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Efficient, Ultrafast, Microwave-Assisted Syntheses of Cycloplatinated Complexes

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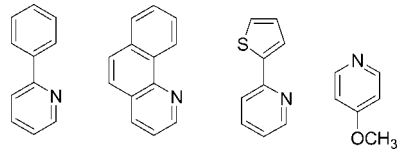
Cyclometallated chloridoplatinum complexes containing neutral monodentate ligands such as 2-phenylpyridine (**1a**), 2-(2′-thienyl)pyridine (**1c**) or 4-methoxypyridine (**1d**), as well as the cyclometallated benzo[*h*]quinoline chlorido complex with 4-methoxypyridine (**2d**), can be synthesised in a few minutes by irradiating the reaction mixture with microwaves. The single-crystal X-ray molecular structures of the solvato complexes **1**·dmso and **2**·dmso as well as **1c**, **1d** and **2d** are reported. The availability of this class of complexes in a few minutes offers the possibility of a combinatorial approach for the preparation of libraries of homologous compounds of potential interest for applicative purposes.

Introduction

Significant research efforts are currently focused on the study of cycloplatinated complexes due to their potential antitumoural activity[1] as well as their photophysical[2] or mesomorphic[3] properties. The creation of a five-membered metallacycle and formation of the chlorido-bridged dimer $[LPt(\mu\text{-}Cl)]_2$ typically occur during standard cycloplatination reactions carried out with K_2PtCl_4 and a ligand HL.[4] Although cyclometallation has been extensively studied and applied, cycloplatination is not a straightforward reaction and often requires rather drastic conditions to take place.

In the last few years, "although microwave effects are still the subject of considerable current debate and controversy",[5] controlled microwave heating has been extensively used in organic synthesis to reduce reaction times and/or improve yields. Microwave-assisted reactions involving transition metals are mainly dedicated to catalytic processes[5,6] or the synthesis of coordination complexes mainly containing iridium[7] and ruthenium,[8] and there is only one example where microwave irradiation has been used to attempt cyclometallation in the synthesis of (2-arylpyridine)-iridium complexes.[9] To the best of our knowledge, cycloplatination has never been studied under microwave irradiation.

Herein we describe new synthetic protocols for the synthesis of dinuclear chlorido-bridged cycloplatinated complexes of the ligands 2-phenylpyridine and benzo[*h*]quinoline (**a** and **b**, respectively), which were selected as representative examples of species that can undergo cycloplatination with the assistance of microwaves.



a b c d

Motivated by literature data reporting the highly cytotoxic properties of a mononuclear Pt^{II} complex bearing ligand **a** both as a cyclometallated and monodentate neutral ligand against some cisplatin-resistant cell lines,[10] this article presents new synthetic strategies for the preparation of mononuclear derivatives with a similar structure that are easily obtained from their corresponding dinuclear complexes. Several new mononuclear Pt^{II} complexes are obtained by both conventional and microwave-assisted syntheses and fully characterised by standard spectroscopic techniques. In addition, the molecular structures of all new synthesised complexes have been determined by single-crystal X-ray analysis.

Results and Discussion

Conventional Synthesis of Cycloplatinated Complexes

Cycloplatination reactions were carried out by treating ligand **a** or **b** with K_2PtCl_4 according to a conventional synthetic procedure. Under the reaction conditions used [24 h in 2-ethoxyethanol (EGEE) at 65 °C], the nature of the products obtained depends on the ligand/salt molar ratio. Thus, with a 1:1 ratio of ligand/Pt^{II} salt the expected cyclo-

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platinated chlorido-bridged dimers **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** were obtained in good yields (95 and 75%, respectively), whereas with an excess of **a** (i.e. a molar ratio of 2:1 or even higher), the mononuclear cycloplatinated complex **1a**, which contains a coordinated molecule of **a**, formed almost quantitatively (95% yield). Ligand **b** gives rise exclusively to the dimeric derivative **[2(μ-Cl)]$_2$** irrespective of the ligand/salt ratio. Complexes **[1(μ-Cl)]$_2$**, **[2(μ-Cl)]$_2$** and **1a** have been reported previously,[11] although it is worthwhile noting that **1a** was either only isolated as a side product (10% yield)[12] or was obtained unexpectedly in a two-step reaction from cisplatin in rather poor overall yield.[9b]

Dissolving **[1(μ-Cl)]$_2$** or **[2(μ-Cl)]$_2$** in dmso gave the mononuclear derivatives **1**·dmso and **2**·dmso, which bear a solvent molecule as ancillary ligand.[13] The ^{1}H NMR spectra of these complexes in $CDCl_3$ show the signal of the methyl protons of the coordinated solvent molecule ($\delta \approx 3.6$ ppm). Moreover, two characteristic doublets with broad ^{195}Pt satellites ($^3J_{Pt,H}$ between 30 and 45 Hz) are observed due to the protons of the carbon atoms in the α-position with respect to the (N,C)Pt metallacycle nitrogen and carbon atoms ($\delta \approx 9.7$ and 8.4 ppm, respectively). The structures of **1**·dmso and **2**·dmso were unequivocally confirmed by single-crystal X-ray diffraction analysis (see below).

