4 (Calkyne), 86.5 (Calkyne), 105.4 (Calkyne), 105.6 (Calkyne), 122.2 (4CHimidazole), 167.7 (2C-Pd). HRMS (positive ESI) [M+Na]: calcd for C23H23I2N3PdSi3Na 822.982, found 822.978.

**Trans**-diiodo-di-[1-methyl-3-(pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II) 2. Fluoride on Amberlyst® A-26 (271 mg, 0.678 mmol, 2.5 mmol/g loading) was added to a solution of the **trans**-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-
yn-1-yl)-imidazol-2-ylidene]-palladium(II) (58 mg, 0.072 mmol) in THF (15 mL). The solution was stirred 2-20 h at room temperature. The resin was then filtered off. The resulting filtrate was concentrated under vacuum to yield 2 as a light yellow powder (33 mg, 69 %). 1H-NMR (CDCl3, 300 MHz, 20°C): δ 2.04 (s, 1H, CHalkyne), 2.06 (s, 1H, CHalkyne), 2.31 (br, 8H, 4CH2), 3.93 (s, 3H, N-CH3), 3.96 (s, 3H, N-CH3), 4.47 (t, J = 6.8 Hz, 2H, N-CH2), 4.49 (t, J = 6.9 Hz, 2H, N-CH2), 6.87 (s, 2H, 2CHimidazole), 6.96 (s, 2H, 2CHimidazole). 13C-NMR (CDCl3, 125 MHz, 20°C): δ 15.7 (2CH3), 28.5 (2CH2), 38.6 (2CH3), 49.4 (N-CH2), 49.5 (N-CH2), 69.8 (CHalkyne), 69.5 (CHalkyne), 82.8 (Calkyne), 82.9 (Calkyne), 121.9-122.3 (4CHimidazole), 167.7 (2C-Pd).

Trans-dibromo-di-[1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-imidazol-2-ylidene]-palladium(II) 4. 1-Methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-1H-imidazol-3-ium bromide (135 mg, 0.386 mmol) and [Pd(OAc)2]3 (49 mg, 0.073 mmol) were dissolved in dichloromethane (10 mL) at -10°C. The mixture was stirred overnight at room temperature. The resulting suspension was filtered through a celite plug and concentrated in vacuo. The residue was purified by a silica gel chromatography with dichloromethane affording the complex 4 (1:1 syn/anti) as a white powder (80 mg, 52%). 1H-NMR (CDCl3, 300 MHz, 20°C): δ 0.19 (s, 9H, Si-(CH3)3), 0.22 (s, 9H, Si-(CH3)3), 4.00 (s, 3H, N-CH3), 4.12 (s, 3H, N-CH3), 5.57 (s, 2H, N-CH2), 5.74 (s, 2H, N-CH2), 6.82 (s, 2H, 2CHimidazole), 6.83 (s, 2H, 2CHimidazole), 7.26-7.30 (m, 4H, Ar-H), 7.37-7.39 (m, 4H, Ar-H), 7.50-7.51 (m, 2H, Ar-H). The 1H NMR spectrum of complex 4 shows a similar signal pattern to that of complexes reported in the literature. 13C-NMR (CDCl3, 125 MHz, 20°C): δ -0.37 (2Si-(CH3)3), 36.0 (CH3), 36.1 (CH3), 54.8 (CH3), 54.9 (CH3), 90.5 (2Calkyne), 104.6 (2Calkyne), 118.9 (2Cimidazole), 124.5 (CHimidazole), 124.6 (CHimidazole), 128.4, 128.5, 128.9, 129.0, 135.4 (C aromatic), 135.5 (C aromatic), 171.1 (2C-Pd). HRMS (positive ESI) [M-Br]: calcd for C30H26Br2N4PdSi2 721.104, found 721.100.

