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4-*tert*-Butylphenyl Solubilized Oligopyridines

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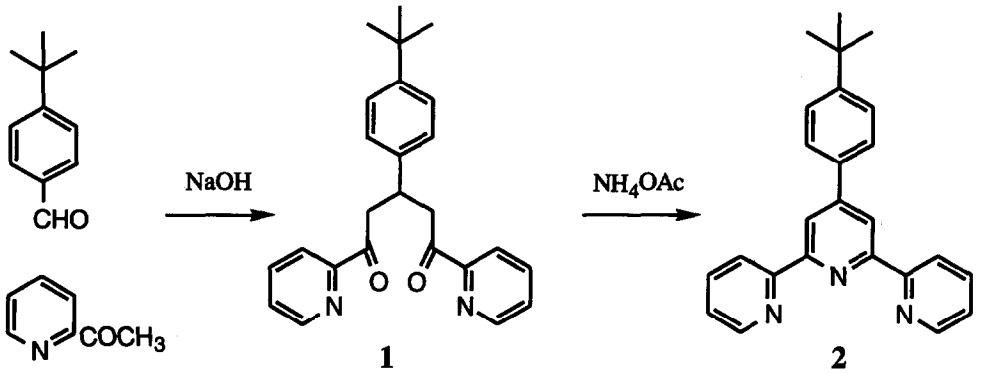
Abstract: Soluble 4-*tert*-butylphenyl substituted derivatives of 2,2':6',2"-terpyridine, 2,2':6',2":6",2"'-quaterpyridine, 2,2':6',2":6",2"':6"',2""-quinquepyridine and 2,2':6',2":6",2"':6"',2"":6"",2""':6""',2""'-sexipyridine have been prepared. The ligands and their metal complexes are more soluble than unsubstituted analogues, but the introduction of the bulky substituent does not perturb any metal centred processes.

Oligopyridines have proved to be extremely versatile ligands for the assembly of metallosupramolecular systems.[1-4] In particular, the lower members of the series (2,2'-bipyridine, 2,2':6',2"-terpyridine and the related ligand 1,10-phenanthroline) have classically been widely used for the preparation of transition metal complexes with specific redox, photochemical or catalytic properties. More recently, the combination of two or more oligopyridine moieties (metal-binding *domains*) in multinucleating ligands has allowed the preparation of dendritic and oligomeric systems which are specifically assembled upon interaction of the multidentate ligands with metal ions.[5-7] The higher members of the series may interact with metal ions in a variety of ways, but controlled twisting about interannular C-C bonds allows the partitioning of the ligand into two or more discrete metal binding domains, and ultimately permits the metal-directed assembly of helicates.[1] The higher oligopyridines tend to be extremely insoluble, although interaction with metal ions yields soluble ionic complexes. The insolubility of the free ligands is primarily due to the efficient graphitic stacking of the planar molecules in the crystal lattice. In view of this limitation, Potts has introduced alkylthio substituents to aid the solubility of the ligands.[2,8] The thioether substituents may be converted to other functional groups, but yields are not always high. Accordingly, we have emphasized the introduction of aryl substituents upon the periphery of oligopyridines utilizing the Kröhnke methadology.[9] This allows us to prepare a very wide range of remotely functionalized derivatives in simple and high-yielding processes.[10,11,12] As a part of our studies upon aryl-substituted oligopyridines and their complexes we now describe the introduction of solubilizing

4-*tert*-butylphenyl substituents onto 2,2':6',2"-terpyridines, 2,2':6',2":6",2"'-quaterpyridines, 2,2':6',2":6",2"':6"',2""-quinquepyridines and 2,2':6',2":6",2"':6"',2"":6"",2""'-sexipyridines.

RESULTS AND DISCUSSION

The strategy adopted for the synthesis of the aryl-substituted oligopyridines uses the methodology developed by Kröhnke.[9] Initially, we prepared a solubilized 2,2':6',2"-terpyridine to develop the methodology and to investigate the effect of the solubilizing group upon the properties of the ligand and its transition metal complexes. The reaction of 4-*tert*-butylbenzaldehyde with 2-acetylpyridine in aqueous ethanolic sodium hydroxide proceeded in a similar manner to the analogous reaction with benzaldehyde.[13] The 1,5-dicarbonyl species **1** was isolated from the reaction of the substituted benzaldehyde with 0.9 equivalents of 2-acetylpyridine as a white solid in 40% yield (Scheme 1). A minor product that was also isolated from the reaction was 3,5-*bis*(4-*tert*-butylphenyl)-2,4-bis(2-pyridylcarbonyl)-1-(2-pyridyl)cyclohexanol which arose from the condensation of three equivalents of 2-acetylpyridine with two equivalents of the substituted benzaldehyde. Analogous cyclic products have previously been observed under similar reaction conditions.[14] Compound **1** underwent a facile ring closure in the presence of ammonium acetate and air to give the 4'-substituted terpyridine **2**. The initially formed dihydro-2,2':6',2"-terpyridine undergoes aerial oxidation under the reaction conditions, to give the desired product, and there is no need for a separate oxidation step.