The reactivity of **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** towards the nucleophiles **a**–**d** (see above), which differ in their basicity and steric hindrance, was tested in bridge-splitting reactions to yield the corresponding monomeric adducts. Thus, refluxing **[1(μ-Cl)]$_2$** or **[2(μ-Cl)]$_2$** in 2-ethoxyethanol for 24 h with bases **a**–**d** gave complexes **1a**, **1c**, **1d** and **2d** in 95, 88, 92 and 98% yields, respectively. No complexes were formed when **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** were treated with the sterically more demanding base **b** even after longer reaction times. In particular, for **[2(μ-Cl)]$_2$**, due to the steric hindrance of the bridge itself, only the less encumbered base **d** led to the formation of a monomeric adduct **2d**.

Microwave-Assisted Cycloplatinations

Since cycloplatinations still suffer from long reaction times of up to a week,[14] the reaction mixtures were irradiated with microwaves to try to reduce the reaction times. The Pt^{II} precursor salts used in cycloplatination reactions are highly sensitive to the experimental conditions as they readily decompose at high temperature and in the presence of oxygen. In a very recent synthesis of (diimine)Pt^{II} complexes,[15] the authors reported that microwave irradiation of a reaction mixture containing K_2PtCl_4 led to degradation to black Pt^0 within a few minutes after heating.

In order to overcome this limitation in the use of Pt^{II} precursor salts, we decided to control the microwave heating by controlling the irradiation power during the synthesis of the new cycloplatinated species. The microwave oven was initially set to reach a maximum temperature of 65 °C after 150 W irradiation. However, this temperature was reached after only 1 min of irradiation; therefore, irradiation was automatically stopped to prevent the maximum temperature from being exceeded. Increasing the reaction time by using the oven cooling option allowed further irradiation of only 1 or 2 W instead of the expected 150 W. In order to prevent the reaction carrying on at 65 °C without microwave irradiation, the reaction vessel was cooled to room temperature in an ice bath and then re-inserted into the microwave oven to be irradiated once more. Three irradiation/cooling cycles of 1 min each were performed; the reaction times reported in Table 3 are quoted relative to the total amount of effective 150 W irradiation time. The bridged dimers **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** were obtained using a 1:1 molar ratio of ligand/metal salt according to this strategy in yields of 55–65%. These low yields are due to the formation of a small amount of black Pt^0.

When 2 equiv. (or more) of ligand **a** was used to reproduce the synthesis of complex **1a**, 250 W irradiation was used in order to work at a higher temperature (110 °C) than that used for the bridge dimers. This allowed quantitative conversion to the desired product **1a** in 1 min, with no sign of K_2PtCl_4 decomposition. Under the same experimental conditions (250 W, 110 °C), but with a smaller quantity of ligand **a**, K_2PtCl_4 salt decomposition was immediately observed.

As for the conventional heating synthesis, the only product isolated upon irradiation of a reaction mixture containing ligand **b** and the Pt^{II} salt, irrespective of the ligand/salt ratio, is the dinuclear complex **[2(μ-Cl)]$_2$**, even after shorter reaction times (<1 min).

The microwave heating protocol was also applied to the bridge-splitting reactions between **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** and bases **a**–**d**, using 250 W of irradiation. Again, an irradiation/external cooling strategy was preferred in order to avoid temperatures higher than those previously established and to ensure that the reaction was performed under 250 W irradiation conditions. Even under these conditions only the mononuclear complexes **1a**, **1c**, **1d** and **2d** were obtained in a few minutes and in good yields (99, 74, 94 and 63% respectively). The spectroscopic characterisation of **1a**, **1c** and **1d** proved the presence of a single product in all cases. Their ^{1}H NMR spectra show three characteristic doublets with broad ^{195}Pt satellites due to the protons of the carbon atoms α to the Pt-coordinated atoms. The crude product resulting from the reaction between **d** and **[2(μ-Cl)]$_2$** contains a mixture of isomers and the ^{1}H NMR spectrum of the crude product suggests a mixture of *trans*-*N*,*N* (**2d**) and *cis*-*N*,*N* (**2d′**) isomers. The clear separation of the distinctive doublets due to the protons of the carbon atoms α to the N–Pt-bonded atoms (δ = 9.82 ppm for **2d** and 9.35 ppm for **2d′**) allowed the relative ratio of the two isomers (85% of **2d** and 15% of **2d′**) to be determined. Recrystallisation of the crude reaction product from a dichloromethane/methanol solution allowed the separation of the *trans*-*N*,*N* isomer **2d**. Since this isomer is the only product formed from the reaction between **[2(μ-Cl)]$_2$** and **d** during the conventional heating routine, it can be inferred that **2d** and **2d′**, which is observed only when the reaction is performed using microwave irradiation, are the thermodynamic and kinetic products, respectively.

Crystal Structure Analysis

The mononuclear complexes **1**·dmso, **2**·dmso, **1a**, **1c**, **1d** and **2d** were characterised by single-crystal X-ray diffraction analysis (Figures 1 and 2). Selected bond lengths and angles are listed in Tables 1 and 2.

