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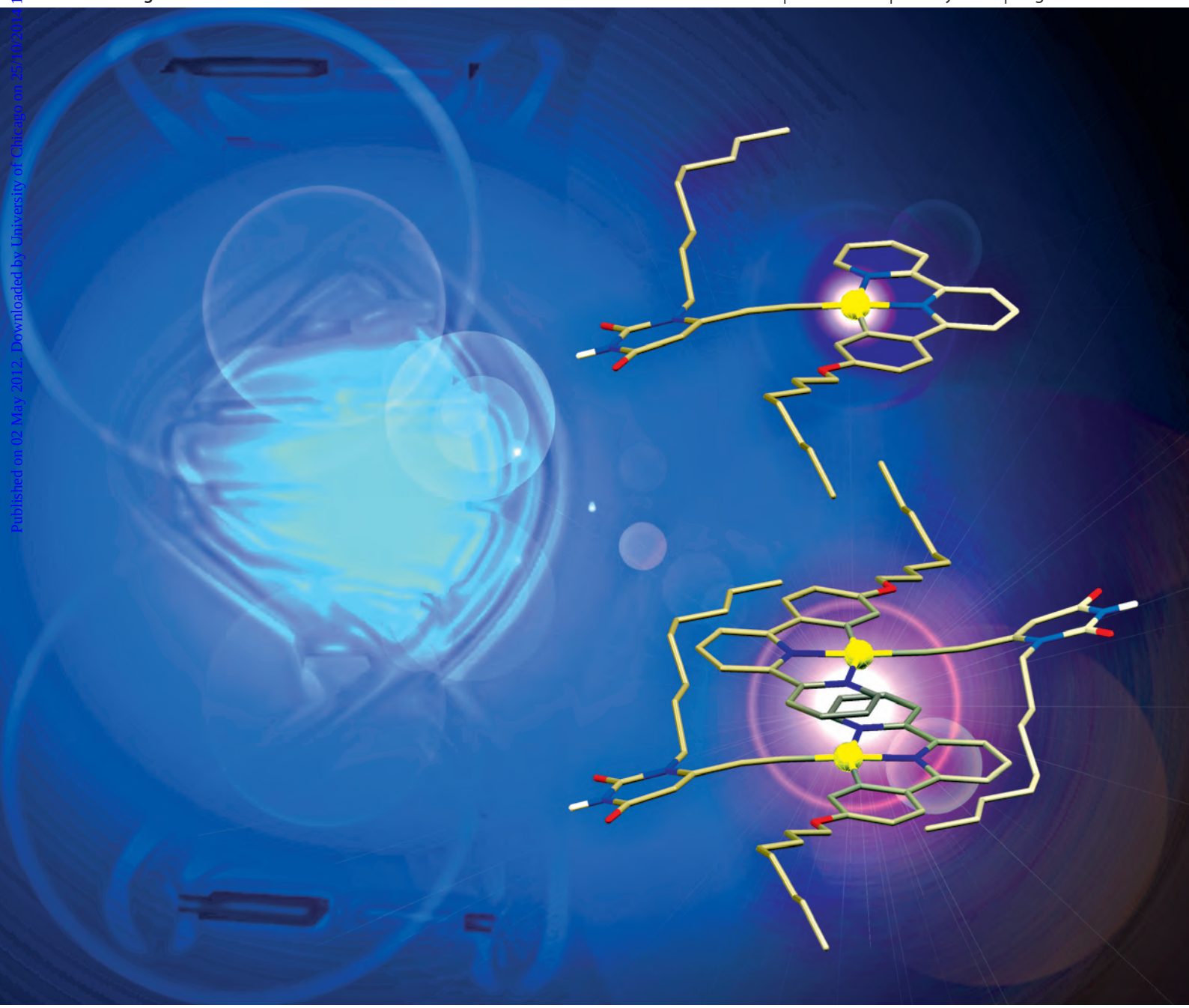

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PAPER

Design and controlled emission properties of bioorganometallic compounds composed of uracils and organoplatinum(II) moieties†

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The bioorganometallic platinum(II) compounds **PtU6** and **PtU5** were designed by the conjugation of the corresponding uracil derivative and the organoplatinum(II) compound [4-octyloxy-(C^N^N)PtCl]. The single crystal X-ray structure determination of **PtU6** revealed the formation of the dimeric structure through intermolecular hydrogen bonds between the uracil moieties of two independent molecules, wherein each hydrogen-bonded dimer was connected through Pt(II)–Pt(II) and π–π interactions. The tuning of the emission properties of the organoplatinum(II) compounds was achieved by changing the direction of hydrogen bonding sites and the molecular scaffold having two 2,6-dihexamidopyridine moieties as a complementary hydrogen bonding site for the uracil moiety, which depends on the regulation of the aggregated structures, to induce the Pt(II)–Pt(II) and π–π interactions.

Introduction

Highly-ordered molecular assemblies are constructed in bio-systems to fulfill unique functions as observed in enzymes, receptors, *etc.* The introduction of functional complexes into highly-ordered biomolecules is considered to be a convenient approach to design novel biomaterials and bio-inspired systems, *etc.* Recently, the field of bioorganometallic chemistry has drawn great attention and undergone rapid development.[1] The conjugation of organometallic compounds with biomolecules such as peptides and nucleobases is predicted to afford such bioconjugates. The architectural control of molecular self-organization is of importance for the development of functional materials[2] and non-covalent bonding is a powerful tool in the construction of architectural molecular assemblies. The regulation of hydrogen bonding is a key factor in the design of various molecular assemblies by virtue of its directionality and specificity.[3] The reversibility and tunable nature of hydrogen bonding is also of fundamental importance in the chemical and/or physical properties of molecular assemblies. The double helical DNA is created by A–T and G–C base pairs, which are mainly controlled by hydrogen bonds, π–π interactions, and hydrophobic effects.[4]

The utilization of self-assembling properties of nucleobases in bio-inspired systems offers the flexibility of exploiting four different binding motifs. A variety of metal-modified nucleobases have been designed to demonstrate molecular architecture through hydrogen bonds.[5] On the other hand, square-planar d^8 transition metal complexes possess intriguing photophysical and photochemical properties. In particular, luminescent platinum(II) complexes with oligopyridine and cyclometalating ligands have attracted much attention because of their interesting luminescence properties based on the metallophilic interaction through $d_z^2 \cdots d_z^2$ and/or π–π interactions.[6] A combination of nucleobases with luminescent platinum(II) complexes has allowed the design of novel bioconjugates. From these points of view, we herein report the design of the bioorganometallic compounds composed of uracils and organoplatinum(II) compounds and the controlled emission properties based on the regulation of aggregation (Fig. 1).

