Electronic Supplementary Material (ESI) for Chemical Communications

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

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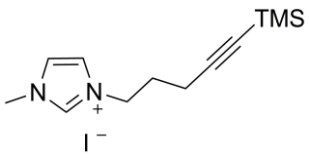
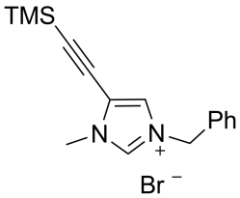
General procedures

All reactions were performed under an inert atmosphere of argon or nitrogen using standard Schlenck 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. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on a Brucker AVANCE 300 spectrometer using the residual solvent peak as reference ($CDCl_3$: 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 derivative[2] and oestrogen bromide derivative[3] have been synthesized according to the procedures described in the literature.

1. Synthesis of the ligands

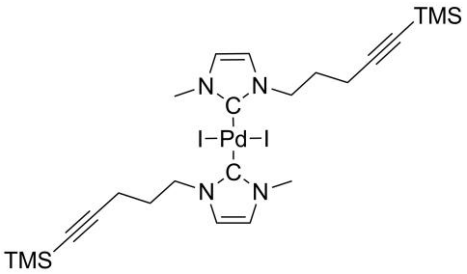


1-Methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-1H-imidazol-3-ium iodide 1. A mixture of 1-methylimidazole (0.50 g, 6.09 mmol), sodium iodide (1.82 g, 12.18 mmol) and 1-chloro-5-(trimethylsilyl)-4-pentyne (1.12 mL, 6.09 mmol) was suspended in dimethylether (8 mL) and the reaction was refluxed at 85°C overnight. 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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 0.10 (s, 9H, Si-$(CH_3)_3$), 2.10 (m, 2H, CH_2), 2.30 (t, J= 6.5 Hz, 2H, CH_2), 4.06 (s, 3H, N-CH_3), 4.42 (t, J = 7.0 Hz, 2H, CH_2), 7.43 (s, 1H, $CH_{imidazole}$), 7.57 (s, 1H, $CH_{imidazole}$), 9.83 (s, 1H, N-CH=N). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 0.08 (Si-$(CH_3)_3$), 16.8 (CH_2), 28.6 (CH_2), 37.3 (CH_3), 48.7 (N-CH_2), 87.3 (C_{alkyne}), 103.8 (C_{alkyne}), 122.5 ($CH_{imidazole}$), 123.8 ($CH_{imidazole}$), 136.8 ($NCH_{imidazolium}$).

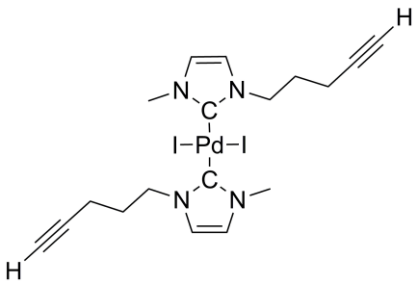


1-Methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-*1H*-imidazol-3-ium bromide. A mixture of 5-(trimethylsilyl)ethynyl-1-methylimidazole (1.04 g, 5.84 mmol) and bromobenzyle (0.69 mL, 5.84 mmol) was dissolved in acetonitrile (30 mL) and the reaction was refluxed at 75°C overnight. The solvent was removed under vacuum. The solid was washed with diethyl ether to yield the 1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-*1H*-imidazol-3-ium bromide as a white solid (1.93 g, 95%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 0.24 (s, 9H, Si-$(CH_3)_3$), 3.98 (s, 3H, N-CH_3), 5.60 (s, 2H, N-CH_2), 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). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ -0.68 (Si-$(CH_3)_3$), 34.8 (CH_3), 53.8 (CH_2), 86.5 (C_{alkyne}), 108.7 (C_{alkyne}), 119.0 ($C_{imidazole}$), 123.8 ($CH_{imidazole}$), 129.3, 129.5, 129.6, 132.5 ($C_{aromatic}$), 138.0 ($NCH_{imidazolium}$).