Complexes **1**·dmso and **2**·dmso are formed when the dinuclear precursors are dissolved in dmso and a molecule of solvent replaces one chlorido ligand in a bridge-splitting reaction. The platinum atom in both **1**·dmso and **2**·dmso is located in a slightly distorted square-planar environment and is surrounded by the C and N atoms of the cyclometallated ligand with the coordinated solvent molecule positioned *trans* to the N atom. The Pt–S distances of 2.21–

Table 1. Selected bond lengths [Å] and angles [°] for complexes **1**·dmso and **2**·dmso.

	1·dmso	**2·dmso**
Pt–C(11)	2.001(4)	2.006(3)
Pt–N	2.055(3)	2.064(3)
Pt–S	2.2181(1)	2.2074(1)
Pt–Cl	2.4187(1)	2.4032(1)
C(11)–Pt–N	80.66(1)	81.65(1)
C(11)–Pt–S	98.95(1)	98.01(9)

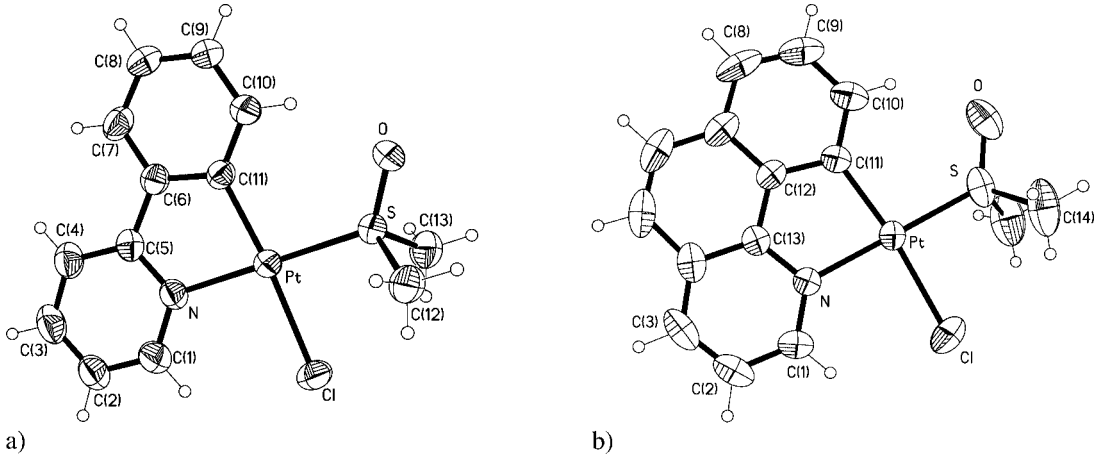

Figure 1. Molecular structures of **1**·dmso (a) and **2**·dmso (b).

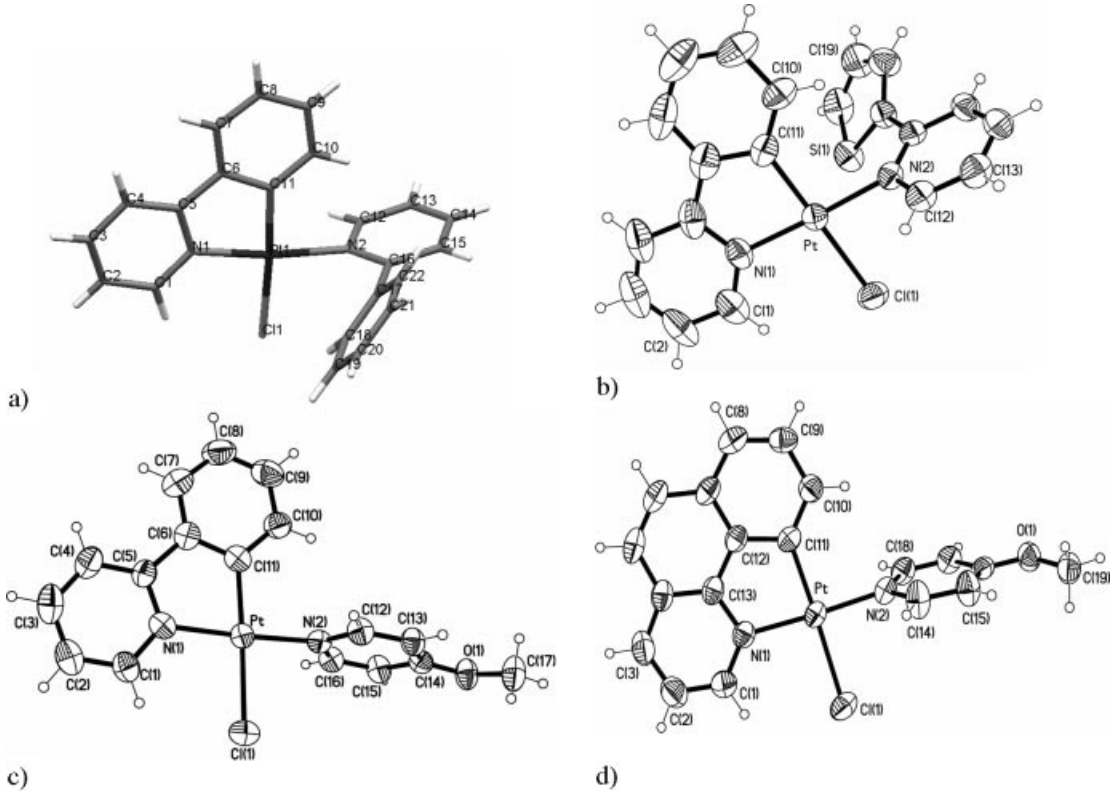

Figure 2. Molecular structures of **1a** (taken from ref.[10b]) (a), **1c** (b), **1d** (c) and **2d** (d).