Results and discussion

The bioorganometallic platinum(II) compounds **PtU6** and **PtU5** were prepared by the reaction of [4-octyloxy-(C^N^N)PtCl] (**2**), which was obtained from the reaction of 6-(4-octyloxyphenyl)-2,2′-bipyridine (**1**) and K_2PtCl_4, with 6-ethynyl-1-octyluracil or 5-ethynyl-1-octyluracil, respectively (Scheme 1). Further structural information was obtained by single-crystal X-ray structure determination (Table 1). The X-ray crystal structure of **PtU6** revealed the formation of dimeric structure through intermolecular hydrogen bonds between the uracil moieties of two independent molecules (Fig. 2a and Table 2). Selected bond distances and angles of **PtU6** are reported in Table 3. The [4-octyloxy-(C^N^N)Pt] moiety is nearly parallel to the uracil

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†Electronic supplementary information (ESI) available: ^{1}H NMR spectra for Job's plots. CCDC reference number 851423 for **PtU6**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2dt30533j

moiety, probably due to the d,π-conjugation; the dihedral angles between the least squares plane of the [4-octyloxy-(C^N^N)Pt] and the uracil moieties are 19.8(3) and 14.8(3)°. Furthermore, each hydrogen-bonded dimer was connected through π–π interactions between the [4-octyloxy-(C^N^N)Pt] ligands as well as the uracil moieties to form π-stacks in a crystal packing, wherein Pt(II)–Pt(II) interaction (the intermolecular Pt–Pt distance is *ca.* 3.3 Å) was observed, as shown in Fig. 2b. These π–π and Pt(II)–Pt(II) interactions might require the orientation of the [4-octyloxy-(C^N^N)Pt] moiety within a limited range of locations parallel to the uracil moiety. In fact, the platinum(II) complex **PtU6** exhibited an emission band around 720 nm, derived from the triplet metal–metal-to-ligand charge transfer (^{3}MMLCT) excited state resulting from Pt(II)–Pt(II) and π–π interactions in the solid state (Fig. 3). In contrast, the platinum(II) complex **PtU5**, wherein the direction of hydrogen bonding sites of the uracil moieties is different from **PtU6**, showed an emission band based on the metal-to-ligand charge transfer (MLCT) and/or ligand-to-ligand charge transfer (LLCT) transition. The synergistic effects of emission properties are considered to depend on the aggregation properties of the platinum(II) complexes.

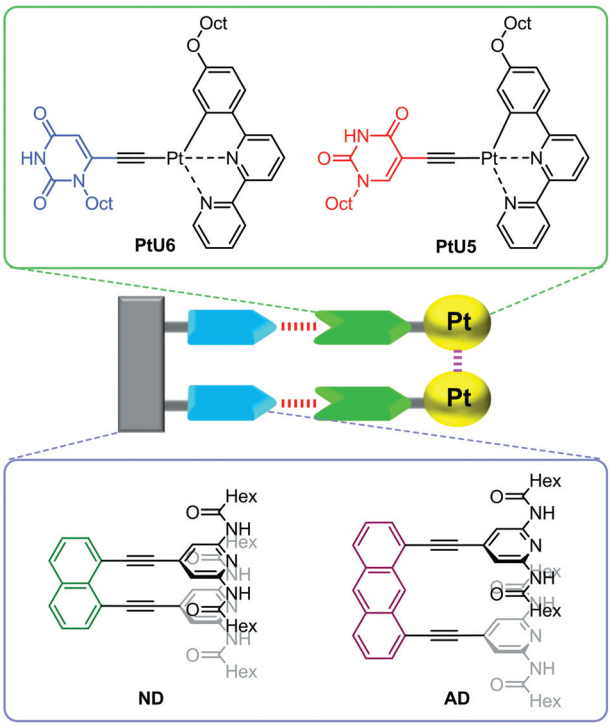
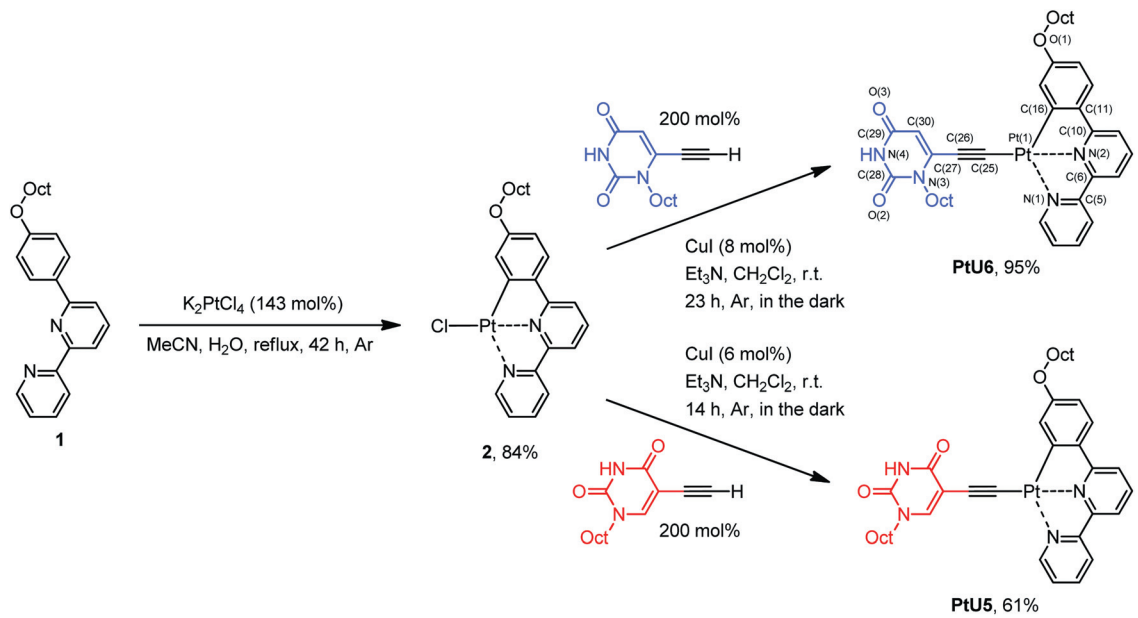


Fig. 1 Design of the bioorganometallic compounds composed of uracils and organoplatinum(II) complexes, and molecular scaffolds.

Table 1 Crystallographic data for **PtU6**

	PtU6
Formula	$C_{38.5}H_{47}N_4O_3Pt_1Cl$
Formula weight	844.36
Crystal system	Triclinic
Space group	$P\bar{1}$ (No. 2)
a, Å	12.1080(4)
b, Å	14.5494(5)
c, Å	20.4353(7)
α, °	89.7533(9)
β, °	88.4541(9)
γ, °	83.7668(9)
V, Å^3	3577.4(2)
Z	4
d_{calcd}, g cm^{-3}	1.568
μ(Mo K$_\alpha$), cm^{-1}	40.236
T, °C	−150
λ(Mo K$_\alpha$), Å	0.71075
$R_1{}^a$	0.065
w$R_2{}^b$	0.214

$^a R_1 = \sum||F_o| - |F_c||/\sum|F_o|$. ^{b} w$R_2 = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$.



Scheme 1 Synthesis of the bioorganometallic platinum(II) compounds **PtU6** and **PtU5**.

