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From 1,2,4-triazines towards substituted pyridines and their cyclometallated Pt complexes

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ABSTRACT

A new, efficient methodology for the synthesis of substituted thienylpyridines includes the synthesis of 3-thienyl-1,2,4-triazines using simple heterocyclisation followed by easy transformation of the triazine ring to a pyridine through an aza Diels–Alder approach. A variety of substituted pyridines can be easily achieved using cheap, commercially available reagents such as bromoacetylarenes, aroyl hydrazides, norbornadiene, and enamines in various combinations. New thienylpyridines form phosphorescent cyclometallated Pt complexes.

A significant research effort has focused on the photophysical and photochemical properties of luminescent cyclometallated Ir and Pt complexes.[1–3] These complexes have found a wide range of applications such as optical chemosensors,[4] photocatalysts,[5] molecular photochemical devices for solar energy conversion[6] and biological labelling reagents.[7] In particular, they are considered advantageous for application as phosphorescent emitters in organic light-emitting diodes (OLEDs).[8,9] Some cyclometallated platinum and iridium complexes of 2-(hetero)arylpyridines, which also contain 1,3-diketonates as auxiliary ligands, were reported to be strongly emissive, and the nature of the cyclometallating ligand was found to affect strongly the energy of the emissive state so that the emission colour could be tuned.[10,11] Thus, the photophysical properties of complexes can be tuned by appropriate ligand design.

It is known that 1,2,4-triazines can be converted into pyridines through an aza Diels–Alder reaction.[12] Thus, a combination of the wide variety of methods for the synthesis of substituted 1,2,4-triazines, coupled with the aza Diels–Alder reaction with various dienophiles, allows for the synthesis of different functionalised pyridines.[13–19] In this Letter we report the application of 1,2,4-triazine chemistry in the development of a new, efficient, flexible and straightforward methodology for the synthesis of ligands capable of forming cyclometallated complexes with Pt^{II}.

The method started with the synthesis of 1,2,4-triazines using the heterocyclisation reaction described by Saraswathi and Srinivasan in 1971, where 2-bromoacetophenone was reacted with two equivalents of acid hydrazides in the presence of a base to give 3,6-disubstituted-1,2,4-triazines.[20] We found that this approach was not always consistent and in some cases the yields of the desired triazines were far from perfect. Thus, the reactions of bromoacetylarenes **1a**–**d** with pyridine-2-carboxylic acid hydrazide **2** resulted in 6-aryl-3-pyridyl-1,2,4-triazines **3a**–**d** in 12–22% yields (Scheme 1). The low yields (compared with the method[21] using cyclisation of hydrazones of 2-oximinoacetophenones and 2-pyridinecarboxaldehyde) are partly compensated by the fact that bromoacetylarenes are more readily available than oximinoacetophenones (e.g., di- and trimethoxy derivatives). Transformations of the pyridyltriazines **3** into arylbipyridines **4** via aza Diels–Alder reactions with 2,5-norbornadiene have been reported.[21]

Fortunately, synthesis of the desired thienyltriazines was more successful. Reactions of bromoacetylarenes **1a,b** and thienylcarboxylic acid hydrazide **5** in the presence of sodium acetate gave 6-aryl-3-thienyl-1,2,4-triazines **6a,b** in 60–65% yields (Scheme 1).[22] The best solvent for the reaction was a mixture of ethanol–acetic acid (3:1). Simple filtration of the resulting crystals from the reaction mixture gave pure product **6**. This synthetic procedure is very simple and can be performed on a multigram scale. The next step in the synthesis of the target ligands is the inverse-electron-demand Diels–Alder reaction. The electron-rich dienophile 1-morpholinocyclopentene reacts readily with electron-deficient 1,2,4-triazines to give cyclopenteno[*c*]pyridines **7a,b** in 55–82% yields