Crystal data for 4: C30H26Br2Pd4Si2, yellow, crystal dimensions 0.05 x 0.05 x 0.02 mm, M = 401.54, triclinic, P-1, a = 5.7239(11), b = 11.368(2), c = 14.203(3) Å, α = 101.46(3), β = 91.89(3), γ = 99.34(3)°, U = 891.7(3) Å³, Z = 2, D = 1.495 g cm⁻³, μ = 7.663 mm⁻¹, F(000) = 404, number of data meas.: 11674 at 173(2) K, number of data with I > 3σ(I): 2802, number of variables: 176, R = 0.116, Rw = 0.317, GOF = 1.168.
**Trans-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II).** Fluoride on Amberlyst® A-26 (384 mg, 0.768 mmol, 2.5 mmol/g loading) was added to a solution of TMS-protected alkyne complexe 4 (51 mg, 0.064 mmol) in THF (20 mL). The solution was stirred 20 h at room temperature. The resin was then filtered off. The resulting filtrate was concentrated under vacuum to yield the trans-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium (II) as a light yellow powder (41 mg, 98%).

**1H-NMR (CDCl₃, 300 MHz, 20°C):** δ 3.45 (s, 1H, CH₃alkyne), 3.48 (s, 1H, CH₃alkyne), 4.01 (s, 3H, N-CH₃), 4.14 (s, 3H, N-CH₃), 5.59 (s, 2H, N-CH₂), 5.75 (s, 2H, N-CH₂), 6.88 (s, 2H, 2CH₃imidazole), 6.89 (s, 2H, 2CH₃imidazole), 7.26-7.56 (m, 10H, Ar-H), 13C-NMR (CDCl₃, 125 MHz, 20°C): δ 36.2 (2CH₃), 54.8 (CH₂), 55.0 (CH₂), 70.2 (2CH₃alkyne), 86.4 (2Calkyne), 117.8 (2Cimidazole), 125.2 (CH₃imidazole), 125.3 (CH₂imidazole), 128.4, 128.6, 128.9, 129.0, 135.3 (2C aromatic), 171.4 (2C-Pd).
3. Synthesis of the Pt(II) complexes

**Trans-diiodo-(N-pyridine)-[1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-imidazol-2-ylidene]-platinum(II)** 8a. A mixture of 1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-IH-imidazol-3-ium bromide (100 mg, 0.286 mmol), sodium iodide (228 mg, 1.521 mmol), platinum dichloride (76 mg, 0.286 mmol) and potassium carbonate (216 mg, 1.585 mmol) was suspended in pyridine (3 mL). The mixture was stirred for 3h at 100°C. The resulting suspension was concentrated in vacuo, then dissolved in dichloromethane, filtered through a celite plug and concentrated in vacuo. The residue was purified by a silica gel chromatography (dichloromethane/cyclohexane 1:1) affording the complex 8a as a yellow-orange powder (184 mg, 81%). ^3H-NMR (CDCl₃, 300 MHz, 20°C): δ 0.27 (s, 9H, Si(CH₃)₃), 4.03 (s, 3H, N-CH₂), 5.73 (m, 2H, CH₂), 6.82 (s, 1H, CHimidazole), 7.36-7.43 (m, 5H, ArH), 7.53 (d, J = 6.5 Hz, 2H, Ar-H), 7.77 (t, J = 7.5 Hz, 1H, Ar-H), 9.08 (d, J = 5.0 Hz, 2H, Ar-H). ^13C-NMR (CDCl₃, 125 MHz, 20°C): δ -0.19 (Si(CH₃)₃), 36.4 (CH₂), 55.2 (CH₂), 90.4 (Calkyne), 105.0 (Calkyne), 118.6 (Cimidazole), 124.2 (Cimidazole), 125.2 (Cpyridine), 128.8 (Caromatic), 129.2 (Caromatic), 129.5 (Caromatic), 135.0 (Caromatic), 137.7 (Cpyridine), 138.7 (C-Pt), 154.0 (Cpyridine). HRMS (positive ESI) [M-I]: calcd for C₂₁H₂₁N₃PtSi 669.051, found 669.050.

**Trans-diiodo-(N-cyclohexylamine)-[1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-imidazol-2-ylidene]-platinum(II)** 8b. ^1H-NMR (CDCl₃, 300 MHz, 20°C): δ 0.21 (s, 9H, Si(CH₃)₃), 1.07-1.40 (br, 5H), 1.71-1.83 (br, 5H), 2.95 (m, 2H, NH₂), 3.26 (m, 1H), 3.88 (s, 3H, CH₃), 5.55 (s, 2H, Nimidazole-CH₂), 6.73 (s, 1H, CHimidazole), 7.32-7.46 (br, 5H, Ar-H). ^13C-NMR (CDCl₃, 125 MHz, 20°C): δ -0.4 (Si(CH₃)₃), 24.8 (CH₂), 25.3 (CH₂), 35.9 (CH₂), 36.0 (CH₂), 54.7 (CH), 54.9 (Nimidazole-CH₂), 90.3 (Calkyne), 104.7 (Calkyne), 118.2 (Cimidazole), 123.8 (Cimidazole), 128.5 (Caromatic), 128.9 (Caromatic), 129.2 (Caromatic), 134.9 (Caromatic), 142.0 (C-Pt). HRMS (positive ESI) [M-I]: calcd for C₂₂H₂₃N₃PtSi 689.113, found 689.130.