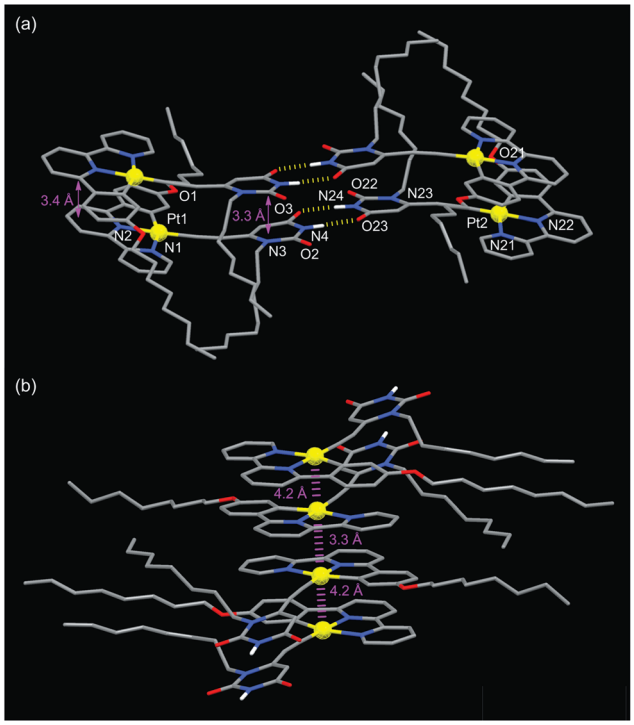


Fig. 2 (a) A hydrogen-bonded dimer through intermolecular hydrogen bonds between the uracil moieties and (b) a portion of a layer containing the π-stacked molecular assembly through π–π interactions between the [4-octyloxy-(C^N^N)Pt] ligands as well as uracil moieties in a crystal packing of **PtU6**.

Table 2 Intermolecular hydrogen bonds for **PtU6**[a]

Donor	Acceptor	D···A (Å)	D–H···A (°)
N(4)	O(23)[b]	2.787(10)	175(5)
N(24)[b]	O(3)	2.819(10)	170(4)
N(24)	O(3)[b]	2.819(10)	170(4)
N(4)[b]	O(23)	2.787(10)	175(5)

[a] Two independent molecules exist in the asymmetric unit. [b] $-X+2, -Y, -Z+1$.

Table 3 Selected bond distances (Å) and angles (°) for **PtU6**

	PtU6[a]	
Bond distances (Å)		
Pt(1)–N(1)	2.112(9)	2.141(9)
Pt(1)–N(2)	1.983(8)	1.985(8)
Pt(1)–C(16)	2.010(11)	2.010(9)
Pt(1)–C(25)	1.949(9)	1.931(9)
C(25)–C(26)	1.211(13)	1.220(13)
C(26)–C(27)	1.437(13)	1.419(13)
C(27)–C(30)	1.340(14)	1.344(14)
N(3)–C(27)	1.390(13)	1.394(13)
N(3)–C(28)	1.399(12)	1.397(12)
N(4)–C(28)	1.358(13)	1.373(13)
N(4)–C(29)	1.389(12)	1.371(13)
C(29)–C(30)	1.433(12)	1.409(13)
O(2)–C(28)	1.234(12)	1.225(12)
O(3)–C(29)	1.234(12)	1.259(12)
Bond angles (°)		
N(1)–Pt(1)–N(2)	77.8(4)	79.1(4)
N(1)–Pt(1)–C(16)	160.3(4)	160.7(4)
N(1)–Pt(1)–C(25)	101.2(4)	99.8(4)
N(2)–Pt(1)–C(16)	82.5(4)	81.7(4)
N(2)–Pt(1)–C(25)	176.3(4)	178.8(4)
C(16)–Pt(1)–C(25)	98.4(4)	99.5(4)
C(27)–N(3)–C(28)	121.0(8)	122.1(8)
N(3)–C(28)–N(4)	116.3(9)	114.7(8)
C(28)–N(4)–C(29)	125.9(8)	126.7(8)
N(4)–C(29)–C(30)	114.7(8)	114.8(9)

[a] Two independent molecules exist in the asymmetric unit.

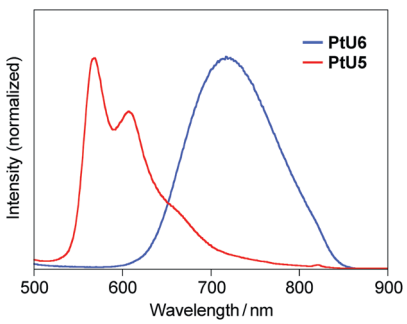
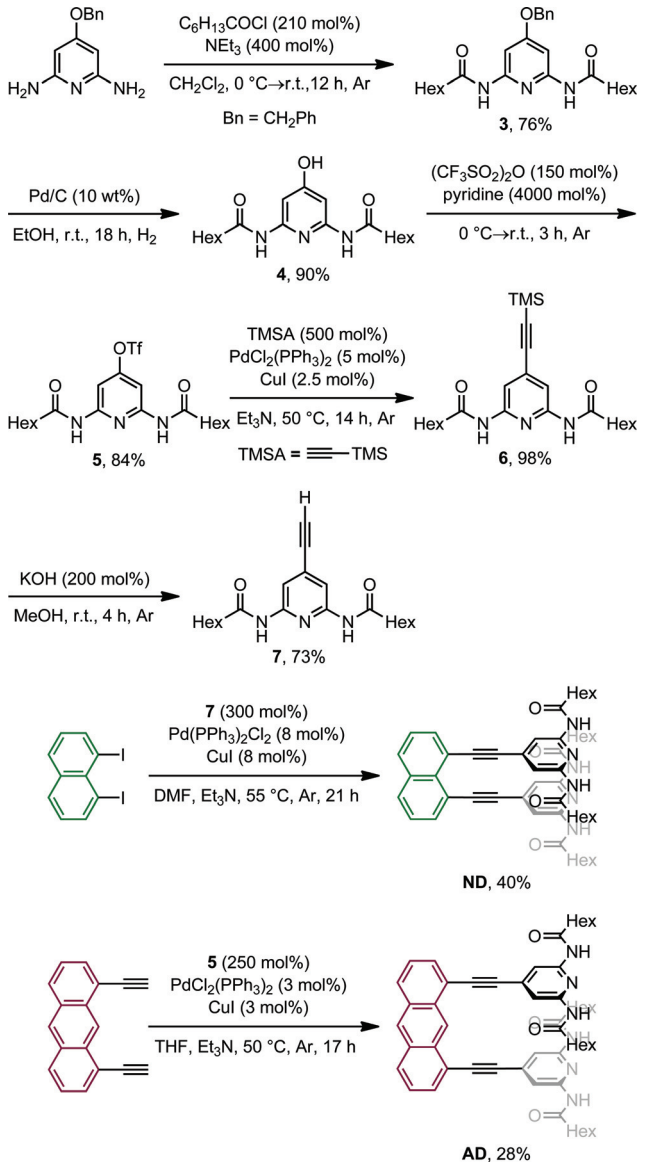


Fig. 3 Emission spectra (λ_{ex} = 470 nm) of **PtU6** and **PtU5** in the solid state at 298 K.

