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Direct platination as a route to conformationally restricted enantiopure C_2-symmetric bisoxazoline pincer complexes

John S. Fossey,[a] Geraint Jones,[b] Majid Motevalli,[a] Huy V. Nguyen,[a] Christopher J. Richards,[a,*] Mark A. Stark[b] and Helen V. Taylor[a]

[a]*Department of Chemistry, Queen Mary, University of London, Mile End Road, E1 4NS, UK*
[b]*Department of Chemistry, Cardiff University, PO Box 912, Cardiff CF10 3TB, UK*

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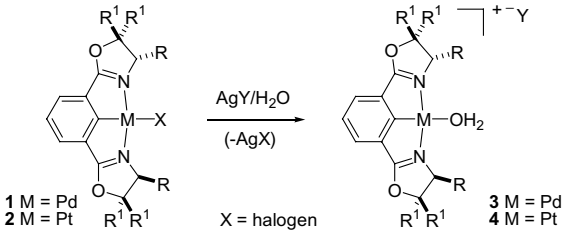
Abstract—(*S*)-3-Amino-4-cyclohexyl-2-methylbutan-2-ol **10** was synthesised in four-steps from (*S*)-2-amino-3-cyclohexanepropanoic acid (47% overall yield). Reaction of **10** with 1,3-bis(ethyl carboximidate)benzene gave (*S*,*S*)-1,3-bis(4′-cyclohexylmethyl-5′,5′-dimethyl-2′-oxazolinyl)benzene **13** in 53% yield. Heating **13** at reflux in acetic acid with K_2PtCl_4 gave (*S*,*S*)-chloro[2,6-bis(5′,5′-dimethyl-4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,C^1,*N*′]platinum(II) **5** (22% yield). Similarly prepared were (*S*,*S*)-chloro[2,6-bis(4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,C^1,*N*′]platinum(II) **6** (9%) and (*S*,*S*)-chloro[2,6-bis(4′-methylethyl-2′-oxazolinyl)-4-nitrophenyl-*N*,C^1,*N*′]platinum(II) **18** (21%). Chloride abstraction from **5** with AgOTf and **6** with AgOTf or $AgSbF_6$, resulted in isolation of the corresponding salts of (*S*,*S*)-aqua[2,6-bis(5′,5′-dimethyl-4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,C^1,*N*′]platinum(II) or (*S*,*S*)-aqua[2,6-bis(4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,C^1,*N*′]platinum(II), respectively. The X-ray crystal structures of **5** and **6** are reported and compared.

1. Introduction

Group 10 C_2-symmetric bisoxazoline pincer complexes of general structures **1** and **2** have recently been the subject of several investigations.[1] Following halide abstraction (Scheme 1), the resulting cationic palladium complexes **3** have been applied as catalysts for cyclopropanation (⩽2% ee),[1a] Michael reactions (up to 34% ee)[1c,e] and silylcyanation (0% ee).[1g] Platinum complexes **4** have been used as catalysts for the aldol reaction of isocyanides and aldehydes (up to 75% ee)[1f] and as stoichiometric controllers of aldimine alkylation (up to 82% ee).[1d] In all of these cases the 5-positions of the oxazoline rings were substituted with hydrogen ($R^1 = H$). Part of our contribution to this previous work was on the asymmetric Michael reaction between α-cyanocarboxylates and methyl vinyl ketone, where the highest ee of 34% was obtained with the relatively long and conformationally flexible $R = CH_2Cy$ substituent.



Scheme 1.

We reasoned that restriction of the conformational freedom of this group by the introduction of *gem*-dimethyl groups at position 5 ($R^1 = Me$) may lead to higher enantioselectivities in the catalysis of this and other reactions. Furthermore, we have also recently found that cationic platinum bisoxazoline complexes give faster rates of reaction than their palladium congeners when employed as catalysts for the Michael and Diels–Alder reactions of nitriles.[2] We therefore set about to synthesise the conformationally restricted C_2-symmetric platinum bisoxazoline pincer complex **5** with the successful outcome of this investigation reported herein. In addition, the X-ray crystal structure of this complex is reported and compared to that of related complex **6**.

* Corresponding author. Tel.: +44-020-7882-3271; fax: +44-020-7882-7427; e-mail: c.j.richards@qmul.ac.uk

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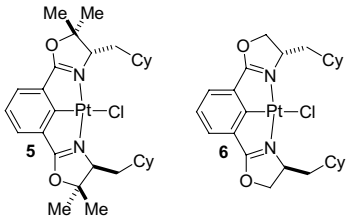
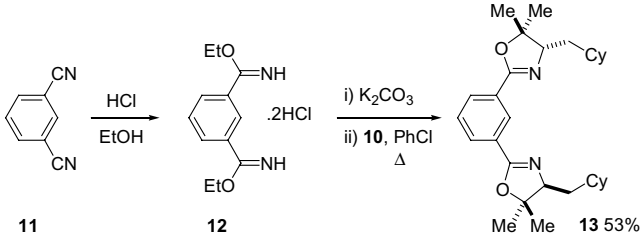




Scheme 3.