**Trans-diiodo-(N-pyridine)-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-platinum(II)**. A mixture of 8a (19 mg, 0.026 mmol) and potassium carbonate (10 mg, 0.072 mmol) was suspended in methanol (4 mL). The mixture was stirred for
6h at room temperature. The resulting suspension was concentrated in vacuo, then dissolved in dichloromethane, filtered through a celite plug and concentrated in vacuo. The residue was then washed with pentane to yield the **trans**-diiodo-\((N\)-pyridine)-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-platinum(II) as a yellow powder (14 mg, 78%). \(^1\)H-NMR (CDCl\(_3\), 300 MHz, 20°C): \(\delta\) 3.47 (s, 1H, CH\(_{\text{ alkyn}}\)), 4.01 (s, 3H, N-CH\(_3\)), 5.70 (s, 2H, CH\(_2\)), 6.82 (s, 1H, CH\(_{\text{imidazole}}\)), 7.31-7.42 (m, 5H, Ar-H), 7.48-7.52 (dd, J = 1.5 Hz, J = 8.1 Hz, 2H, Ar-H), 7.73 (tt, J = 1.2 Hz, J = 7.5 Hz, 1H, Ar-H), 9.04 (m, 2H, Ar-H). \(^13\)C-NMR (CDCl\(_3\), 125 MHz, 20°C): \(\delta\) 36.4 (CH\(_3\)), 55.1 (CH\(_2\)), 70.2 (CH\(_{\text{alkyne}}\)), 86.5 (C\(_{\text{alkyne}}\)), 117.3 (C\(_{\text{imidazole}}\)), 124.4 (CH\(_{\text{imidazole}}\)), 125.0 (CH\(_{\text{pyridine}}\)), 128.2 (CH\(_{\text{aromatic}}\)), 129.0 (CH\(_{\text{aromatic}}\)), 129.3 (CH\(_{\text{aromatic}}\)), 134.7 (C\(_{\text{aromatic}}\)), 137.6 (CH\(_{\text{pyridine}}\)), 139.1 (C-Pt), 153.70 (CH\(_{\text{pyridine}}\)).

**Trans**-diiodo-\((N\)-cyclohexylamine\)-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-platinum(II). A mixture of 8b (61 mg, 0.075 mmol) and potassium carbonate (29 mg, 0.209 mmol) was suspended in methanol (12 mL). The mixture was stirred for 2h at room temperature. The resulting suspension was concentrated in vacuo, then dissolved in dichloromethane, filtered through a celite plug and concentrated in vacuo. The residue was then washed with pentane to yield the **trans**-diiodo-\((N\)-cyclohexylamine\)-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-platinum(II) as a yellow powder (45 mg, 80%). \(^1\)H-NMR (CDCl\(_3\), 300 MHz, 20°C): \(\delta\) 1.07-1.40 (br, 5H), 1.51-1.83 (br, 3H), 2.26 (m, 2H), 2.96 (m, 2H, NH\(_2\)), 3.26 (m, 1H), 3.46 (s, 1H, CH\(_{\text{ alkyn}}\)), 3.91 (s, 3H, CH\(_3\)), 5.57 (s, 2H, N\(_{\text{ imidazole}}\)-CH\(_2\)), 6.79 (s, 1H, CH\(_{\text{imidazole}}\)), 7.32-7.46 (br, 5H, Ar-H). \(^13\)C-NMR (CDCl\(_3\), 125 MHz, 20°C): \(\delta\) 24.8 (CH\(_2\)), 25.2 (CH\(_2\)), 35.7 (CH\(_3\)), 36.0 (CH\(_2\)), 54.7 (CH), 54.9 (N\(_{\text{imidazole}}\)-CH\(_2\)), 70.1 (CH\(_{\text{alkyne}}\)), 86.4 (C\(_{\text{alkyne}}\)), 117.2 (C\(_{\text{imidazole}}\)), 124.4 (CH\(_{\text{imidazole}}\)), 128.5 (CH\(_{\text{aromatic}}\)), 128.9 (CH\(_{\text{aromatic}}\)), 129.2 (CH\(_{\text{aromatic}}\)), 134.8 (C\(_{\text{aromatic}}\)), 142.6 (C-Pt).