To control the aggregate of the organoplatinum(II) complexes with uracil moieties, molecular scaffolds **ND** and **AD** composed of the aromatic rigid naphthalene and anthracene frameworks with two 2,6-dihexamidopyridine moieties as a complementary hydrogen bonding site for the uracil moiety were designed and synthesized according to the synthetic routes shown in Scheme 2.[7] The molecular scaffold **ND** was prepared by the coupling reaction of 1,8-diiodonaphthalene and 2,6-dihexamido-4-ethynylpyridine (**7**) using the palladium-catalyzed Sonogashira coupling procedure in 40% yield. The coupling reaction of 1,8-diethynylanthracene and 4-(2,6-dihexamidopyridyl) trifluoromethanesulfonate (**5**) led to the formation of the molecular scaffold **AD** in 28% yield. The appearance of a new shoulder band at around 500 nm was observed after the addition of 0.5 molar equiv. amount of **ND** to a dichloromethane solution of **PtU6** in the UV-vis spectrum, as shown in Fig. 4a. The absorption at around 500 nm is probably assignable to the MMLCT transition based on the **ND**-induced aggregation of **PtU6** through complementary hydrogen bonding. Only **PtU6** in dichloromethane showed an emission band at 590 nm, which is ascribed to a ^{3}MLCT and/or ^{3}LLCT emission (Fig. 4b). Interestingly, **PtU6** exhibited a new emission band based on a synergistic effect around 730 nm with a concomitant decrease of the ^{3}MLCT–^{3}LLCT emission in the presence of the molecular scaffold **ND** (Fig. 4b). This emission band is assignable to a ^{3}MMLCT emission based on Pt(II)–Pt(II) and π–π interactions between the [4-octyloxy-(C^N^N)Pt] and uracil moieties, as shown in Fig. 4b. The molecular scaffold **ND** was found to play an important role in the aggregation of **PtU6** through complementary hydrogen bonding and π–π interactions between the ligands in a solution state. The 1 : 2 stoichiometry of **ND–PtU6** was confirmed by Job's plots (Fig. 5a). The stepwise association constants (K_1 and K_2 in M^{-1}) were evaluated to be log K_1 =



Scheme 2 Synthesis of the molecular scaffolds **ND** and **AD** composed of the aromatic rigid frameworks naphthalene and anthracene, respectively, with two 2,6-dihexamidopyridine moieties as a complementary hydrogen bonding sites for the uracil moiety.

3.7(3) and log K_2 = 4.1(2), respectively, for a 1 : 2 complexation of **ND** with **PtU6**.[8] The value for the ratio $4K_2/K_1 \approx 16$ clearly indicates the positive homotropic cooperative nature of this complexation. The metallophilic and π–π interactions are likely to induce the positive cooperative effect. Such absorption and emission resulting from Pt(II)–Pt(II) and π–π interactions were hardly observed in the case of **PtU5** (Fig. 4c and d), although a 1 : 2 complexation of **ND** with **PtU5** was confirmed by Job's plots (Fig. 5b). A decrease in K values (log K_1 = 2.95(2) and log K_2 = 2.82(9)) between **ND** and **PtU5** was observed.[8] These results suggest the importance of the direction of hydrogen bonding sites in arranging the [4-octyloxy-(C^N^N)Pt] moieties regularly.

An interbase distance is considered to affect the Pt(II)–Pt(II) and π–π interactions in aggregated complexes, which might be reflected in their absorption and emission properties. The molecular scaffold **AD** was also confirmed to form the 1 : 2 complex with **PtU6** by Job's plots (Fig. 5c), wherein the stepwise association constants (K_1 and K_2) were calculated to be log K_1 = 5.05(4) and log K_2 = 4.189(6), respectively.[8] The addition of 0.5 molar equiv. amount of **AD** composed of anthracene to a dichloromethane solution of **PtU6** caused a new shoulder band around 500 nm assignable to the MMLCT transition based on Pt(II)–Pt(II) and π–π interactions in the UV-vis spectrum (Fig. 6a). The increase of the ^{3}MMLCT emission at around 730 nm based on its synergistic effect and the decrease of the ^{3}MLCT–^{3}LLCT emission were also observed in the emission spectrum by the addition of 0.5 molar equiv. amount of **AD**, as shown in Fig. 6b. In comparison to the emission with the molecular scaffold **ND** composed of naphthalene, the low intensity of the ^{3}MMLCT emission and the high intensity of the ^{3}MLCT emission observed with the **AD** aggregate were probably due to the weak Pt(II)–Pt(II) and π–π interactions based on the longer interbase distance (Fig. 7). The emission properties of **PtU6** were found to be controllable by changing the molecular scaffold size.

Conclusions

In conclusion, bioorganometallic compounds were synthesized to conjugate uracils and organoplatinum(II) compounds. The designed bioorganometallic platinum(II) compound **PtU6** was

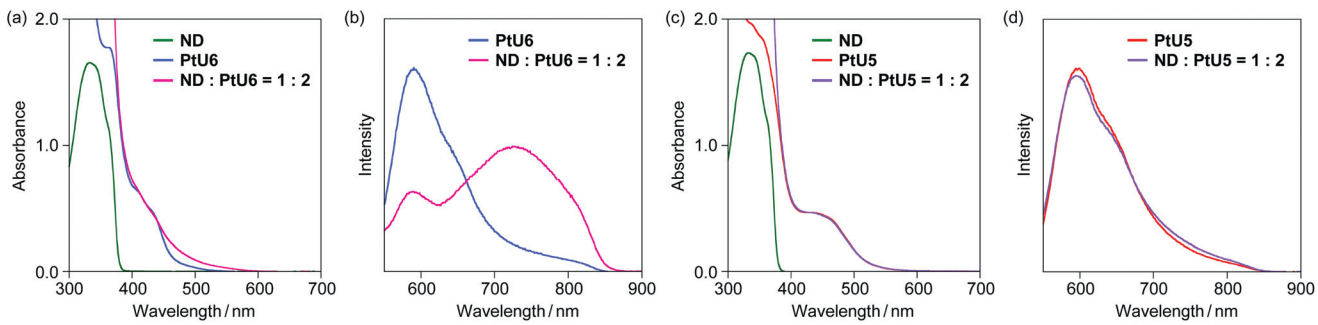


Fig. 4 (a) UV-vis spectra of **ND**, **PtU6**, and **ND–PtU6** (1 : 2) in dichloromethane ([**ND**] = 0.5 × 10^{-3} M, [**PtU6**] = 1.0 × 10^{-3} M) at 298 K, (b) emission spectra (λ_{ex} = 530 nm) of **PtU6** and **ND–PtU6** (1 : 2) in dichloromethane ([**ND**] = 0.5 × 10^{-3} M, [**PtU6**] = 1.0 × 10^{-3} M) at 298 K, (c) UV-vis spectra of **ND**, **PtU5**, and **ND–PtU5** (1 : 2) in dichloromethane ([**ND**] = 0.5 × 10^{-3} M, [**PtU5**] = 1.0 × 10^{-3} M) at 298 K and (d) emission spectra (λ_{ex} = 530 nm) of **PtU5** and **ND–PtU5** (1 : 2) in dichloromethane ([**ND**] = 0.5 × 10^{-3} M, [**PtU5**] = 1.0 × 10^{-3} M) at 298 K.