Scheme 1. Synthesis of the 4-*tert*-butylphenyl substituted terpyridine **2**.

In comparison with the parent unsubstituted and other 4'-substituted terpyridines, the presence of the 4-*tert*-butylphenyl group enhanced the solubility of the ligand and its complexes in common organic solvents. The new ligand behaves in all respects as a substituted 2,2':6',2"-terpyridine, and readily forms complexes with transition metals. The reaction of two equivalents of **2** with methanolic iron(II) sulfate yielded a purple solution, from which the salt $[Fe(\mathbf{2})_2][PF_6]_2$ was readily precipitated as a purple crystalline solid by the addition of $[NH_4][PF_6]$. It is of particular note that this complex is much more soluble in

chlorinated organic solvents than those of other terpyridine ligands. The solubility of the complex $[Fe(\mathbf{2})_2][PF_6]_2$ was determined to be 10.6 mg/ml of dichloromethane. However, the introduction of the substituent has little effect upon the metal centre, and the iron(II)/iron(III) redox process in $[Fe(\mathbf{2})_2][PF_6]_2$ is observed at +0.71 V (MeCN solution, $[^nBu_4N][BF_4]$ supporting electrolyte, potentials quoted *versus* Fc/Fc^+) compared to +0.77 V for $[Fe(tpy)_2][PF6]_2$.[11]

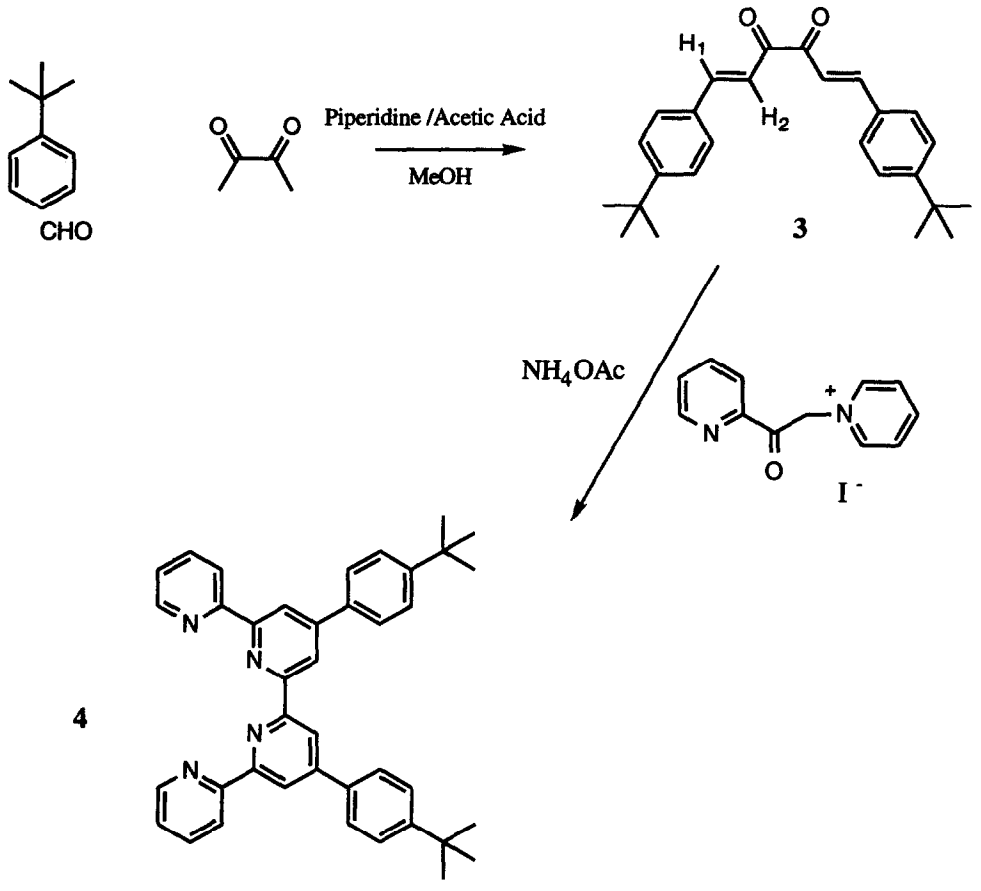
The related complex $[Ru(\mathbf{2})_2][PF_6]_2$ may be prepared in a stepwise manner from $RuCl_3.3H_2O$. The reaction of $RuCl_3.3H_2O$ with **2** in ethanol resulted in the precipitation of the complex $[Ru(\mathbf{2})Cl_3]$ as a brown solid in 60 % yield. Treatment of a suspension of $[Ru(\mathbf{2})Cl_3]$ in methanol with a further equivalent quantity of **2** resulted in the formation of orange-red solutions from which the salt $[Ru(\mathbf{2})_2][PF_6]_2$ was readily precipitated with $[NH_4][PF_6]$. Once again, the increased solubility of the complex was noticed, but there was no significant effect upon the redox properties of the metal (ruthenium(II)/ruthenium(III) +0.89 V compared with +0.92 V for $[Ru(tpy)_2][PF_6]_2$).