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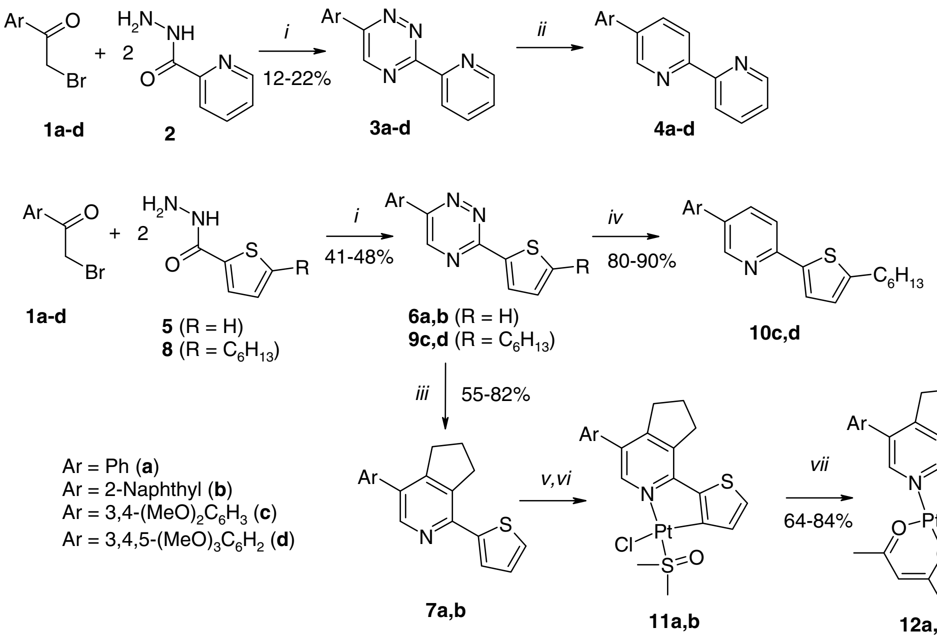

Scheme 1. Synthesis of substituted thienylpyridines. Reagents and conditions: (i) EtOH/AcOH, NaOAc, reflux, 12 h; (ii) 2,5-norbornadiene, *o*-xylene, reflux, 12 h; (iii) 1-morpholinocyclopentene, 220 °C, 0.5 h; (iv) 2,5-norbornadiene, *o*-xylene, 200 °C, 12 h; (v) $K_2[PtCl_4]$, AcOH, reflux, 24 h; (vi) DMSO, reflux, 10 min; (vii) Na *acac*, acetone, rt, 12 h.

(Scheme 1).[23] The reaction is performed in the absence of solvent at high temperature (220 °C). Morpholinocyclopentene must be used in 3–5-fold excess to compensate for partial decomposition.

To increase the solubility of the thienylpyridines and their complexes, we decided to introduce an aliphatic chain to the molecule. Thus, the reactions of 5-hexylthiophene-2-carboxylic acid hydrazide **8** with 2-bromo-3′,4′-dimethoxyacetophenone **1c** and 2-bromo-3′,4′,5′-trimethoxyacetophenone **1d** under the conditions described above resulted in hexylthienyltriazines **9c,d** (Scheme 1). Transformation of triazines **9** to monocyclic pyridines **10c,d** was performed by heating with 2,5-norbornadiene in *o*-xylene in an autoclave at elevated temperatures (200 °C), that allowed the reaction time to be shortened significantly (12 h) with no adverse effect on the yield. There were no cross-coupling reactions, and therefore expensive reagents and complicated reaction conditions are avoided. All the reactions are easily scalable and can be performed on multigram scale.

Cyclometallated Pt^{II} complexes of cyclopentenopyridines **7a,b** were obtained according to an improved method. Thus, heating ligands **7a,b** with equimolar quantities of $K_2[PtCl_4]$ in acetic acid resulted exclusively in the dinuclear bridged complexes, which had low solubility. Addition of the platinum salt as a water solution shortened the reaction time. The intermediate dinuclear complex could be converted easily to a mononuclear DMSO complex by heating in DMSO for a short-time to yield the mononuclear complexes **11a,b**, which could be isolated readily and purified (Scheme 1).[24] DMSO complexes **11** are fairly soluble materials and their reactions with sodium acetylacetonate in acetone proceed quite easily to give target acac complexes **12a,b** in high yields (Scheme 1).[25] The reaction time (0.5–2.0 h) in this case is shorter compared with the synthesis of analogous cyclometallated complexes from poorly soluble bridged binuclear complexes.

Both DMSO **11** and acac **12** complexes were crystalline compounds. Single crystals of **11a**[26] and **12b**[27] suitable for X-ray diffraction crystallography were obtained by slow cooling of the DMSO solution **11a** or slow concentration of the DCM/MeOH solution **12b**. Despite the difference in auxiliary ligands and the aryl substituents, molecules of both complexes **11a** and **12b** pack as centrosymmetric head-to-tail dimers (Figs. 1 and 2). The dimers have a plane-to-plane separation of 3.41 Å for **11a** and 3.48 Å for **12b** indicative of moderate π–π interactions. Short contacts between the thiophene ring and the aryl group of the molecule from the next dimer are evidence of moderate π–π interactions between dimers (see Figs. S1 and S2 in ESI). The shortest distances between the thiophene and the aryl groups are 3.49 Å for **11a** and 3.44 Å for **12b**. There are no metal–metal interactions. Each molecule has a square planar geometry that is only slightly distorted from perfect geometry. There are significant distortions of the phenyl in **11a** (44.6°) and naphthyl in **12b** (49.9°) from the plane of the thienylpyridine moieties because of steric hindrance resulting from the *ortho*-substituent.