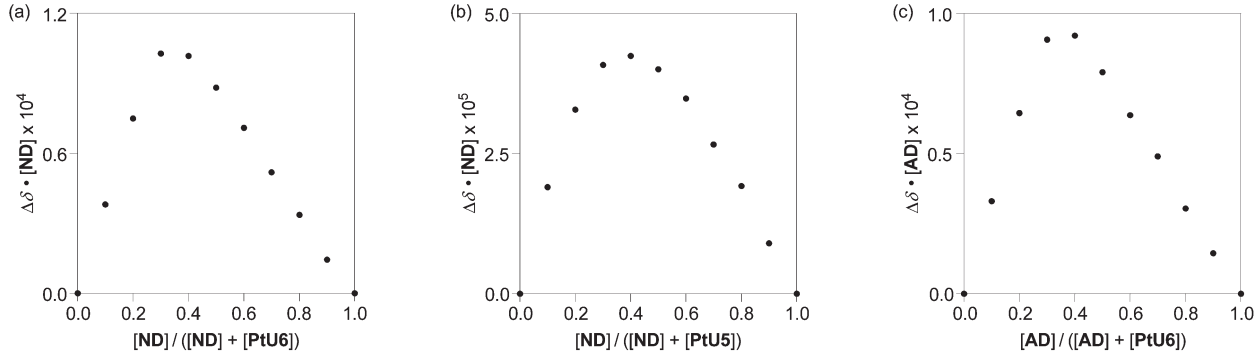


Fig. 5 (a) Job's plots for the complexation of **ND** with **PtU6**, where $\Delta\delta\times$ [**ND**] was plotted against [**ND**]/([**ND**] + [**PtU6**]) at an invariant total concentration of 2.0×10^{-3} M in CD_2Cl_2 at 295 K, (b) Job's plots for the complexation of **ND** with **PtU5**, where $\Delta\delta \times$ [**ND**] was plotted against [**ND**]/([**ND**] + [**PtU5**]) at an invariant total concentration of 2.0×10^{-3} M in CD_2Cl_2 at 295 K and (c) Job's plots for the complexation of **AD** with **PtU6**, where $\Delta\delta \times$ [**AD**] was plotted against [**AD**]/([**AD**] + [**PtU6**]) at an invariant total concentration of 2.0×10^{-3} M in CD_2Cl_2 at 295 K.

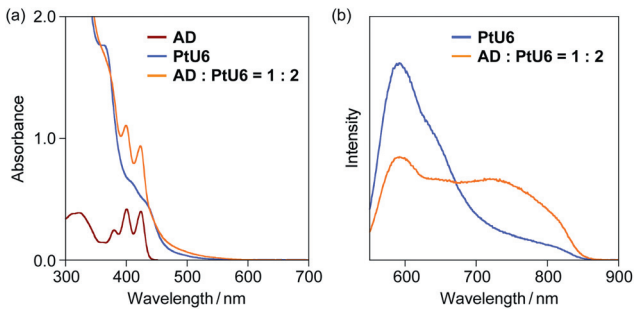


Fig. 6 (a) UV-vis spectra of **AD**, **PtU6**, and **AD–PtU6** (1 : 2) in dichloromethane ([**AD**] = 0.5×10^{-3} M, [**PtU6**] = 1.0×10^{-3} M) at 298 K and (b) emission spectra (λ_{ex} = 530 nm) of **PtU6** and **AD–PtU6** (1 : 2) in dichloromethane ([**AD**] = 0.5×10^{-3} M, [**PtU6**] = 1.0×10^{-3} M) at 298 K.

found to form a dimeric structure through intermolecular hydrogen bonds between the uracil moieties of two independent molecules, wherein each hydrogen-bonded dimer was connected through Pt(II)–Pt(II) and π–π interactions. The tuning of the emission properties of the bioorganometallic platinum(II) compounds was achieved by changing the direction of hydrogen bonding sites and the molecular scaffold size, which depends on the regulation of the aggregated structures, to induce Pt(II)–Pt(II) and π–π interactions. The architectural control of molecular assemblies using pre-organized molecular scaffolds is predicted to be a useful approach to artificial highly-ordered systems without chemical synthesis. Studies on their application to functional materials and catalysts are now in progress.

Experimental

General methods

All the reagents and solvents were purchased from commercial sources and were further purified by the standard methods, where necessary. All manipulations were carried out under Ar. Melting points were determined on a Yanagimoto Micromelting Point Apparatus and were uncorrected. Infrared spectra were obtained with a JASCO FT/IR-480 Plus spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM-ECS 400 (400 MHz) spectrometer with tetramethylsilane as an internal standard. Mass spectra were run on a JEOL JMS DX-303 spectrometer.

6-Ethynyl-1-octyluracil,[9] 5-ethynyl-1-octyluracil,[7] 4-benzyloxy-2,6-pyridinediamine,[10] 1,8-diiodonaphthalene[11] and 1,8-diethynylanthracene[12] were prepared by the methods described in the literature.

Synthesis of 6-(4-octyloxyphenyl)-2,2′-bipyridine (1)

A mixture of *N*-(2-pyridacyl)pyridinium iodide (3.4 g, 10 mmol), 3-dimethylamino-1-(4-octyloxyphenyl)propan-1-one hydrochloride (3.3 g, 10 mmol), and NH_4OAc (17 g, 0.22 mol) in glacial acetic acid (40 mL) was refluxed under Ar for 3 days. After the addition of water and dichloromethane to the resulting mixture, the organic phase was washed in saturated $NaHCO_3$ aqueous solution and brine, and then dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, CH_2Cl_2–EtOAc 49 : 1) to give the desired 6-(4-octyloxyphenyl)-2,2′-bipyridine (**1**) (2.0 g, 5.5 mmol) as a white solid.

1: Yield 55%; mp 61–62 °C; IR (KBr) 3279, 3048, 2917, 2850, 1607, 1582, 1561, 1516, 1455, 1434, 1249, 1182, 1017 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 1.0×10^{-2} M) δ 8.69 (d, 1H, J = 4.0 Hz), 8.63 (d, 1H, J = 8.0 Hz), 8.31 (d, 1H, J = 8.0 Hz), 8.10 (d, 1H, J = 8.8 Hz), 7.90–7.80 (m, 2H), 7.71 (d, 1H, J = 8.0 Hz), 7.32 (dd, 1H, J = 8.0, 4.0 Hz), 7.02 (d, 1H, J = 8.8 Hz), 4.04 (t, 2H, J = 6.4 Hz), 1.86–1.79 (m, 2H), 1.52–1.45 (m, 2H), 1.42–1.26 (m, 8H), 0.90 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1.0×10^{-2} M) 160.1, 156.5, 156.2, 155.5, 149.0, 137.6, 136.9, 131.7, 128.2, 123.7, 121.3, 119.5, 118.6, 114.7, 68.1, 31.8, 29.4, 29.3, 26.1, 22.7, 14.1 ppm; HRMS (FAB) *m/z* Calcd for $C_{24}H_{29}N_2O$ (M^+), 361.2274; Found, 361.2281; Anal. Calcd for $C_{24}H_{28}N_2O$: C, 79.96; H, 7.83; N, 7.77. Found: C, 79.94; H, 7.82; N, 7.67.