The real utility of the *tert*-butylphenyl substituent, however, is demonstrated in the formation of soluble 2,2':6',2":6",2"'-quaterpyridine, 2,2':6',2":6",2"':6"',2""-quinquepyridine and 2,2':6',2":6",2"':6"',2"":6"',2""'-sexipyridine derivatives. We have recently developed a new variation on the Kröhnke synthesis for the preparation of 2,2':6',2":6",2"'-quaterpyridines.[15] The reaction between diacetyl and two equivalents of 4-*tert*-butylbenzaldehyde using piperidine acetate as a catalyst affords **3** as an orange crystalline solid. This product undergoes cyclization by the reaction with the Krohnke reagent in the presence of ammonium acetate to give the 4',4"-disubstituted 2,2':6',2":6",2"'-quaterpyridine **4** as a colourless solid in a yield of 61%. The success of the reaction and loss of conjugation compared to the precurser **3** was indicated by the absence of colour in the product and also by the absence of a carbonyl stretching frequency in its infra-red spectrum. Further characterisation by spectroscopic techniques confirmed the identity of the reaction product as the new potential ligand **4**.

The reaction of 2,6-diacetylpyridine with 2 molar equivalents of 4-*tert*-butylbenzaldehyde in propan-1-ol and diethylamine (Scheme 3) afforded the bischalcone **5** in 48% yield. The subsequent cyclization step in which **5** was reacted with the Kröhnke reagent [9] in methanol in the presence of ammonium acetate afforded 4',4"'-*bis*(4-*tert*-butylphenyl)-2,2':6',2":6",2"':6"',2""-quinquepyridine **6** as a cream solid in 73% yield. In contrast to the insoluble character of ligands such as 2,2':6',2":6",2"':6"',2""-quinquepyridine and 4',4"'-diphenyl-2,2':6',2":6",2"'-2,2':6',2":6",2"':6"',2""-quinquepyridine,[16] **6** is readily soluble in solvents such as chloroform and dichloromethane, although it is only very sparingly soluble in methanol or ethanol. The new ligand **6** is characterised by the presence of a molecular ion at *m/z* 651 in its EI mass spectrum. The ^1H NMR spectrum showed the expected number of peaks and coupling patterns.