Table 2. Selected bond lengths [Å] and angles [°] for complexes **1c**, **1d** and **2d**.

	1c	1d	2d
Pt–$C_{arom.}$	1.976(5), 1.981(4)	1.968(5)	1.981(2)
Pt–$N_{pyr.}$	2.015(4), 2.021(3)	2.015(4)	2.029(2)
Pt–N_{base}	2.027(3), 2.032(3)	2.014(4)	2.024(2)
Pt–Cl	2.405(1), 2.424(2)	2.413(1)	2.390(7)
$C_{arom.}$–Pt–$N_{pyr.}$	81.53(2), 81.55(2)	81.00(2)	82.91(9)
$C_{arom.}$–Pt–N_{base}	95.02(2), 93.39(2)	95.87(2)	94.47(9)
$N_{pyr.}$–Pt–N_{base}	175.77(1), 170.49(1)	176.77(1)	176.93(7)
$C_{arom.}$–Pt–Cl	177.95(1), 174.96(1)	177.75(2)	177.14(7)
$N_{pyr.}$–Pt–Cl	97.36(1), 95.29(1)	96.80(1)	94.89(6)
N_{base}–Pt–Cl	86.17(1), 90.28(1)	86.34(1)	87.78(6)

2.22 Å are similar to those found in a search of the CSD (Cambridge Structural Database, Version 5.26) for a Pt–dmso fragment with the S atom *trans* to an N atom.

The molecular structure of **1a** has already been reported in both its monoclinic and triclinic polymorphs.[9a,10b] The crystals of **1a** isolated here were found to be the triclinic polymorph from a determination of their unit cell parameters. The molecular structures of **1c**, **1d** and **2d** reveal the formation of square-planar derivatives with the nitrogen ligands **c** and **d** bound *trans* to the nitrogen atom of the cyclometallated ligands **a** (**1c** and **1d**) and **b** (**2d**).

The dihedral angles between the two aromatic rings of the cyclometallated ligand **a** in **1c** and **1d** are 2.7(2)° and 3.2(1)° (two molecules of **1c** in the asymmetric unit) and 2.4(2)°, respectively, thereby showing a certain degree of planarity. The pyridyl ring of the Pt^{II}-coordinated ligands **c** and **d** is almost perpendicular to the coordination plane in all cases. The Pt–Cl bond lengths (2.39–2.42 Å) confirm the *trans* influence of the cyclometallated carbon atom, as already observed in complex **1a**.[9a] The shortest value (2.39 Å) is found in complex **2d**, where the higher electron delocalisation of the cycloplatinated ring, and its planarity, result in a stronger Pt–Cl bond than in **1d**.

Analysis of the molecular packing showed the presence of weak hydrogen bonds of the C–H···Cl type. The presence of an oxygen atom in the methoxy substituent of **d** results in the presence of additional intermolecular C–H···O interactions, with distances of 2.7–2.8 Å, in complexes **1d** and **2d**, as shown in Figure 3a, b.

Conclusions

The results obtained from the present comparative investigations, summarised in Table 3, show that microwave irradiation is an easy, efficient and quick way to obtain mononuclear cycloplatinated complexes. Accurate simultaneous control of both temperature and irradiation power is, however, required for these sensitive cycloplatination reactions. The effective irradiation time is an important parameter to be considered when using a controlled microwave heating oven to avoid working without irradiation once the maximum set-up temperature is reached. We found that working with irradiation/external cooling cycles of a few minutes is the best way to control both parameters as it leads to less degradation of the Pt^{II} starting materials in the synthesis of the dinuclear complexes **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** and the absence of decomposition in the case of the mononuclear derivatives **1a**, **1c**, **1d** and **2d**.

As the only difference between the conventional and microwave heating procedures in bridge-splitting reactions of the dinuclear compounds **[1(μ-Cl)]$_2$** and **[2(μ-Cl)]$_2$** is the reaction time, the nature of the obtained products must depend on both the electronic effects exerted by the cyclometallated fragment and the nucleophilicity of the ancillary nitrogen ligands. In particular, the bridge cleavage of **[2(μ-Cl)]$_2$** is only possible with ligand **d** (to yield the expected complex **2d**), whereas with **a** and **c**, which react easily with **[1(μ-Cl)]$_2$** to form the derivatives **1a** and **1c**, no complexes were isolated. This behaviour can be explained on the basis of the metal-chelated ring aromaticity and the π back-bonding of the cyclometallated ligand.[16] The higher electron delocalisation of the cycloplatinated ring formed by **b**, as evidenced by the stronger Pt–Cl bond in **2d** than in **1d** (Table 2), is responsible for the higher stability of the dinuclear complex **[2(μ-Cl)]$_2$**. Consequently, only the smallest and more nucleophilic ligand (**d**) is capable of reacting with **[2(μ-Cl)]$_2$** to give the corresponding mononuclear species.