Synthesis of the platinum(II) complex 2

A mixture of **1** (100 mg, 0.28 mmol) and K_2PtCl_4 (165 mg, 0.40 mol) in acetonitrile–water (8.0 : 8.0 mL) was refluxed under Ar for 42 h and the solvent was evaporated. The product was extracted with dichloromethane. The solvent was evaporated

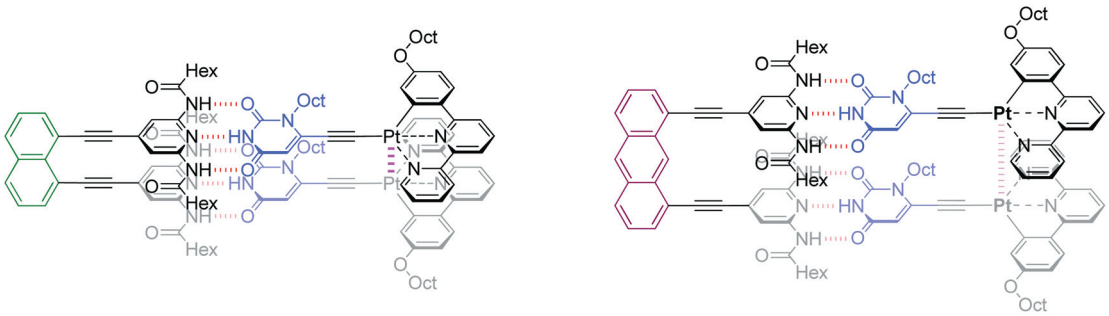


Fig. 7 Schematic representation of the controlled aggregation of the bioorganometallic platinum(II) compound **PtU6** by using molecular scaffolds.

in vacuo and the residue was washed with methanol to give the desired platinum(II) complex **2** (138 mg, 0.23 mmol) as an orange solid.

2: Yield 84%; mp 153–154 °C (decomp.); IR (KBr) 3052, 2925, 2853, 1591, 1544, 1435, 1263, 1203, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 1.0×10^{-2} M) δ 8.99 (d, 1H, J = 5.6, 1.6 Hz), 8.05 (dt, 1H, J = 8.0, 1.6 Hz), 7.90 (d, 1H, J = 8.0 Hz), 7.75 (t, 1H, J = 8.0 Hz), 7.62 (dd, 1H, J = 8.0, 5.6 Hz), 7.47 (d, 1H, J = 8.0 Hz), 7.35 (d, 1H, J = 8.0 Hz), 7.28 (d, 1H, J = 8.8 Hz), 7.13 (d, 1H, J = 2.8 Hz), 6.61 (dd, 1H, J = 8.8, 2.8 Hz), 4.03 (t, 2H, J = 6.4 Hz), 1.82–1.75 (m, 2H), 1.52–1.44 (m, 2H), 1.41–1.26 (m, 8H), 0.90 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1.0×10^{-2} M) 166.8, 161.6, 157.8, 154.7, 149.3, 145.4, 139.8, 139.1, 138.7, 127.8, 126.5, 122.8, 119.7, 118.4, 117.0, 111.1, 68.3, 32.3, 29.8, 29.7, 26.5, 23.1, 14.3 ppm; HRMS (FAB) m/z Calcd for $C_{24}H_{27}ClN_2OPt$ (M^+), 589.1454; Found, 589.1456; Anal. Calcd for $C_{24}H_{27}ClN_2OPt{\cdot}0.5H_2O$: C, 48.12; H, 4.71; N, 4.68. Found: C, 48.29; H, 4.44; N, 4.58.

Synthesis of the bioorganometallic platinum(II) complex PtU6

To a dichloromethane (3.0 mL) solution of 6-ethynyl-1-octyluracil (50 mg, 0.20 mmol), **2** (59 mg, 0.10 mmol), and CuI (1.5 mg, 7.9 μmol) was added triethylamine (1.2 mL, 8.6 mmol) under Ar at room temperature in the dark. The resulting mixture was stirred at room temperature for 23 h and the solvent was evaporated. The residue was washed with methanol, and the bioorganometallic platinum(II) complex **PtU6** was isolated as a dark red solid (76 mg, 95 μmol) by recrystalization from dichloromethane and methanol.

PtU6: yield 95%; mp 240–241 °C (decomp.); IR (KBr) 3427, 2925, 2853, 2089, 1696, 1651, 1561, 1456, 1435, 1262, 1202, 1041 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2, 2.0×10^{-3} M) δ 8.97 (dd, 1H, J = 5.2, 1.6 Hz), 8.28 (br, 1H), 8.11 (td, 1H, J = 7.6, 1.6 Hz), 7.95 (d, 1H, J = 7.6 Hz), 7.84 (t, 1H, J = 8.0 Hz), 7.63–7.57 (m, 2H), 7.52 (d, 1H, J = 8.0 Hz), 7.37 (d, 1H, J = 8.4 Hz), 7.18 (d, 1H, J = 2.4 Hz), 6.62 (dd, 1H, J = 8.4, 2.4 Hz), 5.83 (s, 1H), 4.22 (t, 2H, J = 7.6 Hz), 4.00 (t, 2H, J = 6.4 Hz), 1.87–1.75 (m, 4H), 1.50–1.11 (m, 20H), 0.89 (t, 3H, J = 6.8 Hz), 0.77 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2, 2.0×10^{-3} M) 165.7, 163.2, 162.1, 158.6, 154.7, 152.1, 151.5, 143.6, 142.7, 140.0, 139.9, 139.4, 128.2, 126.9, 124.2, 123.3, 118.7, 117.0, 110.5, 103.2, 97.2, 68.3, 46.7, 32.3, 29.8, 29.7, 29.3, 27.3, 26.5, 23.1, 23.0, 14.3 ppm; HRMS (FAB) m/z Calcd for $C_{38}H_{47}N_4O_3Pt^{194}$ (M^+), 801.3275; Found, 801.3268; Anal. Calcd for $C_{38}H_{46}N_4O_3Pt_1{\cdot}0.5H_2O$: C, 56.28; H, 5.84; N, 6.91. Found: C, 56.47; H, 5.53; N, 6.96.

Synthesis of the bioorganometallic platinum(II) complex PtU5

To a dichloromethane (4.0 mL) solution of 5-ethynyl-1-octyluracil (75 mg, 0.30 mmol), **2** (89 mg, 0.15 mmol), and CuI (1.8 mg, 9.5 μmol) was added triethylamine (1.8 mL, 13 mmol) under Ar at room temperature in the dark. The resulting mixture was stirred at room temperature for 14 h and the solvent was evaporated. The product was extracted with dichloromethane. After evaporation of the solution, the bioorganometallic platinum(II) complex **PtU5** was isolated as an orange solid (73 mg, 91 μmol) by reprecipitation from dichloromethane and ether.