2. Synthesis of the biscarbenic Pd(II) complexes

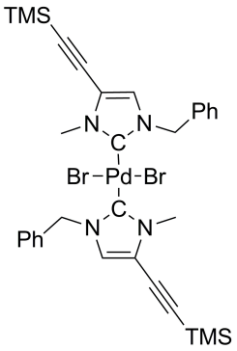


***Trans*-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II)**. The imidazolium **1** (125 mg, 0.359 mmol) was dissolved in THF (10 mL) and palladium (II) acetate (40 mg, 0.179 mmol) was added. The mixture was stirred for 2h at 75°C. The resulting suspension was 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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 0.17 (s, 9H, Si-$(CH_3)_3$), 0.18 (s, 9H, Si-$(CH_3)_3$), 2.31 (br, 8H, 4CH_2), 3.92 (s, 3H, N-CH_3), 3.95 (s, 3H, N-CH_3), 4.47 (br, 4H, 2N-CH_2), 6.86 (br, 2H, 2$CH_{imidazole}$), 6.96 (br, 2H, 2$CH_{imidazole}$). The ^{1}H 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.[4,5] ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 0.19 (2Si-$(CH_3)_3$), 17.0 (CH_2), 17.1 (CH_2), 28.3 (2CH_2), 38.5 (CH_3), 38.6 (CH_3), 49.3 (N-CH_2), 49.5 (N-CH_2), 86.4 (C_{alkyne}), 86.5 (C_{alkyne}), 105.4 (C_{alkyne}), 105.6 (C_{alkyne}), 122.2 (4$CH_{imidazole}$), 167.7 (2C-Pd). HRMS (positive ESI) [M+Na]: calcd for $C_{24}H_{40}I_2N_4PdSi_2Na$ 822.982, found 822.978.



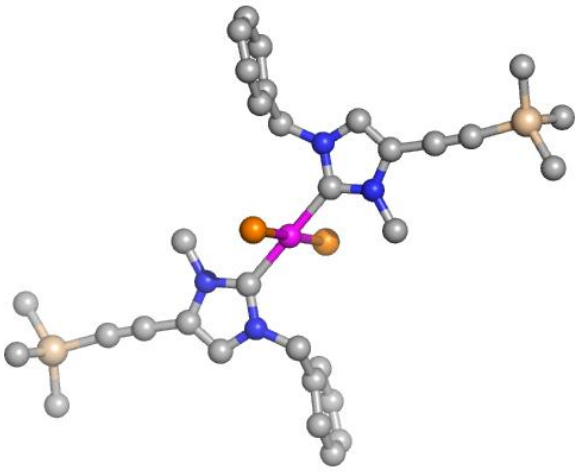
***Trans*-diiodo-di-[1-methyl-3-(pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II) 2**. Fluoride on Amberlyst® A-26 (271 mg, 0.678 mmol, 2.5 mmol/g loading) was added to a solution of the *trans*-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-

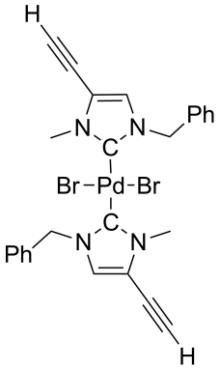
yn-1-yl)-imidazol-2-ylidene]-palladium (II) (58 mg, 0.072 mmol) in THF (15 mL). The solution was stirred 2-20 h at room temperature. The resin was then filtered off. The resulting filtrate was concentrated under vacuum to yield **2** as a light yellow powder (33 mg, 69 %). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 2.04 (s, 1H, CH_{alkyne}), 2.06 (s, 1H, CH_{alkyne}), 2.31 (br, 8H, $4CH_2$), 3.93 (s, 3H, N-CH_3), 3.96 (s, 3H, N-CH_3), 4.47 (t, *J* = 6.8 Hz, 2H, N-CH_2), 4.49 (t, *J* = 6.9 Hz, 2H, N-CH_2), 6.87 (s, 2H, $2CH_{imidazole}$), 6.96 (s, 2H, $2CH_{imidazole}$). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 15.7 ($2CH_2$), 28.5 ($2CH_2$), 38.6 ($2CH_3$), 49.4 (N-CH_2), 49.5 (N-CH_2), 69.8 (CH_{alkyne}), 69.5 (CH_{alkyne}), 82.8 (C_{alkyne}), 82.9 (C_{alkyne}), 121.9-122.3 ($4CH_{imidazole}$), 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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 0.19 (s, 9H, Si-$(CH_3)_3$), 0.22 (s, 9H, Si-$(CH_3)_3$), 4.00 (s, 3H, N-CH_3), 4.12 (s, 3H, N-CH_3), 5.57 (s, 2H, N-CH_2), 5.74 (s, 2H, N-CH_2), 6.82 (s, 2H, $2CH_{imidazole}$), 6.83 (s, 2H, $2CH_{imidazole}$), 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 ^{1}H NMR spectrum of complex **4** shows a similar signal pattern to that of complexes reported in the literature.[4,5] ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ -0.37 ($2Si-(CH_3)_3$), 36.0 (CH_3), 36.1 (CH_3), 54.8 (CH_2), 54.9 (CH_2), 90.5 ($2C_{alkyne}$), 104.6 ($2C_{alkyne}$), 118.9 ($2C_{imidazole}$), 124.5 ($CH_{imidazole}$), 124.6 ($CH_{imidazole}$), 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 $C_{32}H_{40}BrN_4PdSi_2$ 721.104, found 721.100.