**4. Ruthenium(II)-catalyzed Alkyne Azide Cycloaddition (RuAAC)**

**Compound 3.** To a solution of Cp\(^*\)RuCl(PPh\(_3\))\(_2\) (3.0 mg, 3.160 \(\mu\)mol) in tetrahydrofuran (0.5 mL) were added a solution of the alkyne derivative 2 (26 mg, 0.040 mmol) in tetrahydrofuran (1.5 mL) and a solution of benzyl azide (11 mg, 0.087 mmol) in tetrahydrofuran (1 mL). The mixture was then heated overnight at 75°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using a mixture of dichloromethane/cyclohexane 3:1 followed by dichloromethane and then ethyl acetate to afford the compound 3 as an yellow-brown oil (10 mg, 27%). \(^1\)H-NMR (CDCl\(_3\), 300 MHz, 20°C): \(\delta\) 2.30 (br, 4H, 2CH\(_2\)), 2.64 (br, 4H, 2CH\(_2\)), 3.95 (s, 6H, N\(_{\text{imidazole}}\)-CH\(_3\)), 3.97 (s, 6H, N\(_{\text{imidazole}}\)-CH\(_3\)), 4.35
Compound 5. To a solution of Cp*RuCl(PPh₃)₂ (2.4 mg, 3.100 μmol) in tetrahydrofuran (0.5 mL) were added a solution of the trans-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II) (27 mg, 0.037 mmol) in tetrahydrofuran (0.5 mL) and a solution of benzyl azide (11 mg, 0.084 mmol) in tetrahydrofuran (0.5 mL). The mixture was then heated overnight at 60°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using dichloromethane followed by ethyl acetate to afford the compound 5 as an yellow-brown oil (30 mg, 87%). ¹H-NMR (CDCl₃, 300 MHz, 20°C): δ 3.56 (s, 3H, N-CH₃), 3.64 (s, 3H, N-CH₃); 5.35 (s, 2H, Nimidazole-CH₂), 5.36 (s, 2H, Nimidazole-CH₂), 5.64 (s, 2H, Nimidazole-CH₂), 5.74 (s, 2H, Nimidazole-CH₂), 6.47 (s, 1H, CHimidazole), 6.48 (s, 1H, CHimidazole), 6.94-7.55 (br, 20H, Ar-H); 7.77 (s, 1H, CHimidazole), 7.79 (s, 1H, CHimidazole). ¹³C-NMR (CDCl₃, 125 MHz, 20°C): δ 36.2 (N-CH₃), 36.3 (N-CH₃), 53.2 (2Nimidazole-CH₂), 55.4 (Nimidazole-CH₂), 55.4 (Nimidazole-CH₂), 121.1, 122.6, 125.0, 127.9, 128.1, 128.8, 129.0, 129.1, 129.2, 129.3, 129.5, 129.7, 132.3, 132.4, 132.5, 132.6, 133.7, 134.5, 134.6, 135.5, 135.6, 136.6, 173.1 (C-Pd), 173.2 (C-Pd). HRMS (positive ESI) [M+]: calcd for C₃₂H₃₈Nd₄Pd 795.137, found 795.139.