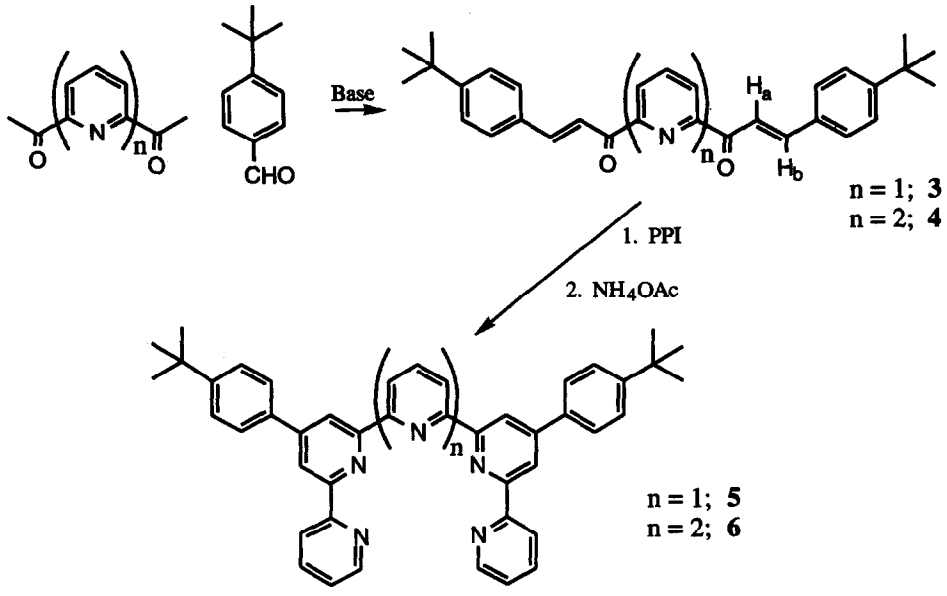
Unsubstituted 2,2':6',2":6",2"':6"',2"":6"",2""'-sexipyridine is only sparingly soluble [17] in organic solvents, which makes it difficult to purify and characterise. This has led us to develop metal-directed methods for the synthesis and isolation of such ligands, which rely upon the solubility of their metal complexes.[18] A smooth reaction between 6,6'-diacetyl-2,2'-bipyridine [19] and 4-*tert*-butylbenzaldehyde in propan-1-ol containing dimethylamine yielded the bischalcone **7** as a yellow solid. The reaction of **7**

with the Kröhnke reagent gave the new ligand 4',4'''-*bis*(4-*tert*butylphenyl)-2,2':6',2'':6'',2''':6''',2'''':6'''',2''''':6''''',2'''''-sexipyridine **8** as a pale brown solid. The compound **8** was readily soluble in chlorinated organic solvents. This facilitates characterisation of the free ligand without necessitating the need to form soluble complexes of the ligand with transition metal ions.



Scheme 2. Synthesis of 4',4''-*bis*(4-tert-butylphenyl)-2,2':6',2'':6'',2''':6''',2''''-quaterpyridine **4**.

The 4-*tert*-butylphenyl solubilizing group should be applicable to solubilizing the higher oligopyridines and so facilitate their characterisation. This would also enable the higher oligopyridines to be incorporated into metallosupramolecular systems, which otherwise might be prevented from so doing by the inherent insolubility of the free ligand in organic solvents. We are currently extending these studies to the preparation of the higher homologues, and are presently investigating the coordination behaviour of these new ligands.



Scheme 3. Synthetic route to 4',4"'-*bis*(4-*tert*-butylphenyl)-2,2':6',2":6",2"':6"',2""-quinquepyridine **6** and 4',4""-*bis*(4-*tert*butylphenyl)-2,2':6',2":6",2"':6"',2"":6"",2""'-sexipyridine **8**.

EXPERIMENTAL

1,6-*Bis*(2-pyridyl)-4-(4-*tert*-butylphenyl)-penta-1,5-dione (1)

2-Acetylpyridine (0.3 ml, 2.5 mmol) and 4-*tert*-butylbenzaldehyde (2.0 g, 2.8 mmol) were stirred for 1 h in ethanol (20 ml) containing aqueous NaOH (10 ml, 2M). The white solid that precipitated was collected by filtration, washed with a little aqueous methanol and dried to give **1** (193 mg, 40%) as a white powder; m.p. 129-130°C; δ_H (300 MHz, $CDCl_3$) 1.26 (9H, s, $C(CH_3)_3$), 3.55 (4H, qd CH_2), 4.12(1H, t, CH), 7.28 (4H, m, H_3,$H_{o/m}$), 7.42 (2H, qd, H_5), 7.78 (2H, td, H_4), 7.93 (2H, d, $H_{o/m}$), 8.64 (2H, d, H_6); *m/z* (EI) 386 $(M+H)^+$.