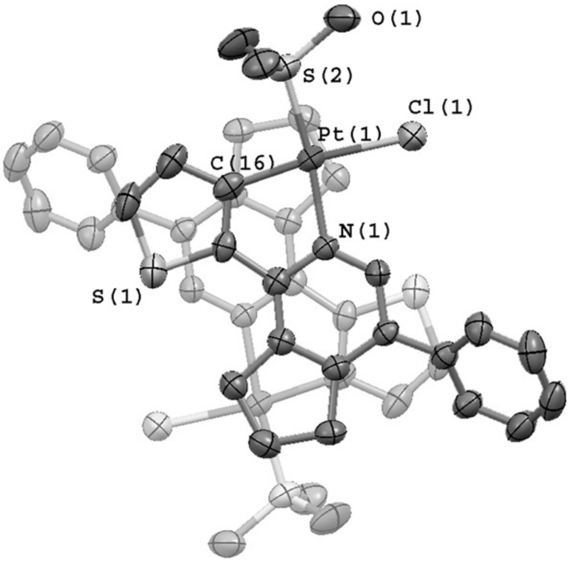

Figure 1. Crystal structure of dimer **11a**. One of the **11a** molecules has been lightened in colour for clarity. The solvent molecule and hydrogens are omitted. Selected bond lengths (Å) and angles (°): Pt(1)–C(16) 1.988(5), Pt(1)–N(1) 2.077(3), Pt(1)–Cl(1) 2.3901(12), Pt(1)–S(2) 2.2035(11) Å, C(16)–Pt(1)–N(1) 80.48(15), Cl(1)–Pt(1)–S(2) 94.27(4).[28]

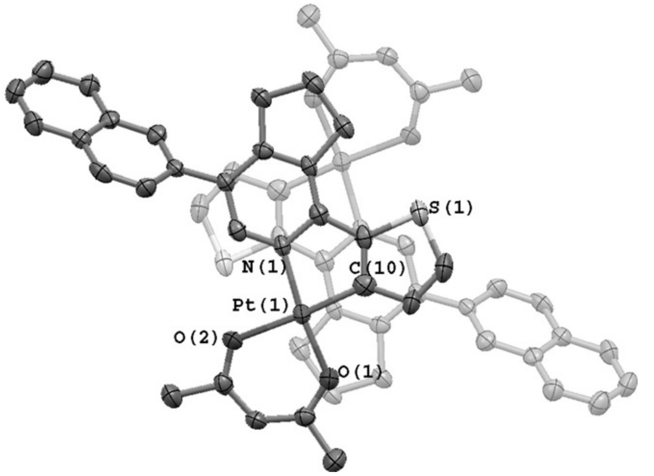

Figure 2. Crystal structure of dimer**12b**. One of the **12b** molecules has been lightened in colour for clarity. The solvent molecule and hydrogens are omitted. Selected bond lengths (Å) and angles (°): Pt(1)–C(10) 1.965(8), Pt(1)–N(1) 2.013(5), Pt(1)–O(1) 1.998(4), Pt(1)–O(2) 2.095(5) Å, C(10)–Pt(1)–N(1) 91.5(2), O(1)–Pt(1)–O(2) 92.39(18).[28]

Complexes **12** exhibit phosphorescence in DCM solutions at room temperature similar to the acac Pt^{II} cyclometallated complex of unsubstituted 2-thienylpyridine (*thpy*) [Pt(acac)(*thpy*)].[10] However, the emission maxima of **12a,b** are slightly red-shifted (578 nm for **12a** and 587 nm for **12b**) compared with the emission maximum of [Pt(acac)(*thpy*)] (575 nm).[10] Increasing the conjugation system of the ligand is expected to shift the electronic transitions bathochromically, as observed on changing the phenyl group to a naphthyl group (**12a→12b**), which leads to an 11 nm red-shift. So, changes in the aryl substituent allow tuning of the emission. Detailed photophysical studies of cyclometallated Pt complexes of new substituted thienylpyridines will be reported in other work.