PtU5: yield 61%; mp 197–199 °C (decomp.); IR (KBr) 3088, 3039, 2928, 2852, 2106, 1695, 1659, 1581, 1547, 1435, 1351, 1225, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 2.5×10^{-2} M) δ 9.36 (d, 1H, J = 5.2 Hz), 8.32 (s, 1H), 8.07 (t, 1H, J = 7.6 Hz), 7.94 (d, 1H, J = 7.6 Hz), 7.80 (t, 1H, J = 8.0 HzH), 7.63 (dd, 1H, J = 7.6, 5.2 Hz), 7.58 (d, 1H, J = 8.0 Hz), 7.48 (d, 1H, J = 8.0 Hz), 7.44 (s, 1H), 7.39 (d, 1H, J = 2.4 Hz), 7.37 (d, 1H, J = 8.4 Hz), 6.60 (dd, 1H, J = 8.4, 2.4 Hz), 4.07 (t, 2H, J = 6.4 Hz), 3.72 (t, 2H, J = 7.2 Hz), 1.83–1.68 (m, 4H), 1.52–1.25 (m, 20H), 0.91–0.87 (m, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2, 2.0×10^{-3} M) 165.7, 163.4, 162.1, 158.7, 154.9, 152.5, 150.2, 144.8, 143.7, 139.6, 139.4, 139.3, 128.2, 126.6, 124.0, 122.9, 118.4, 116.9, 112.6, 110.3, 104.8, 94.7, 68.3, 49.1, 32.3, 32.2, 29.9, 29.8, 29.7, 29.6, 29.5, 26.9, 26.5, 23.1, 23.0, 14.3, 14.2 ppm; HRMS (FAB) m/z Calcd for $C_{38}H_{47}N_4O_3Pt^{194}$ (M^+), 801.3275; Found, 801.3267; Anal. Calcd for $C_{38}H_{46}N_4O_3Pt_1{\cdot}0.5H_2O$: C, 56.28; H, 5.84; N, 6.91. Found: C, 56.49; H, 5.55; N, 6.98.

Synthesis of 2,6-dihexamido-4-ethynylpyridine (7)

2,6-Dihexamido-4-ethynylpyridine (**7**) was synthesized from 4-benzyloxy-2,6-pyridinediamine in 5 steps. To a dichloromethane (100 mL) solution of 4-benzyloxy-2,6-pyridinediamine (2.2 g, 10 mmol) and triethylamine (5.6 mL, 40 mmol) was added a dichloromethane (50 mL) solution of heptanoylchloride (3.3 mL, 21 mmol) dropwise under Ar at 0 °C. The resulting mixture was stirred at room temperature for 12 h. The resulting mixture was diluted with dichloromethane, washed with saturated $NaHCO_3$ aqueous solution and brine, and then dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the residue

was chromatographed on a silica-gel column (eluent, CH_2Cl_2) to give **3** (3.3 g, 7.6 mmol).

3: Yield 76%; mp 54–56 °C; IR (KBr) 3424, 3325, 2953, 2926, 2860, 2367, 1692, 1673, 1583, 1541, 1503, 1440 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) δ 7.66 (s, 2H), 7.61 (s, 2H), 7.46–7.32 (m, 5H), 5.14 (s, 2H), 2.33 (t, J = 7.5 Hz, 4H), 1.70–1.63 (m, 4H), 1.38–1.28 (m, 12H), 0.89 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) 172.0, 168.8, 151.3, 136.5, 128.9, 128.5, 128.1, 96.2, 70.5, 38.1, 31.9, 29.2, 25.6, 22.9, 14.2 ppm; HRMS (FAB) m/z Calcd for $C_{26}H_{38}N_3O_3$ (M^+), 440.2908; Found, 440.2924.

Benzyl ether **3** (5.6 g, 13 mmol) was dissolved in a mixture of ethanol (60 mL). Pd/C (10 wt%, 0.59 g) was added and the reaction mixture was placed under H_2, stirred at room temperature for 18 h and filtered through celite. The solvent was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, EtOAc) to give **4** (4.0 g, 12 mmol).

4: Yield 90%; mp 80–82 °C; IR (KBr) 3271, 2956, 2929, 2858, 1657, 1597, 1464, 1435, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 1.0 × 10^{-2} M) δ 10.03 (s, 1H), 7.67 (s, 2H), 7.55 (s, 2H), 2.38 (t, J = 7.6 Hz, 4H), 1.75–1.68 (m, 4H), 1.41–1.25 (m, 12H), 0.89 (t, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 1.0 × 10^{-2} M) 172.6, 168.0, 150.1, 98.0, 38.1, 31.5, 28.8, 25.4, 22.5, 14.0 ppm; HRMS (FAB) m/z Calcd for $C_{19}H_{32}N_3O_3$ (M^+), 350.2438; Found,350.2454; Anal. Calcd for $C_{19}H_{31}N_3O_3$: C, 65.30; H, 8.94; N, 12.02. Found: C, 65.05; H, 8.94; N, 11.84.

To a pyridine (6.5 mL, 80 mmol) solution of **4** (700 mg, 2.0 mmol) was added trifluoromethanesulfonic anhydride (0.5 mL, 3.0 mmol) dropwise under Ar at 0 °C. The reaction mixture was stirred at room temperature for 3 h. After removal of the solvent, the residue was poured into water and extracted with ether. The ether extract was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, hexane–EtOAc 4 : 1) to give **5** (810 mg, 1.7 mmol).

5: Yield 84%; mp 49–51 °C; IR (KBr) 3396, 3261, 3120, 3040, 2958, 2931, 2862, 2362, 1686, 1605, 1523, 1433, 1212 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) δ 7.93 (s, 2H), 7.80 (s, 2H), 2.38 (t, J = 7.7 Hz, 4H), 1.73–1.64 (m, 4H), 1.40–1.29 (m, 12H), 0.89 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) 172.2, 159.0, 151.8, 119.0, 101.9, 38.0, 31.9, 29.2, 25.4, 22.9, 14.2 ppm; HRMS (FAB) m/z Calcd for $C_{20}H_{31}F_3N_3O_5S$ (M^+), 482.1931; Found, 482.1949.

To a triethylamine (24 mL) solution of **5** (1.9 g, 4.0 mmol), $PdCl_2(Ph_3P)_2$ (0.14 g, 0.20 mmol), and CuI (19 mg, 0.10 mmol) was added trimethylsilylacetylene (2.8 mL, 20 mmol) under Ar at room temperature. The reaction mixture was stirred at 50 °C for 14 h. After removal of the solvent, the residue was poured into water and extracted with dichloromethane. The dichloromethane extract was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, CH_2Cl_2) to give **6** (1.7 g, 3.9 mmol).

6: Yield 98%; IR (KBr) 3282, 2958, 2947, 2858, 2168, 1675, 1609, 1557, 1419, 1211 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) δ 7.93 (s, 2H), 7.86 (s, 2H), 2.34 (t, J = 7.6 Hz, 4H), 1.70–1.62 (m, 4H), 1.36–1.27 (m, 12H), 0.88 (t, J = 7.0 Hz, 6H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) 172.0, 150.3, 135.6, 111.6, 102.8, 99.7, 38.0, 31.9, 29.2, 25.6, 22.9, 14.2, −0.3 ppm; HRMS (FAB) m/z Calcd for $C_{24}H_{40}N_3O_2Si$ (M^+), 430.2884; Found, 430.2899.