4'-(4-*tert*-Butylphenyl-2,2':6',2"-terpyridine (2)

A solution of **1** (160 mg, 0.44 mmol), and ammonium acetate (1 g, excess) in glacial acetic acid (10 ml) was heated at reflux for 2 h. The reaction mixture was neutralised with aqueous Na_2CO_3 and extracted with CH_2Cl_2 (2 x 30 ml). Removal of the solvent *in vacuo* afforded a green oil from which a light green solid was obtained upon the addition of water (20 ml). This was collected by filtration to give **2** as a light green solid (120 mg, 75 %); m.p. 174-175°C; δ_H (300 MHz, $CDCl_3$) 1.39 (9H, s, $C(CH_3)_3$), 7.35 (2H, dd, H_5), 7.53 (2H, d, H_m), 7.85 (2H, d, H_o), 7.88 (2H, dd, H_4), 8.67 (2H, d, H_3), 8.73 (2H, d, H_6), 8.75 (2H, s, $H_{3'}$); *m/z* (EI) 365 $(M)^+$ 350 $(M-CH_3)^+$.

1,6-*Bis*(4-*tert*-butylphenyl)hexa-1,5-diene-3,4-dione (3)

Piperidine (0.1 ml, 1mmol) and glacial acetic acid (0.06 ml, 1 mmol) were added to a stirred solution of 4-*tert*-butylbenzaldehyde (3.2 g, 0.02 mol) and diacetyl (0.44 ml, 5 mmol) in methanol (3 ml). The mixture was heated at reflux for 2 h and concentrated to ~0.5 ml *in vacuo.* before cooling. The bright orange crystals which formed were isolated by filtration washed with cold ethanol and characterised as **3** (320 mg, 17%) m.p. 165-166°C; δ_H (300 MHz, $CDCl_3$) 1.35 (18H, s, $C(CH_3)_3$), 7.62 (2H, d, H_1), 7.47 (4H, d, $H_{o/m}$), 7.60 (4H, d, $H_{o/m}$), 7.85 (2H, d, H_2); *m/z* (CI) 375 $(M)^+$.

4',4''-*Bis*(4-*tert*-butylphenyl)-2,2':6',2'':6'',2''':6''',2''''-quaterpyridine (4)

3 (150 mg, 0.4 mmol) was added to a solution of *N*-[1-oxo-2-(2-pyridyl)ethyl]-pyridinium iodide (260 mg, 0.8 mmol) and NH_4OAc (300 mg, 4 mmol) in ethanol (10 ml) and the mixture heated at reflux for 4 h. After cooling, the precipitate that had formed was collected by filtration to give **4** as an off-white solid (140 mg, 61%); m.p. > 250°C; δ_H (300 MHz, $CDCl_3$) 1.42 (18H, s, $C(CH_3)_3$), 7.38 (2H, dt, H_4), 7.60 (4H, d, H_m), 7.92 (6H, d, H_o,H_3), 8.70-8.80 (6H, m, $H_{3'/5'}$,H_5,H_6), 8.96 (2H, d, $H_{3'/5'}$); *m/z* (EI) 574 $(M)^+$, 559 $(M\text{-}CH_3)^+$, 543 $(M\text{-}2CH_3)^+$.

2,6-*Bis*(4-*tert*-butylphenylcinnamoyl)pyridine (5)

2,6-Diacetylpyridine (2.0 g, 12 mmol), 4-*tert*-butylbenzaldehyde (5 ml, ~30 mmol) and diethylamine (5 ml) were heated to reflux in propan-1-ol (30 ml) for 18 h and allowed to cool. After standing for 3 h the yellow solid that precipitated was collected by filtration and washed thoroughly with ice-cold methanol to give **5** (2.6 g, 48%); m.p. 168 - 170°C; δ_H (300 MHz, $CDCl_3$) 1.39 (18H, s, $C(CH_3)_3$), 7.50 (4H, d, H_m), 7.74 (4H, d, H_o), 8.03 (2H, d, H_b), 8.08 (1H, t, H_4), 8.38 (2H, d, H_3), 8.47 (2H, d, H_a) ; *m/z* (EI) 451 $(M)^+$.

4',4'''-*Bis*(4-*tert*-butylphenyl)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (6)

5 (0.45 g, 1 mmol), *N*-[1-oxo-2-(2-pyridyl)ethyl]-pyridinium iodide (0.65 g, 2 mmol) and ammonium acetate (4 g) were heated to reflux in methanol (15 ml) for 15 h and then cooled. The product was collected by filtration to give **6** (0.475 g, 73%) as a fine cream powder; m.p. > 295°C; δ_H (300 MHz, $CDCl_3$) 1.43 (18H, s, $C(CH_3)_3$), 7.37 (2H, qd, H_5), 7.59 (4H, d, $H_{o/m}$), 7.91 (6H, m, H_4, $H_{o/m}$), 8.07 (1H, t, $H_{4'}$), 8.74 (6H, m, H_3, H_6, $H_{3'}$), 8.79 (2H, d, $H_{3'/5'}$), 9.04 (2H, d, $H_{5'/3'}$); *m/z* (EI) 651 $(M)^+$.