The synthesis of **1a**, which is quantitative in 1 min, is a large step forward in the preparation of highly cytotoxic compounds. Furthermore, due to their structural similarities to known cytotoxic compounds, complexes **1c**, **1d** and **2d** should also be of interest for potential therapeutic applications. The availability of this class of complexes in only a

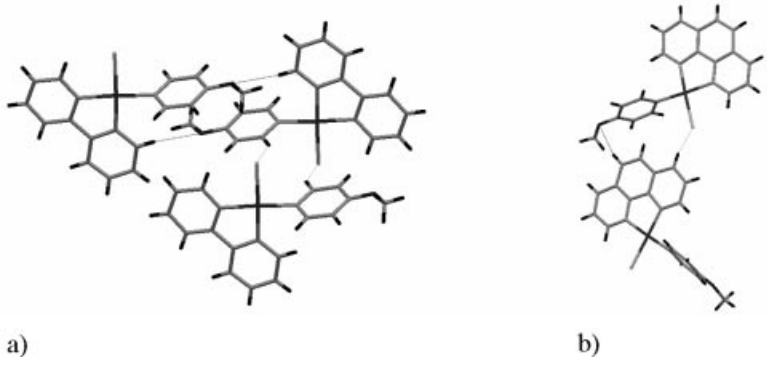

Figure 3. View of the intermolecular interactions in complexes **1d** (a) and **2d** (b).

Table 3. Comparative study between conventional and microwave-assisted syntheses.

	Conventional heating		Microwave-assisted			
	Reaction time	Yield [%]	Reaction time	Yield [%]	Power [W]	Max. temp. [°C]
[1(μ-Cl)]$_2$	48 h	95	3 min	55	150	65
[2(μ-Cl)]$_2$	48 h	75	3 min	65	150	65
1a	24 h	95	1 min	99	250	110
1c	24 h	88	6 min	74	250	110
1d	24 h	92	6 min	94	250	110
2d	24 h	98	6 min	63	250	110

few minutes by microwave-assisted synthesis is a considerable advantage as it offers the possibility of a combinatorial approach to the preparation of families of compounds for large-scale screening studies.[17]

Experimental Section

General: 2-Phenylpyridine, benzo[*h*]quinoline, 2-(2′-thienyl)pyridine, 4-methoxypyridine, potassium tetrachloroplatinate and all solvents were obtained from Aldrich and used as received. Microwave reactions were performed using a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC). This instrument consists of a continuous focused microwave power delivery system with operator-selectable power output (0–300 W). The reactions were performed in glass vessels (capacity 50 mL) equipped with a condenser under atmospheric pressure. The temperature of the contents of the vessel was monitored using an optical fibre inserted through a specially designed glass-tube directly into the centre of the reaction vessel. The contents of the vessel were stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel. ^{1}H NMR (500 MHz) spectra were recorded with a Bruker Avance 500 spectrometer with tetramethylsilane (TMS) as internal standard. Elemental analyses were performed with a Perkin–Elmer 2400 analyzer. The thermal behaviour was monitored with a Zeiss Axioscope polarizing microscope equipped with a Linkam CO 600 heating stage.

[1(μ-Cl)]$_2$. Conventional Heating Synthesis: An aqueous degassed solution (5 mL) of potassium tetrachloroplatinate (500 mg, 1.2 mmol) was added, under N_2, to a stirred degassed solution of 2-phenylpyridine (**a**; 185 mg, 1.2 mmol) in 2-ethoxyethanol (15 mL) and the reaction mixture heated to 80 °C for 48 h. After cooling in an ice bath, distilled water was added. The obtained yellow-green precipitate was filtered, washed with ethanol and dried under vacuum. Yield: 435 mg (95%). **Microwave-Assisted Synthesis:** The product was synthesised by treating ligand **a** (224 mg, 1.4 mmol) with potassium tetrachloroplatinate (600 mg, 1.4 mmol) in a degassed solution (N_2) of 2-ethoxyethanol/H_2O (3:1, v/v, 20 mL) and irradiating this mixture with 150 W of microwave radiation. The temperature was prevented from rising above 65 °C by stopping the irradiation and quickly cooling the reaction mixture. Three irradiation/cooling cycles of 1 min were performed. Upon completion, the black Pt^0 precipitate was filtered off and distilled water added. The yellow-green precipitate obtained was washed with dichloromethane and dried under vacuum. Yield: 305 mg (55%). $C_{22}H_{16}Cl_2N_2Pt_2$ (769.44): calcd. C 34.34, H 2.10, N 3.64; found C 34.73, H 1.98, N 3.61. M.p. > 350 °C. NMR spectroscopic data are not available because **[1(μ-Cl)]$_2$** is only soluble in solvents such as dmso or dmf in which bridge splitting occurs upon dissolution to give complexes containing a solvent molecule as ancillary ligand (for example **1**·dmso).