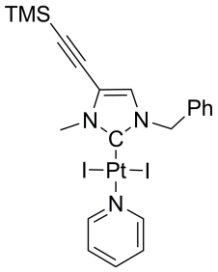
Crystal data for **4**: $C_{16}H_{20}BrN_2Pd_{0.5}Si$, yellow, crystal dimensions 0.05 x 0.05 x 0.02 mm, *M* = 401.54, triclinic, P-1, *a* = 5.7239(11), *b* = 11.368(2), *c* = 14.203(3) Å, α = 101.46(3), *β* = 91.89(3), γ = 99.34(3)°, *U* = 891.7(3) Å^3, *Z* = 2, D_c = 1.495 g cm^{-3}, μ = 7.663 mm^{-1}, *F*(000) = 404, number of data meas.: 11674 at 173(2) K, number of data with $I > 3\sigma(I)$: 2802, number of variables: 176, *R* = 0.116, *Rw* = 0.317, GOF = 1.168.



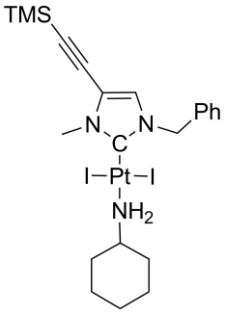


***Trans*-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II)**. Fluoride on Amberlyst® A-26 (384 mg, 0.768 mmol, 2.5 mmol/g loading) was added to a solution of TMS-protected alkyne complexe **4** (51 mg, 0.064 mmol) in THF (20 mL). The solution was stirred 20 h at room temperature. 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 %). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 3.45 (s, 1H, CH_{alkyne}), 3.48 (s, 1H, CH_{alkyne}), 4.01 (s, 3H, N-CH_3), 4.14 (s, 3H, N-CH_3), 5.59 (s, 2H, N-CH_2), 5.75 (s, 2H, N-CH_2), 6.88 (s, 2H, $2CH_{imidazole}$), 6.89 (s, 2H, $2CH_{imidazole}$), 7.26-7.56 (m, 10H, Ar-H). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 36.2 ($2CH_3$), 54.8 (CH_2), 55.0 (CH_2), 70.2 ($2CH_{alkyne}$), 86.4 ($2C_{alkyne}$), 117.8 ($2C_{imidazole}$), 125.2 ($CH_{imidazole}$), 125.3 ($CH_{imidazole}$), 128.4, 128.6, 128.9, 129.0, 135.3 ($2C_{aromatic}$), 171.4 (2C-Pd).

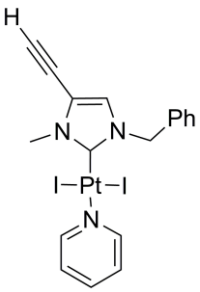
3. Synthesis of the Pt(II) complexes



***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)-*1H*-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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 0.27 (s, 9H, Si-$(CH_3)_3$), 4.03 (s, 3H, N-CH_3), 5.73 (m, 2H, CH_2), 6.82 (s, 1H, $CH_{imidazole}$), 7.36-7.43 (m, 5H, Ar-H), 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). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ -0.19 (Si-$(CH_3)_3$), 36.4 (CH_3), 55.2 (CH_2), 90.4 (C_{alkyne}), 105.0 (C_{alkyne}), 118.6 ($C_{imidazole}$), 124.2 ($CH_{imidazole}$), 125.2 ($CH_{pyridine}$), 128.8 ($CH_{aromatic}$), 129.2 ($CH_{aromatic}$), 129.5 ($CH_{aromatic}$), 135.0 ($C_{aromatic}$), 137.7 ($CH_{pyridine}$), 138.7 (C-Pt), 154.0 ($CH_{pyridine}$). HRMS (positive ESI) [M-I]: calcd for $C_{21}H_{25}IN_3PtSi$ 669.051, found 669.050.

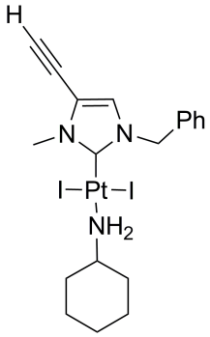


***Trans*-diiodo-(*N*-cyclohexylamine)-[1-methyl-3-benzyl-5-((trimethylsilyl)ethynyl)-imidazol-2-ylidene]-platinum(II) 8b**
^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 0.21 (s, 9H, Si-$(CH_3)_3$), 1.07-1.40 (br, 5H), 1.71-1.83 (br, 5H), 2.95 (m, 2H, NH_2), 3.26 (m, 1H), 3.88 (s, 3H, CH_3), 5.55 (s, 2H, $N_{imidazole}$-CH_2), 6.73 (s, 1H, $CH_{imidazole}$), 7.32-7.46 (br, 5H, Ar-H). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ -0.4 (Si-$(CH_3)_3$), 24.8 (CH_2), 25.3 (CH_2), 35.9 (CH_3), 36.0 (CH_2), 54.7 (CH), 54.9 ($N_{imidazole}$-CH_2), 90.3 (C_{alkyne}), 104.7 (C_{alkyne}), 118.2 ($C_{imidazole}$), 123.8 ($CH_{imidazole}$), 128.5 ($CH_{aromatic}$), 128.9 ($CH_{aromatic}$), 129.2 ($CH_{aromatic}$), 134.9 ($C_{aromatic}$), 142.0 (C-Pt). HRMS (positive ESI) [M-I]: calcd for $C_{22}H_{33}IN_3PtSi$ 689.113, found 689.130.