Compound 6. To a solution of Cp*RuCl(PPh₃)₂ (2.4 mg, 3.100 μmol) in tetrahydrofuran (1 mL) were added a solution of trans-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II) (27 mg, 0.037 mmol) in tetrahydrofuran (1 mL) and a solution of H₃(C-(OCH₂CH₃))₂N⁺ (19 mg, 0.082 mmol) in tetrahydrofuran (1 mL). The mixture was then heated 2h at 60°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using dichloromethane followed by ethyl acetate and then a mixture of ethyl acetate/methanol 3:1 to afford the compound 6 as an yellow-brown oil (31 mg, 76%). ¹H-NMR (CDCl₃, 300 MHz, 20°C): δ 3.13-4.09 (br, 40H, 2O-CH₃, 14CH₂ and 2NCH₂), 4.35 (m, 4H, 2Nimidazole-CH₂), 5.69 (s, 2H, Nimidazole-CH₂), 5.86 (s, 2H, Nimidazole-CH₂), 7.23-7.74 (br, 10H, Ar-H), 7.79 (s, 1H, CHimidazole), 7.82 (s, 1H, CHimidazole). ¹³C-NMR (CDCl₃, 125 MHz, 20°C): δ 36.2 (NCH₃), 36.3 (NCH₃), 48.4 (2Nimidazole-CH₂), 54.8 (Nimidazole-CH₂), 54.9 (Nimidazole-CH₂), 59.0 (2O-CH₃), 69.7 (O-CH₂), 70.3 (O-CH₂), 70.3 (O-CH₂), 70.5 (O-CH₂), 70.5 (O-CH₂), 71.9 (O-CH₂), 120.1, 123.5, 123.6, 126.2, 126.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.7, 128.8,
128.8, 128.8, 128.9, 128.9, 134.8, 135.5, 135.6, 172.3 (C-Pd), 172.4 (C-Pd). HRMS (positive ESI) [M+Na]: calcd for C_{44}H_{62}Br_{2}N_{10}O_{8}PdNa 1145.204, found 1145.190.

**Compound 7.** To a solution of Cp*RuCl(PPh_{3})_{2} (1.4 mg, 1.840 μmol) in tetrahydrofuran (0.5 mL) were added a solution of the trans-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II) (15 mg, 0.023 mmol) in tetrahydrofuran (1 mL) and a solution of H_{2}C=(OCH_{2}CH_{2})_{6}-N_{3}^1 (18 mg, 0.050 mmol) in tetrahydrofuran (1 mL). The mixture was then heated 30 min at 65°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using dichloromethane/methanol 10:0.7 to afford the compound 7 as an yellow-brown oil (23 mg, 72%).

^{1}H-NMR (CDCl_{3}, 300 MHz, 20°C): δ 3.34-3.99 (br, 60-64 H, 2O-CH_{3}, 14 CH_{2} and 2N-CH_{3}), 4.31 (br, 4H, N-triazole-CH_{2}); 5.65 (s, 2H, N-imidazole-CH_{2}), 5.81 (s, 2H, N-imidazole-CH_{2}), 7.22-7.56 (br, 12H, Ar-H), 7.76 (s, 1H, CH-triazole), 7.79 (s, 1H, CH-triazole).

^{13}C-NMR (CDCl_{3}, 125 MHz, 20°C): δ 36.2 (N-CH_{3}), 36.3 (N-CH_{3}), 48.4 (2CH_{2}), 54.8 (N-imidazole-CH_{2}), 54.9 (N-imidazole-CH_{2}), 59.0 (2OCH_{3}), 69.7, 70.0, 70.2, 70.6, 71.3, 120.9, 123.6, 126.2, 128.3, 128.4, 128.5, 128.7, 128.8, 128.9, 129.0, 132.0, 132.1, 134.8, 135.6, 172.3 (C-Pd). MALDI [M-Br]: found 1308.104.

**Compound 9.** To a solution of the alkyne derivative 8a (13 mg, 0.015 mmol) in tetrahydrofuran (1 mL) were added a solution of Cp*RuCl(PPh_{3})_{2} (0.5 mg, 0.680 μmol) in tetrahydrofuran (0.2 mL) and a solution of benzyl azide (7 mg, 0.053 mmol) in tetrahydrofuran (0.5 mL). The mixture was then heated 2h at 70°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using a mixture of dichloromethane and cyclohexane 1:1 followed by ethyl acetate to afford the compound 9 as a yellow-brown oil (12 mg, 82%).