6,6'-*Bis*(4-*tert*-butylphenylcinnamoyl)-2,2'-bipyridine (7)

6,6'-Diacetyl-2,2'-bipyridine (0.72 g, 3 mmol) 4-*tert*-butylbenzaldehyde (1.2 g, 7.5 mmol) and diethylamine (2 ml) were dissolved in n-propanol (12 ml) and heated at reflux for 12 h. Collection of the precipitate by filtration afforded **7** (0.92 g, 58%) as a pale yellow solid; m.p. 247-248°C; δ_H (300 MHz, $CDCl_3$) 1.36 (18H, s, $C(CH_3)_3$), 7.49 (4H, d, H_m) 7.71 (4H, d , H_o), 8.02 (2H, d, H_a), 8.11 (2H, t, H_4), 8.27 (2H, dd, H_3), 8.43 (2H, d, H_b), 8.81 (2H, dd, H_5); *m/z* (EI) 729 $(M+H)^+$.

4',4''''-*Bis*(4-*tert*-butylphenyl)-2,2':6',2'':6'',2''':6''',2'''':6'''',2''''':sexipyridine (8)

A solution of **7** (0.30 g, 0.57 mmol), *N*-[1-oxo-2-(2-pyridyl)ethyl]-pyridinium iodide (0.40 g, 1.2 mmol) and $[NH_4]OAc$ (0.5 g, excess) in glacial acetic acid was heated at reflux for 3 h. After cooling, water (50 ml) was added and the precipitate collected. Recrystallisation from CH_2Cl_2/MeOH afforded **7**

(0.31 g, 75%) as a pale brown solid; m.p. >250°C; δ_H (300 MHz, $CDCl_3$) 1.40 (18H, s, $C(CH_3)_3$), 7.35 (2H, m, H_5), 7.60 (4H, d, $H_{o/m}$), 7.89 (6H, m, H_4,$H_{o/m}$), 8.07 (2H, t, $H_{4''}$), 8.74, (10H, m, H_3,H_6,$H_{3''}$,$H_{5''}$,$H_{3'/5'}$), 8.96 (2H, d, $H_{3'/5'}$); *m/z* (EI) 728 $(M)^+$.

$[Fe(2)_2][PF_6]_2$

A methanolic solution of NH_4PF_6 was added to a solution of **2** (200 mg, 0.5 mmol) and $[Fe(H_2O)_6][SO_4]$ (71 mg, 0.27 mmol) in methanol (50 ml). The precipitate was isolated by filtration and washed with ether to give the complex as a fine purple solid (295 mg, 50%); m.p. > 250°C; δ_H (300 MHz, $CDCl_3$) 1.50 (9H, s, $C(CH_3)_3$), 7.08 (2H, dd, H_5), 7.19 (2H, d, H_6), 7.86 (2H, d, H_m), 7.90 (2H, dd, H_4), 8.27 (2H, d, H_o), 8.61 (2H, d, H_3), 9.18 (2H, s, $H_{3'}$).

$[Ru(2)_2][PF_6]_2$

A solution of **2** (150 mg, 0.4 mmol) and $RuCl_3.3H_2O$(107 mg, 0.5 mmol) in ethanol (10 ml) was heated at reflux for 90 mins. The dark brown solid corresponding to Ru(**2**)Cl_3 was isolated by filtration and washed with a small volume of cold methanol. An aliquot of the solid (50 mg, 0.08 mmol) then heated at reflux for 1 h in methanol (10 ml) containing 4-ethylmorpholine (3 drops) and a further portion of **2** (32 mg, 0.08 mmol). After cooling, a methanolic solution of NH_4PF_6 was added to the dark brown solution and the precipitate collected and washed with a small volume of cold aqueous methanol. This afforded a red/brown solid of $[Ru(2)_2][PF_6]_2$ (36 mg, 50%). m.p. > 250°C; δ_H (300 MHz, $CDCl_3$) 1.45 (9H, s, $C(CH_3)_3$), 7.18 (2H, dd, H_5), 7.43 (2H, d, H_6), 7.81 (2H, d, H_m), 7.95 (2H, dd, H_4), 8.16 (2H, d, H_o), 8.65 (2H, d, H_3) 9.01 (2H, s, $H_{3'}$).

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