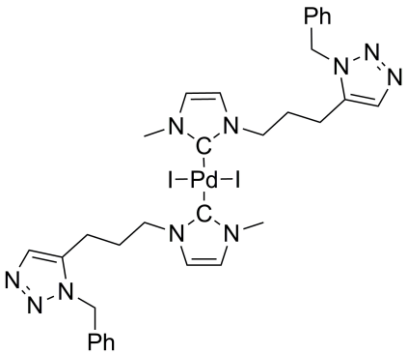
***Trans*-diiodo-(*N*-pyridine)-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-platinum(II)**. A mixture of **8a** (19 mg, 0.026 mmol) and potassium carbonate (10 mg, 0.072 mmol) was suspended in methanol (4 mL). The mixture was stirred for

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): δ 3.47 (s, 1H, CH_{alkyne}), 4.01 (s, 3H, N-CH_3), 5.70 (s, 2H, CH_2), 6.82 (s, 1H, $CH_{imidazole}$), 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): δ 36.4 (CH_3), 55.1 (CH_2), 70.2 (CH_{alkyne}), 86.5 (C_{alkyne}), 117.3 ($C_{imidazole}$), 124.4 ($CH_{imidazole}$), 125.0 ($CH_{pyridine}$), 128.2 ($CH_{aromatic}$), 129.0 ($CH_{aromatic}$), 129.3 ($CH_{aromatic}$), 134.7 ($C_{aromatic}$), 137.6 ($CH_{pyridine}$), 139.1 (C-Pt), 153.70 ($CH_{pyridine}$).



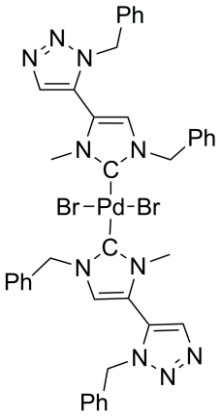
***Trans*-diiodo-(*N*-cyclohexylamine)-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-platinum(II)**. A mixture of **8b** (61 mg, 0.075 mmol) and potassium carbonate (29 mg, 0.209 mmol) was suspended in methanol (12 mL). The mixture was stirred for 2h at room temperature. The resulting suspension 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): δ 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_{alkyne}), 3.91 (s, 3H, CH_3), 5.57 (s, 2H, $N_{imidazole}$-CH_2), 6.79 (s, 1H, $CH_{imidazole}$), 7.32-7.46 (br, 5H, Ar-H). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 24.8 (CH_2), 25.2 (CH_2), 35.7 (CH_3), 36.0 (CH_2), 54.7 (CH), 54.9 ($N_{imidazole}$-CH_2), 70.1 (CH_{alkyne}), 86.4 (C_{alkyne}), 117.2 ($C_{imidazole}$), 124.4 ($CH_{imidazole}$), 128.5 ($CH_{aromatic}$), 128.9 ($CH_{aromatic}$), 129.2 ($CH_{aromatic}$), 134.8 ($C_{aromatic}$), 142.6 (C-Pt).

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

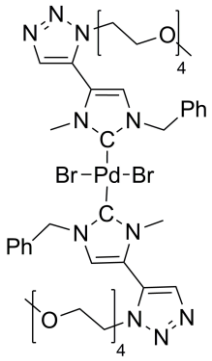


Compound 3. To a solution of Cp*RuCl(PPh_3)$_2$ (3.0 mg, 3.160 µmol) in tetrahydrofuran (0.5 mL) were added a solution of the alkyne derivative **2** (26 mg, 0.040 mmol) in tetrahydrofuran (1.5 mL) and a solution of benzyl azide (11 mg, 0.087 mmol) in tetrahydrofuran (1 mL). The mixture was then heated 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): δ 2.30 (br, 4H, 2CH_2), 2.64 (br, 4H, 2CH_2), 3.95 (s, 6H, $N_{imidazole}$-CH_3), 3.97 (s, 6H, $N_{imidazole}$-CH_3), 4.35

(br, 4H, $N_{imidazole}$-CH_2), 5.54 (s, 2H, $N_{triazole}$-CH_2), 5.57 (s, 2H, $N_{triazole}$-CH_2), 6.68-6.70 (br, 2H, CH), 6.85-6.88 (br, 2H, CH), 7.25-7.70 (br, 12H, Ar-H). HRMS (positive ESI) [M-I]: calcd for $C_{32}H_{38}IN_{10}Pd$ 795.137, found 795.139.