^{1}H-NMR (CDCl_{3}, 300 MHz, 20°C): δ 3.57 (s, 3H, CH_{3}), 5.37 (s, 2H, N-triazole-CH_{2}), 5.73 (s, 2H, N-imidazole-CH_{2}), 6.43 (s, 1H, CH-imidazole), 7.19-7.51 (br, 13H, 10Ar-H and 3CH_{pyridine}), 7.81 (s, 1H, CH-triazole), 9.04 (d, 2H, CH_{pyridine}). ^{13}C-NMR (CDCl_{3}, 125 MHz, 20°C): δ 36.1 (CH_{3}), 52.7 (N-triazole-CH_{2}), 55.2 (N-imidazole-CH_{2}), 120.1, 121.6, 124.4, 125.1, 125.3, 127.8, 128.7, 128.8, 129.1, 129.3, 129.5, 134.1, 134.6, 136.4, 137.7, 153.8. HRMS (positive ESI) [M-I]: calcd for C_{25}H_{24}Br_{2}Pt 730.075, found 730.085.
**Compound 10.** To a solution of Cp*RuCl(PPh₃)₂ (2.0 mg, 2.418 μmol) in tetrahydrofuran (3 mL) were added a solution of the alkyne derivative 8b (45 mg, 0.060 mmol) in tetrahydrofuran (3 mL) and a solution of benzyl azide (24 mg, 0.181 mmol) in tetrahydrofuran (4 mL). The mixture was then heated 20h at 70°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using a mixture of ethyl acetate and cyclohexane 1:2 to afford the compound 10 as an yellow-brown oil (37 mg, 70%). ¹H-NMR (CDCl₃, 300 MHz, 20°C): δ 1.10-1.85 (br, 8H, CH₂ cyclohexylamine), 2.30 (m, 2H, CH₂ cyclohexylamine), 3.00 (br, 2H, NH₂), 3.29 (m, 1H, CH₂ cyclohexylamine), 3.47 (s, 3H, CH₃), 5.35 (s, 2H, N₃), 5.59 (s, 2H, N₃), 6.38 (s, 1H, CH₃), 7.01 (m, 2H, 2Ar-H), 7.25-7.46 (br, 8H, 8Ar-H), 7.77 (s, 1H, CH₃). ¹³C-NMR (CDCl₃, 125 MHz, 20°C): δ 24.8 (CH₃), 25.3 (CH₃), 35.9 (CH₃), 36.0 (CH₂), 52.7 (N₃), 54.9 (N₃), 55.0 (CH), 120.0 (C₆H₅), 121.4 (C₆H₅), 124.5 (C₆H₅), 127.7 (CH₃), 128.6 (CH₃), 128.7 (CH₃), 129.0 (CH₃), 129.3 (CH₃), 129.4 (CH₃), 134.1 (C₆H₅), 134.7 (C₆H₅), 136.3 (C₆H₅), 144.3 (C-Pt). HRMS (positive ESI) [M+H]: calcd for C₂₃H₂₄N₃Pt 878.050, found 878.039.

**Compound 11.** To a solution of Cp*RuCl(PPh₃)₂ (9.0 mg, 0.011 mmol) in tetrahydrofuran (3 mL) were added a solution of the alkyne derivative 8a (55 mg, 0.076 mmol) in tetrahydrofuran (4 mL) and a solution of Fmoc-Lys(N₃)-OMe (66 mg, 0.162 mmol) in tetrahydrofuran (4 mL). The mixture was then heated 2h at 70°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using dichloromethane followed by a mixture of ethyl acetate and dichloromethane 1:5 to afford the compound 11 as an yellow-brown oil (51 mg, 59%). ¹H-NMR (CDCl₃, 300 MHz, 20°C): δ 1.67-1.78 (br, 6H, 3CH₂), 3.74 (s, 3H, OCH₃), 3.80 (s, 3H, N₃), 4.10-4.24 (br, 3H), 5.26 (m, 1H, CH₂Fmoc), 5.79 (s, 2H, N₃), 6.78 (s, 1H, CH₃), 7.19-7.78 (br, 17H, 13Ar-H, CH₃ and 3CH₃). ¹³C-NMR (CDCl₃, 125 MHz, 20°C): δ 22.3, 29.4, 32.0, 36.3 (N₃), 47.2, 48.4, 52.6, 53.5, 55.1 (N₃), 67.1, 120.0, 121.5, 125.1, 127.1, 127.7, 128.8, 129.1, 129.3, 134.7, 135.7, 137.6, 141.3, 143.8, 153.7 (CH₃). HRMS (positive ESI) [M-I]: calcd for C₄₂H₂₃N₇O₇Pt 1005.191, found 1005.194.