[2(μ-Cl)]$_2$. Conventional Heating Synthesis: The cycloplatination reaction of benzo[*h*]quinoline (**b**) was carried out as described for the preparation of **[1(μ-Cl)]$_2$**. Yellow-green solid. Yield: 365 mg (75%). **Microwave-Assisted Synthesis:** Complex **[2(μ-Cl)]$_2$** was prepared as described for **[1(μ-Cl)]$_2$**. Yellow-green solid. Yield: 383 mg (65%). $C_{26}H_{16}Cl_2N_2Pt_2$ (817.48): calcd. C 38.20, H 1.97, N 3.43; found C 38.49, H 2.01, N 3.09. Mp > 350 °C. NMR spectroscopic data are not available for the same reason as for **[1(μ-Cl)]$_2$**.

1·dmso: Distilled water was added to a solution of **[1(μ-Cl)]$_2$** (380 mg, 0.5 mmol) in dmso (10 mL). The resulting yellow-green powder was filtered off, dried under vacuum and recrystallised from dichloromethane/ethanol to yield **1**·dmso quantitatively (455 mg). M.p. 208 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 9.60 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 4.5, $^3J_{Pt,H}$ = 33 Hz, 1 H), 8.32 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 7.5, $^3J_{Pt,H}$ = 37.5 Hz, 1 H), 7.85 (t, $^3J_{H,H}$ = 8 Hz, 1 H), 7.71 (d, $^3J_{H,H}$ = 8 Hz, 1 H), 7.50 (d, $^3J_{H,H}$ = 7 Hz, 1 H), 7.26–7.16 (m, 3 H) 3.65 (s, 6 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): δ = 166.0, 150.1, 144.4, 140.4, 140.2, 134.1, 130.8, 125.3, 123.8, 121.9, 118.6, 47.3 ppm. $C_{13}H_{14}ClNOPtS$ (462.85): calcd. C 33.73, H 3.05, N 3.03; found C 33.95, H 2.94, N 3.25.

2·dmso: Distilled water was added to a solution of **[2(μ-Cl)]$_2$** (408 mg, 0.5 mmol) in dmso (10 mL). The resulting yellow-green powder was filtered off, dried under vacuum and recrystallised from dichloromethane/ethanol to yield **2**·dmso quantitatively (485 mg). M.p. 227 °C. ^{1}H NMR (500 MHz, CDCl3, 25 °C): δ = 9.80 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5.5, $^3J_{Pt,H}$ = 30.5 Hz, 1 H), 8.51 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 6.5, $^3J_{Pt,H}$ = 43.5 Hz, 1 H), 8.35 (d, $^3J_{H,H}$ = 8 Hz, 1 H), 7.81 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H), 7.69 (d, $^3J_{H,H}$ = 8 Hz, 1 H), 7.70–7.56 (m, 3 H) 3.71 (s, 6 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): δ = 178.0, 154.8, 143.9, 133.7, 127.0, 126.6, 124.8, 124.5, 122.7, 121.5, 118.2, 117.5, 115.4, 47.3 ppm. $C_{15}H_{14}ClNOPtS$ (486.87): calcd. C 37.00, H 2.90, N 2.88; found C 36.76, H 1.94, N 3.01.

1a. Conventional Heating Synthesis: An aqueous degassed solution of potassium tetrachloroplatinate (500 mg, 1.2 mmol in 3 mL of H_2O) was added to a stirred degassed solution of **a** (372 mg, 2.4 mmol) in 2-ethoxyethanol (9 mL) under N_2 and the reaction mixture heated to 80 °C overnight. After cooling in an ice bath, distilled water was added and the yellow precipitate produced was filtered off, washed with cold ethanol and dried under vacuum. Further crystallisation from a dichloromethane/ethanol solution yielded yellow crystals of **1a**. Yield: 615 mg (95%). **Microwave-Assisted Synthesis:** The product was synthesised by treating ligand **a** (340 mg, 2.2 mmol) with potassium tetrachloroplatinate (400 mg, 1 mmol) in a degassed solution (N_2) of 2-ethoxyethanol/H_2O (3:1, v/v, 20 mL) and irradiating this mixture with 250 W of microwave radiation for 1 min (maximum temperature reached: 110 °C). The reaction mixture was then cooled rapidly and the yellow precipitate formed was filtered off. Recrystallisation from dichloromethane/ethanol solution yielded **1a** quantitatively (591 mg). M.p. 225 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 9.60 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5, $^3J_{Pt,H}$ = 34 Hz, 1 H), 9.23 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5.5, $^3J_{Pt,H}$ = 39 Hz, 1 H), 8.08 (m, 2 H), 7.92 (td, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 2 Hz, 1 H), 7.67 (td, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 2 Hz, 1 H), 7.47 (d, $^3J_{H,H}$ = 8 Hz, 1 H) 7.35–7.26 (m, 5 H), 7.03 (td, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1.5 Hz, 1 H), 6.96 (td, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1.5 Hz, 1 H) 6.86 (td, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1.5 Hz, 1 H), 6.17 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 6.5, $^3J_{Pt,H}$ = 39 Hz, 1 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): δ = 167.2, 162.3, 154.4, 151.2, 144.2, 141.1, 139.9, 138.4, 137.7, 130.82, 129.8, 129.6, 129.3, 127.8, 127.3, 123.8, 123.2, 123.1, 121.7, 118.0 ppm. $C_{22}H_{17}ClN_2Pt$ (539.91): calcd. C 48.94, H 3.17, N 5.19; found C 48.78, H 3.25, N 5.33.