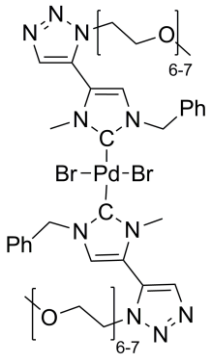


Compound 5. To a solution of Cp*RuCl(PPh_3)$_2$ (2.4 mg, 3.100 μmol) in tetrahydrofuran (0.5 mL) were added a solution of the *trans*-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II) (27 mg, 0.037 mmol) in tetrahydrofuran (0.5 mL) and a solution of benzyl azide (11 mg, 0.084 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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 3.56 (s, 3H, N-CH_3), 3.64 (s, 3H, N-CH_3); 5.35 (s, 2H, $N_{triazole}$-CH_2), 5.36 (s, 2H, $N_{triazole}$-CH_2), 5.64 (s, 2H, $N_{imidazole}$-CH_2), 5.74 (s, 2H, $N_{imidazole}$-CH_2), 6.47 (s, 1H, $CH_{imidazole}$), 6.48 (s, 1H, $CH_{imidazole}$), 6.94-7.55 (br, 20H, Ar-H); 7.77 (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), 53.2 (2$N_{triazole}$-CH_2), 55.4 ($N_{imidazole}$-CH_2), 55.4 ($N_{imidazole}$-CH_2), 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-Br]: calcd for $C_{40}H_{38}BrN_{10}Pd$ 843.154, found 843.149.

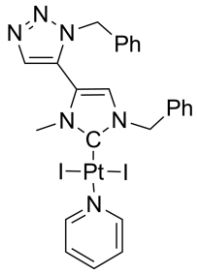


Compound 6. To a solution of Cp*RuCl(PPh_3)$_2$ (2.4 mg, 3.100 μmol) in tetrahydrofuran (1 mL) were added a solution of *trans*-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II) (27 mg, 0.037 mmol) in tetrahydrofuran (1 mL) and a solution of H_3C-(OCH_2CH_2)$_4$-N_3[1] (19 mg, 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 ethylacetate and then a mixture of ethyl acetate/methanol 3:1 to afford the compound **6** as an yellow-brown oil (31 mg, 76%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 3.13-4.09 (br, 40H, 2O-CH_3, 14CH_2 and 2N-CH_3), 4.35 (m, 4H, 2$N_{triazole}$-CH_2), 5.69 (s, 2H, $N_{imidazole}$-CH_2), 5.86 (s, 2H, $N_{imidazole}$-CH_2), 7.23-7.74 (br, 10H, Ar-H), 7.79 (s, 1H, $CH_{triazole}$), 7.82 (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 (2$N_{triazole}$-CH_2), 54.8 ($N_{imidazole}$-CH_2), 54.9 ($N_{imidazole}$-CH_2), 59.0 (2O-CH_3), 69.7 (O-CH_2), 70.3 (O-CH_2), 70.3 (O-CH_2), 70.3 (O-CH_2), 70.5 (O-CH_2), 70.5 (O-CH_2), 71.9 (O-CH_2), 120.1, 123.5, 123.6, 126.2, 126.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.7, 128.8,

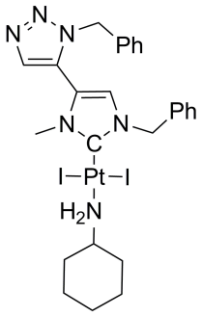
128.8, 128.8, 128.9, 128.9, 134.8, 135.5, 135.6, 172.3 (C-Pd), 172.4 (C-Pd). HRMS (positive ESI) [M+Na]: calcd for $C_{44}H_{62}Br_2N_{10}O_8PdNa$ 1145.204, found 1145.190.



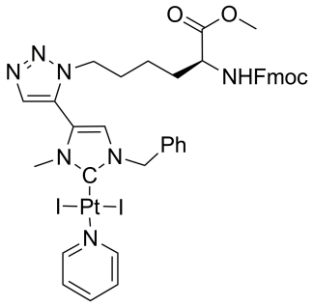
Compound 7. To a solution of Cp*RuCl(PPh_3)$_2$ (1.4 mg, 1.840 μmol) in tetrahydrofuran (0.5 mL) were added a solution of the *trans*-dibromo-di-[1-methyl-3-benzyl-5-(ethynyl)-imidazol-2-ylidene]-palladium(II) (15 mg, 0.023 mmol) in tetrahydrofuran (1 mL) and a solution of H_3C-(OCH_2CH_2)$_{6\text{-}7}$-N_3[1] (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, 60-64H, 2O-CH_3, 14CH_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.