**16β-Hydroxymethyl-16α-(6'-azidoocyt)-1,3,5(10)-estratrien-3,17β-diol 12.** 16β-hydroxymethyl-16α-(6'-bromooctyl)-1,3,5(10)-estratrien-3,17β-diol obtained as reported in literature³ (160 mg, 0.324 mmol) was dissolved in methanol (10 mL).
and sodium azide (105 mg, 1.62 mmol) was added to this solution. The solution was placed to reflux for 20 h under stirring. The solvent was evaporated and diethyl ether (100 mL) was added to the residue. The ethereal solution was washed with water (3x50 mL), dried over anhydrous sodium sulphate, filtered and concentrated affording the product 12 as a white solid (104 mg, 71%). 

$^1$H-NMR (CDCl$_3$, 300 MHz, 20°C): $\delta$ 0.87 (s, 3H, CH$_3$ estrogen), 0.98-2.00 (m, 26H, 2CH and 12 CH$_2$ estrogen), 2.69-2.83 (m, 3H, CH$_2$ and CH$_3$ estrogen), 3.24-3.54 (m, 3H, CHOH and CH$_2$OH estrogen), 3.80 (br d, 1H, OH), 4.78 (br s, 1H, OH), 6.57 (d, $J$=2.7 Hz, 1H, Ar-H estrogen), 6.63 (dd, $J_1$=8.4 Hz, $J_2$=2.7 Hz, 1H, 1Ar-H estrogen), 7.15 (d, $J$=8.7 Hz, 1H, 1Ar-H estrogen).

$^{13}$C-NMR (CDCl$_3$, 125 MHz, 20°C): $\delta$ 11.9 (CH$_3$ estrogen), 22.7, 24.5, 26.3, 27.4, 28.7, 29.6, 30.2, 33.3, 36.3 (Nimidazole-CH$_3$), 38.0, 39.3, 43.8, 44.9, 47.0, 47.9, 51.5, 67.0 (CH$_2$OH estrogen), 90.5, 112.7, 115.3 (CH arson), 126.4 (CH arson), 132.5 (CH arson), 153.5 (COH arson). HRMS (positive ESI) [M+Na]: calcd for C$_{27}$H$_{41}$N$_3$O$_3$Na 478.304, found 478.307.

**Compound 13.** To a solution of Cp*RuCl(PPh$_3$)$_2$ (2.8 mg, 3.516 $\mu$mol) in tetrahydrofuran (2 mL) were added a solution of the alkyne derivative 8a (43 mg, 0.059 mmol) in tetrahydrofuran (4 mL) and a solution of the oestrogen derivative 12 (27 mg, 0.059 mmol) in tetrahydrofuran (4 mL). The mixture was then heated overnight at 70°C. The solvent was then removed under vacuum. The residue was purified by a silica gel chromatography using a mixture of ethyl acetate and cyclohexane 1:2 and then 1:1 to afford the compound 13 as a yellow-brown oil (17 mg, 24%).