1c. Conventional Heating Synthesis: 2-(2′-Thienyl)pyridine (**c**; 400 mg, 2.5 mmol) was added to a stirred solution of **[1(μ-Cl)]$_2$** (765 mg, 1 mmol) in 2-ethoxyethanol (15 mL) and the reaction mixture heated to 80 °C overnight. The solvent was then evaporated and the resulting solid was dissolved in dichloromethane (5 mL). Addition of ethanol (15 mL) caused the formation of a precipitate. Recrystallisation of this precipitate from dichloromethane/ethanol gave yellow crystals of **1c**. Yield: 955 mg (88%). **Microwave-Assisted Synthesis:** This product was synthesised by treating ligand **c** (27 mg, 0.17 mmol) with the chlorido-bridged dimer **[1(μ-Cl)]$_2$** (63 mg, 0.08 mmol) in degassed (N_2) 2-ethoxyethanol (15 mL) and irradiating this mixture at 250 W for 2 min (maximum temperature reached: 110 °C). After each irradiation step, the mixture was cooled in an ice bath and the irradiation cycle repeated three times. Distilled water was then added and the resulting yellow precipitate filtered off and recrystallised from a dichloromethane/ethanol solution. Yield: 66 mg (74%). M.p. 258 °C (dec). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 9.70 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5, $^3J_{Pt,H}$ = 35 Hz, 1 H), 9.24 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5, $^3J_{Pt,H}$ = 45 Hz, 1 H), 8.01 (dd, $^3J_{H,H}$ = 4, $^3J_{H,H}$ = 1.5 Hz, 1 H), 7.90–7.79 (m, 3 H) 7.62 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H), 7.41 (dd, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1 Hz, 1 H), 7.38 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 1 Hz, 1 H), 7.26 (m, 1 H), 7.14 (td, $^3J_{H,H}$ = 7, $^3J_{H,H}$ = 1.5 Hz, 1 H), 7.04 (td, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1 Hz, 1 H), 6.98 (dd, $^3J_{H,H}$ = 5, $^3J_{H,H}$ = 4 Hz, 1 H), 6.87 (td, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1 Hz, 1 H), 6.21 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 7, $^3J_{Pt,H}$ = 42.5 Hz, 1 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): δ = 167.4, 155.4, 154.6, 151.4, 144.1, 141.6, 138.7, 137.6, 130.7, 130.2, 130.1, 129.5, 129.4, 127.0, 126.3, 123.5, 123.4, 123.3, 121.9, 118.2 ppm. $C_{20}H_{15}ClN_2PtS$ (545.94): calcd. C 44.00, H 2.77, N 5.13; found C 44.20, H 3.05, N 5.25.

1d. Conventional Heating Synthesis: The preparation of **1d** was carried out as described for **1c**. Yellow solid. Yield: 903 mg (92%). **Microwave-Assisted Synthesis:** Complex **1d** was prepared as described for **1c** from **[1(μ-Cl)]$_2$** and 4-methoxypyridine (**d**). Yellow solid. Yield: 76 mg (94%). M.p. 245 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 9.70 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5.5, $^3J_{Pt,H}$ = 31 Hz, 1 H), 8.78 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 7, $^3J_{Pt,H}$ = 39.5 Hz, 2 H), 7.81 (td, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 1.5 Hz, 1 H), 7.64 (d, $^3J_{H,H}$ = 8 Hz, 1 H), 7.47 (dd, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1.5 Hz, 1 H), 7.14–7.08 (m, 2 H), 6.99 (td, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 1.5 Hz, 1 H), 6.92 (d, $^3J_{H,H}$ = 7 Hz, 2 H), 6.44 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 6.5, $^3J_{Pt,H}$ = 41.5 Hz, 1 H), 3.95 (s, 3 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): δ = 171.9, 152.5, 149.1, 140.4, 130.7, 127.2, 125.4, 124.9, 124.6, 123.1, 122.9, 120.9, 119.9, 110.6, 55.45 ppm. $C_{17}H_{15}ClN_2OPt$ (493.94): calcd. C 41.35, H 3.06, N 5.67; found C 41.38, H 3.29, N 5.98.

2d. Conventional Heating Synthesis: Complex **2d** was prepared as described for **1c** from **[2(μ-Cl)]$_2$** and **d**. Yellow solid. Yield: 1 g (98%). **Microwave-Assisted Synthesis:** The reaction was performed as described for **1c**. The ^{1}H NMR spectrum of the crude reaction product shows signals for an isomeric mixture (see text) containing **2d** (85%) and **2d′** (15%). Recrystallisation of the crude yellow solid from a dichloromethane/ethanol solution allowed the major thermodynamic isomer **2d** to be separated. Yield: 53 mg (63%). M.p. 268 °C (dec). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 9.82 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 5.5, $^3J_{Pt,H}$ = 35 Hz, 1 H), 8.90 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 7, $^3J_{Pt,H}$ = 37.5 Hz, 2 H), 8.26 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 1 Hz, 1 H), 7.74 (d, $^3J_{H,H}$ = 9 Hz, 1 H), 7.58 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H), 7.55 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H), 7.47 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 5.5 Hz, 1 H), 7.35 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H), 6.95 (d, $^3J_{H,H}$ = 7 Hz, 2 H), 6.71 (d with broad ^{195}Pt satellites, $^3J_{H,H}$ = 7.5, $^3J_{Pt,H}$ = 37.5 Hz, 1 H), 3.96 (s, 3 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): δ = 166.4, 156.9, 154.8, 150.3, 141.6, 139.8, 137.6, 133.6, 129.3, 129.1, 127.9, 126.4, 123.5, 121.6, 120.9, 112.0, 56.1 ppm. $C_{19}H_{15}ClN_2OPt$ (517.87): calcd. C 44.07, H 2.92, N 5.41; found C 44.38, H 3.09, N 5.71.