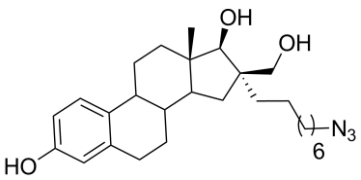
Compound 9. To a solution of the alkyne derivative **8a** (13 mg, 0.015 mmol) in tetrahydrofuran (1 mL) were added a solution of Cp*RuCl(PPh_3)$_2$ (0.5 mg, 0.680 μmol) in tetrahydrofuran (0.2 mL) and a solution of benzyl azide (7 mg, 0.053 mmol) in tetrahydrofuran (0.5 mL). The mixture was then heated 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 an 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 3$CH_{pyridine}$), 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 $C_{25}H_{24}IN_6Pt$ 730.075, found 730.085.



Compound 10. To a solution of Cp*RuCl(PPh_3)$_2$ (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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 1.10-1.85 (br, 8H, CH_2 $_{cyclohexylamine}$), 2.30 (m, 2H, CH_2 $_{cyclohexylamine}$), 3.00 (br, 2H, NH_2), 3.29 (m, 1H, $CH_{cyclohexylamine}$), 3.47 (s, 3H, CH_3), 5.35 (s, 2H, $N_{triazole}$-CH_2), 5.59 (s, 2H, $N_{imidazole}$-CH_2), 6.38 (s, 1H, $CH_{imidazole}$), 7.01 (m, 2H, 2Ar-H), 7.25-7.46 (br, 8H, 8Ar-H), 7.77 (s, 1H, $CH_{triazole}$). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 24.8 (CH_2), 25.3 (CH_2), 35.9 (CH_3), 36.0 (CH_2), 52.7 ($N_{triazole}$-CH_2), 54.9 ($N_{imidazole}$-CH_2), 55.0 (CH), 120.0 ($C_{imidazole}$), 121.4 ($CH_{triazole}$), 124.5 ($CH_{imidazole}$), 127.7 ($CH_{aromatic}$), 128.6 ($CH_{aromatic}$), 128.7 ($CH_{aromatic}$), 129.0 ($CH_{aromatic}$), 129.3 ($CH_{aromatic}$), 129.4 ($CH_{aromatic}$), 134.1 ($C_{aromatic}$), 134.7 ($C_{aromatic}$), 136.3 ($C_{triazole}$), 144.3 (C-Pt). HRMS (positive ESI) [M+H]: calcd for $C_{26}H_{33}I_2N_6Pt$ 878.050, found 878.039.

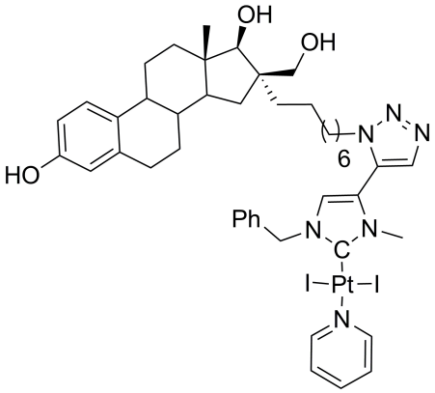


Compound 11. To a solution of Cp*RuCl(PPh_3)$_2$ (9.0 mg, 0.011 mmol) in tetrahydrofuran (3 mL) were added a solution of the alkyne derivative **8a** (55 mg, 0.076 mmol) in tetrahydrofuran (4 mL) and a solution of Fmoc-Lys(N_3)-OMe (66 mg, 0.162 mmol) in tetrahydrofuran (4 mL). The mixture was then heated 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%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 1.67-1.78 (br, 6H, $3CH_2$), 3.74 (s, 3H, OCH_3), 3.80 (s, 3H, $N_{imidazole}$-CH_3), 4.10-4.24 (br, 3H), 5.26 (m, 1H, CH_{Fmoc}), 5.79 (s, 2H, $N_{imidazole}$-CH_2), 6.78 (s, 1H, $CH_{imidazole}$), 7.19-7.78 (br, 17H, 13Ar-H, $CH_{triazole}$ and $3CH_{pyridine}$), 9.04 (d, 2H, $CH_{pyridine}$). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 22.3, 29.4, 32.0, 36.3 ($N_{imidazole}$-CH_3), 47.2, 48.4, 52.6, 53.5, 55.1 ($N_{imidazole}$-CH_2), 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 ($CH_{pyridine}$), 155.9 ($NHCO_2$), 172.5 (CO_2). HRMS (positive ESI) [M-I]: calcd for $C_{40}H_{41}IN_7O_4Pt$ 1005.191, found 1005.194.



16β-Hydroxymethyl-16α-(6'-azidooctyl)-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 literature[3] (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): δ 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 $_{estrogen}$), 3.24-3.54 (m, 3H, CHOH and CH_2OH $_{estrogen}$), 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, J1=8.4 Hz, J2=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): δ 11.9 ($CH_{3\ estrogen}$), 22.7, 24.8, 26.2, 27.4, 28.8, 29.5, 30.4, 31.9, 33.2, 38.0, 39.3, 43.9, 44.9, 47.0, 47.7, 49.2, 51.5, 67.0 (CH_2OH $_{estrogen}$), 90.7 (CHOH $_{estrogen}$), 112.7 (CH $_{arom}$), 115.3 (CH $_{arom}$), 126.4 (CH $_{arom}$), 132.5 (CH $_{arom}$), 138.1 (CH $_{arom}$), 153.5 (COH $_{arom}$). HRMS (positive ESI) [M+Na]: calcd for $C_{27}H_{41}N_3O_3Na$ 478.304, found 478.307.