$^1$H-NMR (CDCl$_3$, 300 MHz, 20°C): $\delta$ 0.87 (s, 3H, CH$_3$ estrogen), 0.98-2.50 (br, 24H, 2CH and 11CH$_2$), 2.79 (br, 3H, CH$_2$ and 1CH), 3.48 (br, 2H), 3.77 (br, 2H), 3.81 (s, 3H, Nimidazole-CH$_3$), 4.18 (br, 1H, OH), 5.02 (br, 1H, OH), 5.80 (s, 2H, Nimidazole-CH$_2$), 6.73 (br, 1H, Ar-H), 6.63 (m, 1H, Ar-H), 6.73 (s, 1H, CH$_2$imidazole), 7.13 (d, $J$ = 9.0 Hz, 1H, 1Ar-H), 7.32-7.43 (br, 5H, Ar-H), 7.56 (m, 2H, 2CH$_2$pyridine), 7.74 (br, 1H, CH$_2$pyridine), 7.80 (s, 1H, CH$_2$imidazole), 9.05 (d, $J$ = 5.4 Hz, 2H, 2CH$_2$pyridine). $^{13}$C-NMR (CDCl$_3$, 125 MHz, 20°C): $\delta$ 11.9 (CH$_3$ estrogen), 24.4, 26.5, 27.4, 28.7, 29.6, 30.2, 33.3, 36.3 (Nimidazole-CH$_3$), 38.0, 39.3, 43.8, 44.9, 47.0, 47.9, 51.5, 67.0 (CH$_2$OH-CH$_2$), 90.5, 112.7, 115.3, 120.5, 121.3, 124.4, 125.0 (2CH$_2$pyridine), 126.4, 128.2, 128.8, 128.9, 129.0, 129.3, 132.6, 134.7, 135.7, 137.7 (CH$_2$pyridine), 138.2, 141.3 (C-Pt), 153.5, 153.8 (2CH$_2$pyridine). HRMS (positive ESI) [M+Na]: calcd for C$_{63}$H$_{92}$N$_6$O$_3$PtNa 1202.220, found 1202.218.
NB: Attempts to functionalise the NHC-complexes using the copper(I)-catalysed azide alkyne cycloaddition failed as mentioned by the selected examples in the table below.\(^6\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkyne</th>
<th>Azide</th>
<th>Copper source</th>
<th>Reductive agent</th>
<th>Ligand</th>
<th>Solvent</th>
<th>Time*</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1</td>
<td>BuN(_3)</td>
<td>(2.1 equiv.)</td>
<td>CuSO(_4) .5H(_2)O</td>
<td>ascorbic acid (0.8 equiv.)</td>
<td>none</td>
<td>H(_2)O/THF 1:2</td>
<td>6 h</td>
<td>Degradation (dark insoluble formed)</td>
</tr>
<tr>
<td>2</td>
<td>BuN(_3)</td>
<td>(2.3 equiv.)</td>
<td>CuSO(_4) .5H(_2)O</td>
<td>sodium ascorbate (12 equiv.)</td>
<td>none</td>
<td>DMF/H(_2)O 4:1</td>
<td>18 h</td>
<td>Degradation (dark insoluble formed)</td>
</tr>
<tr>
<td>3</td>
<td>BuN(_3)</td>
<td>(2.3 equiv.)</td>
<td>CuSO(_4) .5H(_2)O</td>
<td>sodium ascorbate</td>
<td>TBTA</td>
<td>DMF/H(_2)O</td>
<td>24 h</td>
<td>Starting material</td>
</tr>
<tr>
<td>4</td>
<td>BuN(_3)</td>
<td>(2.3 equiv.)</td>
<td>CuI (1.9 equiv.) + DIPEA (2.5 equiv.)</td>
<td>none</td>
<td>none</td>
<td>CH(_2)Cl(_2)</td>
<td>20 h</td>
<td>Side products</td>
</tr>
<tr>
<td>5</td>
<td>BuN(_3)</td>
<td>(2.5 equiv.)</td>
<td>CuI (1.9 equiv.) + DIPEA (2.5 equiv.)</td>
<td>none</td>
<td>none</td>
<td>CH(_2)Cl(_2)</td>
<td>20 h</td>
<td>Insoluble formed</td>
</tr>
<tr>
<td>6</td>
<td>BuN(_3)</td>
<td>(2.5 equiv.)</td>
<td>CuI (0.3 equiv.) + DIPEA (2.5 equiv.)</td>
<td>TBTA (0.4 equiv.)</td>
<td>THF</td>
<td>1 h</td>
<td>Insoluble formed</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>mPEG(_n)=N, (1 equiv.)</td>
<td>CuSO(_4) .5H(_2)O</td>
<td>ascorbic acid (0.6 equiv.)</td>
<td>none</td>
<td>tBuOH/Me OH/H(_2)O 1:5:1</td>
<td>1 h</td>
<td>Insoluble formed</td>
<td></td>
</tr>
</tbody>
</table>

*Reactions were carried out at room temperature.
5. NMR studies on \textit{trans}-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)]imidazol-2-ylidene]-palladium(II)

Effect of the temperature on the signals of N-CH$_3$ groups of the \textit{trans}-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)]imidazol-2-ylidene]-palladium(II) isomers ($^1$H-NMR in C$_6$D$_6$, 300 MHz).
References

4. R. Jothibasu, K.-W. Huang and H. V. Huynh, *Organometallics* 2010, **29** (17), 3746.
6. For a review listing all used conditions for the CuAAC, see: M. Meldal and C. W. Tornøe, *Chem. Rev.* 2008, **108**, 2952.