X-ray Diffraction Studies: X-ray data were collected with a Bruker-Nonius X8 Apex CCD area detector equipped with a graphite-monochromated Mo-K_α radiation source (λ = 0.71073). Data reduction was performed using the SAINT programs; absorption corrections based on multiscan techniques were performed with SADABS.[18] All structures were solved by the Patterson method (SHELXS/L program in the SHELXTL-NT software package)[19] and refined by full-matrix least-squares based on F^2. All non-hydrogen atoms were refined anisotropically and hydrogen atoms were included as idealised atoms riding on the respective carbon atoms with C–H bond lengths appropriate to the carbon atom hybridisation. CCDC-646172 to -646176 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal Data for 1·dmso: $C_{13}H_{14}ClNOPtS$, M_r = 462.85 g mol^{-1}, size 0.28 × 0.20 × 0.02 mm, monoclinic, space group $P2_1/c$, a = 9.6290(8), b = 18.9145(1), c = 7.3691(6) Å, β = 91.238(3)°, F(000) = 872, V = 1341.80 (2) Å^3, T = 298 K, Z = 4, $D_{calcd.}$ = 2.291 g cm^{-3}, μ = 10.798 mm^{-1}, $2\theta_{max}$ = 56.6°. The structure was solved by the Patterson method and refined on F^2 to R_1 (wR_2) = 0.0278 (0.0609) using 2916 reflections with $I > 2\sigma(I)$. GOF = 1.056.

Crystal Data for 2·dmso: $C_{15}H_{14}ClNOPtS$, M_r = 486.87 g mol^{-1}, size 0.32 × 0.16 × 0.16 mm, orthorhombic, space group $Pnma$, a = 11.2795(2), b = 6.9794(1), c = 18.399(3) Å, F(000) = 920, V = 1448.5 (4) Å^3, T = 298 K, Z = 4, $D_{calcd.}$ = 2.233 Mg m^{-3}, μ = 10.009 mm^{-1}, $2\theta_{max}$ = 56.6°. The structure was solved by the Patterson method and refined on F^2 to R_1 (wR_2) = 0.0178 (0.0359) using 1768 reflections with $I > 2\sigma(I)$. GOF = 1.072.

Crystal Data for 1c: $C_{20}H_{15}ClN_2PtS$, M_r = 545.94 g mol^{-1}, size 0.32 × 0.28 × 0.16 mm, monoclinic, space group $P2_1/n$, a = 17.962(2), b = 9.0825(1), c = 22.107(3) Å, β = 92.111(2)°, F(000) = 2080, V = 3604.1(8) Å^3, T = 298 K, Z = 8, $D_{calcd.}$ = 2.012 g cm^{-3}, μ = 8.055 mm^{-1}, $2\theta_{max}$ = 56.6°. The structure was solved by the Patterson method and refined on F^2 to R_1 (wR_2) 0.0297 (0.0685) using 7268 reflections with $I > 2\sigma(I)$. GOF = 1.029.

Crystal Data for 1d·CHCl$_3$: $C_{18}H_{16}Cl_4N_2OPt$, M_r = 613.22 g mol^{-1}, size 0.40 × 0.20 × 0.02 mm, triclinic, space group $P\bar{1}$, a = 9.3783(7), b = 9.4050(7), c = 13.2499(9) Å, α = 73.945(3)°, β = 82.691(3)°, γ = 63.670(2)°, F(000) = 584, V = 1006.57(13) Å^3, T = 298 K, Z = 2, $D_{calcd.}$ = 2.023 g cm^{-3}, μ = 7.511 mm^{-1}, $2\theta_{max}$ = 50.7°. The structure was solved by the Patterson method and refined on F^2 to R_1 (wR_2) 0.0272 (0.0559) using 3192 reflections with $I > 2\sigma(I)$. GOF = 1.076.

Crystal Data for 2d: $C_{19}H_{15}ClN_2OPt$, M_r = 517.87 g mol^{-1}, size 0.46 × 0.40 × 0.20 mm, monoclinic, space group $P2_1/n$, a = 9.1327(13), b = 10.1178(14), c = 18.010(3) Å, β = 90.165(6)°, $F(000)$ = 984, V = 1664.2(4) Å^3, T = 298 K, Z = 4, $D_{calcd.}$ = 2.067 g cm^{-3}, μ = 8.599 mm^{-1}, $2\theta_{max}$ = 61.0°, The structure was solved by the Patterson method and refined on F^2 to R_1 (wR_2) 0.0203 (0.0419) using 4244 reflections with $I > 2\sigma(I)$. GOF = 1.032.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra are shown in Figures S1–S6.

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