Compound 13. To a solution of $Cp^*RuCl(PPh_3)_2$ (2.8 mg, 3.516 μmol) 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 an yellow-brown oil (17 mg, 24%). ^{1}H-NMR ($CDCl_3$, 300 MHz, 20°C): δ 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, $N_{imidazole}$-CH_3), 4.18 (br, 1H, OH), 5.02 (br, 1H, OH), 5.80 (s, 2H, $N_{imidazole}$-CH_2), 6.73 (br, 1H, Ar-H), 6.63 (m, 1H, Ar-H), 6.73 (s, 1H, $CH_{imidazole}$), 7.13 (d, *J* = 9.0 Hz, 1H, 1Ar-H), 7.32-7.43 (br, 5H, Ar-H), 7.56 (m, 2H, 2$CH_{pyridine}$), 7.74 (br, 1H, $CH_{pyridine}$), 7.80 (s, 1H, $CH_{triazole}$), 9.05 (d, *J* = 5.4 Hz, 2H, 2$CH_{pyridine}$). ^{13}C-NMR ($CDCl_3$, 125 MHz, 20°C): δ 11.9 ($CH_{3\ estrogen}$), 24.5, 26.3, 27.4, 28.7, 29.6, 30.2, 33.3, 36.3 ($N_{imidazole}$-CH_3), 38.0, 39.3, 43.8, 44.9, 47.0, 47.6, 48.8, 55.2 ($N_{imidazole}$-CH_2), 67.0 (CH_2-OH), 90.5, 112.7, 115.3, 120.5, 121.3, 124.4, 125.0 (2$CH_{pyridine}$), 126.4, 128.2, 128.8, 128.9, 129.0, 129.3, 132.6, 134.7, 135.7, 137.7 ($CH_{pyridine}$), 138.2, 141.3 (C-Pt), 153.5, 153.8 (2$CH_{pyridine}$). HRMS (positive ESI) [M+Na]: calcd for $C_{45}H_{58}I_2N_6O_3PtNa$ 1202.220, found 1202.218.

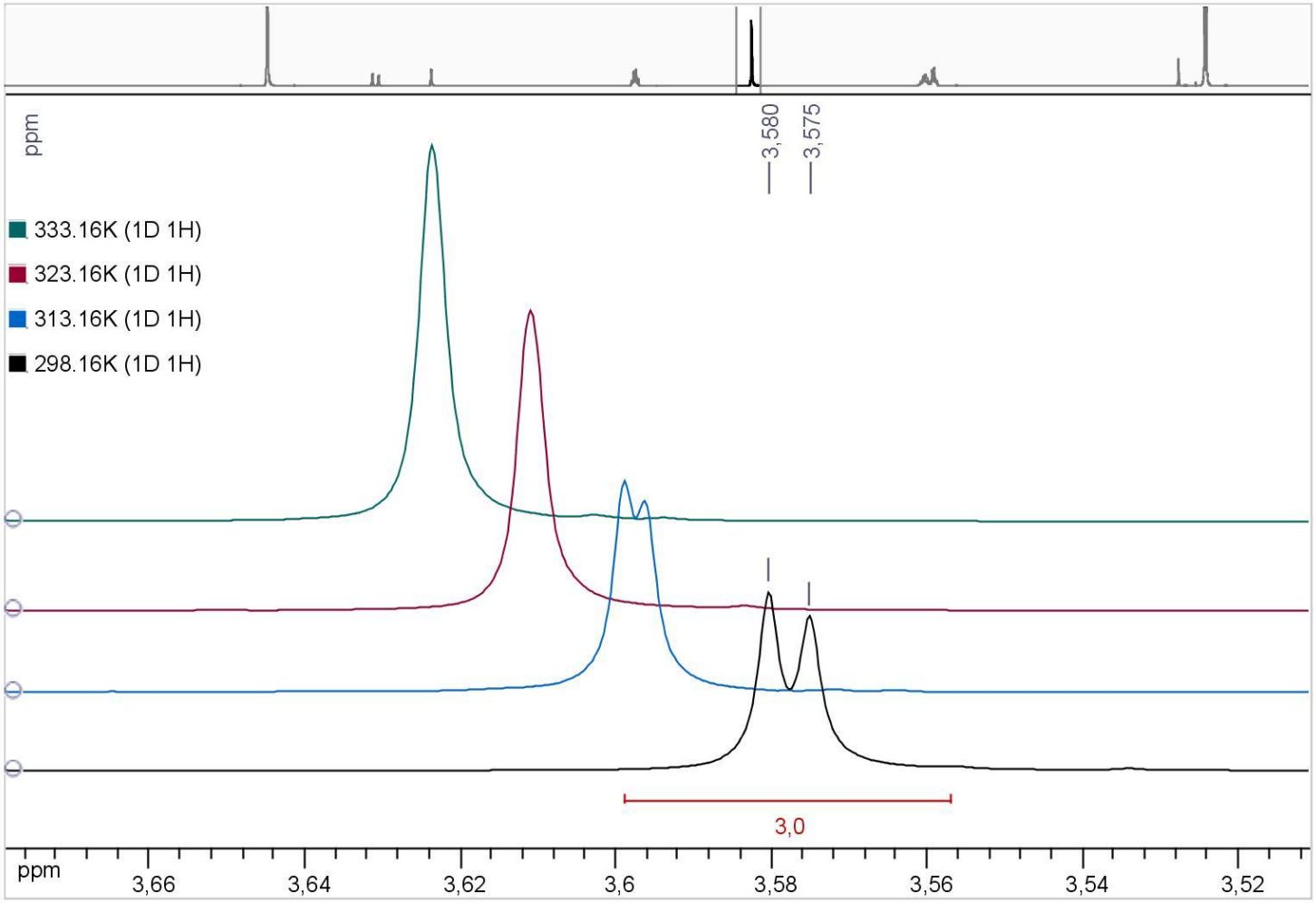
NB: Attempts to functionalise the NHC-complexes using the copper(I)-catalysed azide alkyne cycloaddition failed as mentioned by the selected examples in the table below.[6]