In conclusion, an efficient and straightforward method for the synthesis of aryl-substituted thienylpyridines has been demonstrated. A wide variety of substituted pyridines can readily be accessed by using cheap, commercially available reagents, such as bromoacetylarenes, aroyl hydrazides, norbornadiene, and enamines in various combinations. Different substitution patterns allow the luminescence of cyclometallated Pt complexes to be tuned based on these new ligands.

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Supplementary data

Supplementary data (experimental details, spectral data for all new compounds, and crystal packing of complexes **11a** and **12b**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.138.

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22. *Typical procedure for the synthesis of thienyltriazines* **6**: A mixture of 2-bromoacetophenone **1a,b** (10 mmol), thiophene-2-carboxylic acid hydrazide **5** (2.84 g, 20 mmol), sodium acetate (1.0 g, 12 mmol), ethanol (30 ml) and acetic acid (10 ml) was heated under reflux for 12 h. The reaction mixture was allowed to cool to room temperature and the precipitated solid was filtered off, washed with ethanol and dried. The product was used in the next step without further purification.
23. *Typical procedure for the preparation of 2-(2′-thienyl)cyclopenteno[c]pyridines* **7a**,**b**: A mixture of 6-aryl-3-thienyl-1,2,4-triazine **6** (4.0 mmol) and 1-morpholinocyclopentene (3 ml, 18.8 mmol) was stirred at 220 °C under an argon atmosphere for 0.5 h. The reaction mixture was diluted with DCM and passed through a short column (silica gel, DCM as eluent). The fractions containing the product were combined, and the solvent was evaporated to dryness. The residue was treated with ethanol (10 ml), and the solid so formed was separated by filtration and washed with cold ethanol (5 ml).
24. *Typical procedure for the preparation of DMSO Pt complexes* **11a,b**: To a stirred solution of **7** (2.2 mmol) in acetic acid (30 ml) was added a solution of potassium tetrachloroplatinate (415 mg, 1 mmol) in water (1 ml). The reaction mixture was heated at reflux under nitrogen for 24 h. A precipitated solid of the chloro-bridged dinuclear intermediate was filtered off, washed with acetic acid (5 ml), ethanol (5 ml) and dried under vacuum. To this solid was added DMSO (2 ml) and the mixture was heated under reflux for 10 min. Complex **11** precipitated upon cooling, and the crystals were filtered off and washed with DMSO (1 ml) and acetone (3 ml) to give pure compounds.
25. *Typical procedure for the preparation of acac Pt complexes* **12a**,**b**: A mixture of **11a,b** (0.1 mmol), sodium acetylacetonate monohydrate (1.0 mmol) and acetone (10 ml) was stirred at 50 °C for 12 h. The reaction mixture was then diluted with water (50 ml). The precipitated solid was filtered off and purified by column chromatography (silica gel, DCM).
26. *X-ray crystallography of complex* **11a**. Single crystals of **11a** suitable for X-ray crystallography were obtained by slow cooling of a saturated DMSO solution of **11a**. Crystal data for **11a** were collected with an *Xcalibur 3 CCD* (graphite monochromator, MoKα): $C_{20}H_{20}ClNOPtS_2$ C_2H_6OS, FW = 663.16, triclinic, a = 7.7173(8) Å, b = 12.3254(11) Å, c = 13.4726(14) Å, α = 103.455(11)°, β = 105.379(9)°, γ = 96.111(8)°, V = 1182.2(2) $Å^3$, T = 295(2) K, space group $P-1$, Z = 2, 9395 reflections were collected, and 5444 independent reflections were used in all the calculations. Number of parameters 280. R_1 = 0.0280, wR_2 = 0.0635. GOOF 1.003. Method SHELXL-97.
27. *X-ray crystallography of complex* **12b**. Single crystals of **12b** suitable for X-ray crystallography were obtained by slow concentration of a DCM/MeOH solution of **12b**. Crystal data for **12b** were collected with an *Xcalibur 3 CCD* (graphite monochromator, MoKα): $C_{27}H_{23}NO_2PtS$, FW = 620.61, monoclinic, a = 12.3573(13) Å, b = 7.9005(6) Å, c = 23.828(2) Å, α = 90.00°, β = 104.851(8)°, γ = 90.00°, V = 2248.6(3) $Å^3$, T = 295(2) K, space group $P2_1/c$, Z = 4, 12197 reflections were collected, and 4520 independent reflections were used in all the calculations. Number of parameters 289. R_1 = 0.0395, wR_2 = 0.0882. GOOF 1.007. Method SHELXL-97.
28. Crystallographic data (excluding structure factors) for the structures in this Letter have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 668782 **11a** and 681703 **12b**. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].