A mixture of **6** (1.6 g, 3.7 mmol) and KOH (0.41 g, 7.3 mmol) in methanol (55 mL) was stirred at room temperature under Ar for 4 h. The resulting mixture was diluted with ethyl acetate, washed with water and brine, and then dried over Na_2SO_4. The ethyl acetate extract was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, CH_2Cl_2–EtOAc 9 : 1) to give **7** (0.98 g, 2.7 mmol).

7: Yield 73%; mp 45–47 °C; IR (KBr) 3566, 3402, 3278, 2955, 2927, 2857, 2116, 1672, 1613, 1557, 1507, 1419, 1212 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) δ 7.97 (s, 2H), 7.67 (s, 2H), 3.31 (s, 1H), 2.35 (t, J = 7.6 Hz, 4H), 1.72–1.64 (m, 4H), 1.38–1.29 (m, 12H), 0.89 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2, 5.0 × 10^{-2} M) 171.9, 150.4, 134.7, 111.9, 81.8, 81.5, 38.1, 31.9, 29.2, 25.6, 22.9, 14.2 ppm; HRMS (FAB) m/z Calcd for $C_{21}H_{32}N_3O_2$ (M^+), 358.2489; Found, 358.2499; Anal. Calcd for $C_{21}H_{31}N_3O_2{\cdot}0.5H_2O$: C, 68.82; H, 8.80; N, 11.47. Found: C, 68.78; H, 8.76; N, 11.19.

Synthesis of the molecular scaffold ND

To a DMF (7.5 mL) solution of 1,8-diiodonaphthalene (92 mg, 0.24 mmol), **7** (0.26 g, 0.72 mmol), $PdCl_2(Ph_3P)_2$ (15 mg, 20 μmol) and CuI (4.8 mg, 25 μmol) was added triethylamine (2.5 mL, 18 mmol) at room temperature. The resulting mixture was stirred under Ar at 55 °C for 21 h. The resulting mixture was diluted with dichloromethane, washed with water and brine, and then dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, $CHCl_3$–EtOAc 19 : 1) to give **ND** (79 mg, 95 μmol) as a white solid.

ND: yield 40%; mp 178–180 °C; IR (KBr) 3296, 3050, 2954, 2928, 2856, 2211, 1703, 1672, 1610, 1555, 1420, 1260, 1213, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 5.0 × 10^{-3} M) δ 7.95–7.91 (m, 4H), 7.77 (s, 4H), 7.55–7.52 (m, 6H), 2.30 (t, 8H, J = 7.7 Hz, H_m), 1.65(q, J = 7.7 Hz, 8H), 1.39–1.28 (m, 24H), 0.90 (t, J = 7.0 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$, 5.0 × 10^{-3} M) 171.3, 149.8, 136.1, 135.9, 134.4, 131.7, 130.9, 126.2, 120.0, 111.5, 95.1, 93.9, 37.9, 32.0, 29.3, 25.6, 22.9, 14.2 ppm; HRMS (FAB) m/z Calcd for $C_{53}H_{67}N_6O_4$ (M^+), 839.5218; Found, 839.5220; Anal. Calcd for $C_{52}H_{66}N_6O_4{\cdot}H_2O$: C, 72.87; H, 8.00; N, 9.80. Found: C, 73.14; H, 7.78; N, 9.69.

Synthesis of the molecular scaffold AD

To a tetrahydrofuran (3.5 mL) solution of 1,8-diethynylanthracene (91 mg, 0.40 mmol), **5** (0.48 g, 1.0 mmol), $PdCl_2(Ph_3P)_2$ (8.4 mg, 12 μmol), and CuI (2.3 mg, 12 μmol) was added triethylamine (1.5 mL, 11 mmol) at room temperature. The mixture was stirred under Ar at 50 °C for 17 h. The resulting mixture was diluted with dichloromethane, washed with water and brine, and then dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the residue was chromatographed on a silica-gel column (eluent, CH_2Cl_2–MeOH 19 : 1) to give **AD** (98 mg, 0.11 mmol) as a pale yellow solid.

AD: Yield 28%; mp 213–215 °C; IR (KBr) 3057, 2955, 2927, 2856, 2208, 1708, 1609, 1556, 1501, 1418, 1264, 1212, 1166 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2, 5.0 × 10^{-3} M) δ 9.56 (s, 1H), 8.56 (s, 1H), 8.12 (d, J = 8.8 Hz, 2H), 7.98 (s, 4H),

7.88 (d, J = 6.8 Hz, 2H), 7.55 (dd, J = 8.8, 6.8 Hz, 2H), 2.27 (t, J = 7.6 Hz, 8H), 1.65–1.56 (m, 8H), 1.37–1.26 (m, 24H), 0.91 (t, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, CD_2Cl_2, 5.0 × 10^{-3} M) 171.4, 150.1, 135.8, 132.0, 131.9, 131.8, 130.3, 128.2, 125.7, 124.3, 120.9, 111.6, 93.7, 91.9, 37.9, 32.0, 29.4, 25.5, 23.0, 14.2 ppm; HRMS (FAB) m/z Calcd for $C_{56}H_{69}N_6O_4$ (M^+), 889.5375; Found, 889.5370.

Physical measurements

UV-vis spectra were obtained using a Hitachi U-3500 spectrophotometer in a deaerated dichloromethane solution under nitrogen at 298 K. Emission spectra were collected using a Shimadzu RF-5300PC spectrofluorophotometer in a deaerated dichloromethane solution under nitrogen at 298 K.

^{1}H NMR titrations

The CD_2Cl_2 solution of **ND** or **AD** with a concentration 0.5 × 10^{-3} M containing various amounts of **PtU6** or **PtU5** was prepared and ^{1}H NMR spectra were measured at 295 K. The changes in chemical shift of **ND** or **AD** signals as a function of **PtU6** or **PtU5** were then analyzed. The titration data for three different signals were used to determine the association constant in each experiment.

Job's plots

For each component of the complex, 5.0 mL CD_2Cl_2 solutions of accurately measured and identical concentrations (2.0 × 10^{-3} M) were prepared. The two solutions were then combined to give a series of samples of identical total concentration (2.0 × 10^{-3} M) containing different mole fractions of the two components. The ^{1}H NMR spectrum of each sample was then measured at 295 K, and these spectra were used to produce a graph of $\Delta\delta$ × [H] against [H]/([H] + [G]) shown as the Job's plots.†

X-Ray structure analysis

All the measurements for **PtU6** were made on a Rigaku R-AXIS RAPID diffractometer using graphite monochromated Mo K_α radiation. The structure of **PtU6** was solved by direct methods[13] and expanded using Fourier techniques. All the calculations were performed using the Crystal Structure crystallographic software package[14] except for the refinement, which was performed using SHELXL-97.[15] The non-hydrogen atoms were refined anisotropically. The H atoms involved in hydrogen bonding were located in electron density maps. The remainder of the H atoms were placed in idealized positions and allowed to ride with the C atoms to which each was bonded. Crystallographic details are given in Table 1. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 851423 for **PtU6**.†

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