Entry	Alkyne	Azide	Copper source	Reductive agent	Ligand	Solvent	Time*	*Comments*
1	**2** (4,7 mM)	BnN_3 (2,1 equiv.)	$CuSO_4.5H_2O$ (0,4 equiv.)	ascorbic acid (0,8 equiv.)	none	H_2O/THF 1:2	6 h	*Degradation (dark insoluble formed)*
2	**2** (1,8 mM)	BnN_3 (2,3 equiv.)	$CuSO_4.5H_2O$ (6,6 equiv.)	sodium ascorbate (12 equiv.)	none	DMF/H_2O 4:1	18 h	*Degradation (dark insoluble formed)*
3	**2** (7,5 mM)	BnN_3 (2,3 equiv.)	$CuSO_4.5H_2O$ (0,4 equiv.)	sodium ascorbate (0,8 equiv.)	TBTA (0,26 equiv.)	DMF/H_2O 4:1	24 h	*Starting material*
4	**2** (7 mM)	BnN_3 (2,3 equiv.)	CuI (1,9 equiv.) + DIPEA (2,5 equiv.)	none	none	CH_2Cl_2	20 h	*Side products*
5	**2** (8,8 mM)	BnN_3 (2,5 equiv.)	CuI (1,9 equiv.) + DIPEA (2,5 equiv.)	none	none	CH_2Cl_2	20 h	*Insoluble formed*
6	**TMS-deprotected 4** (10 mM)	BnN_3 (2,5 equiv.)	CuI (0,3 equiv.) + DIPEA (2,5 equiv.)	none	TBTA (0,4 equiv.)	THF	1 h	*Insoluble formed*
7	**TMS-deprotected 8a** (10 mM)	$mPEG_{n=4}$-N_3 (1,1 equiv.)	$CuSO_4.5H_2O$ (0,3 equiv.)	ascorbic acid (0,6 equiv.)	none	tBuOH/MeOH/H_2O 1:5:1	1 h	*Insoluble formed*

*Reactions were carried out at room temperature.

5. NMR studies on *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 *trans*-diiodo-di-[1-methyl-3-(5-(trimethylsilyl)pent-4-yn-1-yl)-imidazol-2-ylidene]-palladium(II) isomers (^{1}H-NMR in C_6D_6, 300 MHz).



References

[1] D. Samanta, K. Kratz, X. Zhang and T. Emrick, *Macromolecules* 2008, **41**, 530.
[2] E. D. Goddard-Borger and R. V. Stick, *Org. Lett.* 2007, **9** (19), 3797.
[3] C. Descoteaux, J. Provencher-Mandeville, I. Mathieu, V. Perron, S. K. Mandal, E. Asselin and G. Berubea, *Bioorg. Med. Chem. Lett.* 2003, **13**, 3927.
[4] R. Jothibasu, K.-W. Huang and H. V. Huynh, *Organometallics* 2010, **29** (17), 3746.
[5] J. Pytkowicz, S. Roland , P. Mangeney, G. Meyer and A. Jutand, *J. Organomet. Chem.* 2003, **678**, 166.
[6] For a review listing all used conditions for the CuAAC, see: M. Meldal and C. W. Tornøe, *Chem. Rev.* 2008, **108**, 2952.