2. Results and discussion

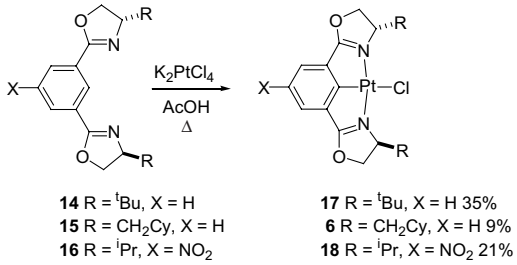
Platinum bisoxazoline complexes have previously been synthesised by either: (a) transmetallation of a 2-trimethylstannyl substituent employing Zeise's salt $K[PtCl_3(C_2H_4)](H_2O)$ as the source of platinum,[1d] or (b) direct cycloplatination with K_2PtCl_4 of precursor 1,3-bis(2-oxazolinyl)benzenes containing only hydrogen at position 2.[2] Although the yields of the achiral bisoxazoline pincer complexes resulting from the latter approach were modest (up to 49%), the simplicity of this method was ideal for rapidly testing the viability of synthesising target complex **5**.

The amino alcohol **10** required for this oxazoline was synthesised as outlined in Scheme 2. Using methodology related to the synthesis of other enantiopure amino tertiary alcohols,[1a,3] (*S*)-2-amino-3-cyclohexanepropanoic acid was first esterified to give **7** followed by *N*-protection and treatment of the product **8** with excess methylmagnesium bromide. Hydrolysis of the trifluoroacetamide functionality of **9** gave **10** as a colourless crystalline solid after purification by Kugelrohr distillation. Conversion of 1,3-dicyanobenzene **11** into the imidate hydrogen chloride salt **12** was carried out as previously described.[4] Following neutralisation with potassium carbonate, the free base was combined with **10** and the resulting mixture heated at reflux in chlorobenzene for 16 h to give the desired bisoxazoline **13** (Scheme 3).

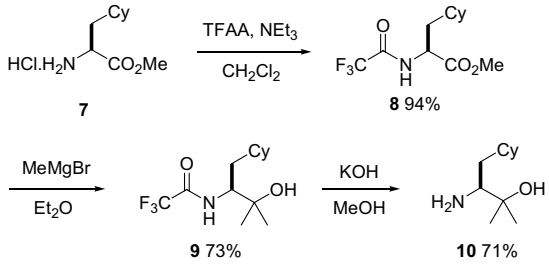
Prior to the attempted platination of **13**, we first applied the metallation methodology to the synthesis of other C_2-symmetric bisoxazoline platinum complexes. Thus using the conditions previously developed,[2] bisoxazoline **14** was heated with potassium tetrachloroplatinate in acetic acid for 48 h resulting in the formation of complex **17**, the physical and spectral characteristics of which essentially identical to those previously reported.[1f] The new complex **6** was similarly prepared from **15**, and the methodology further applied to the 5-nitro substituted bisoxazoline **16**, which gave the functionalised pincer complex **18** (Scheme 4).

We have previously identified that the other reaction occurring in this metallation protocol is the ring-opening of the oxazolines under acidic conditions.[2] As a consequence, the pincer complexes are formed in rather modest yield, but in its favour the method leads directly to the platanacycles from 1,3-bisoxazolines, which in turn are available in one- or two-steps from commercially available starting materials. In contrast, higher yields were reported for the introduction of platinum by transmetallation of a 2-trimethylstannyl substituent.[1f] However, these organometallics must be synthesised from precursor 2-bromo-1,3-bisoxazolines, for which the aromatic starting material, 2-bromoisophthalic acid, is not commercially available and must be synthesised.[5] In our hands we found the direct route described herein is significantly more practical, especially for the synthesis of functionalised complexes exemplified by **18**.

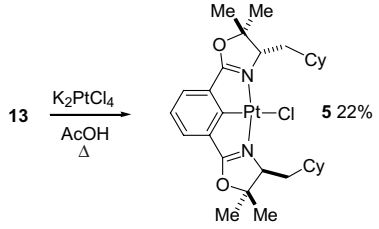
Satisfyingly, we also found that the methodology was applicable to the platination of **13** resulting in the isolation of **5**, the first bisoxazoline pincer complex substituted at the 5-position of the oxazoline rings (Scheme 5). It is noteworthy that attempts to generate a



Scheme 4.



Scheme 2.



Scheme 5.

palladium pincer complex from **13** via regioselective 2-lithiation and transmetallation with $PdBr_2(COD)$ proved unsuccessful. In contrast, this lithiation/transmetallation methodology is applicable to the synthesis of a palladium congener of **6**.[1e] The identity of **5** was confirmed by X-ray crystal structure analysis (Fig. 1), and to enable comparison of the structural and conformational properties of this molecule we also performed an X-ray analysis of related complex **6** (Fig. 2, Table 1).[6]

The two complexes display very similar bond lengths and angles for the distorted square planar platinum centres. The only significant difference is the shorter Pt–C bond of **5** and a reduction in N–CH–CH_2 bond angles in **5** (e.g., 109.2° vs 110.9°). As anticipated, the main differences lie in the conformation of the methylenecyclohexyl groups attached to the oxazoline rings, for which the changes on comparing **5** (R = Me) to **6** (R = H) are represented in Figure 3. In particular, the averaged rotation of 77° to orientate the cyclohexyl methine towards the R = Me substituents, results in a significant increase in the size of the 'walls' that define the C_2-symmetric cleft containing the exchangeable coordination site. This was quantified by measuring the angle from the C_2-axis to the outermost edge of the van der Waals surface of the cyclohexyl groups (Fig. 3).

Finally we wished to confirm that the chloride ligands of both complexes could be replaced by an exchangeable neutral ligand such as H_2O. This has previously been a requirement of the use of related systems in catalysis.[1] Treatment of **6** with silver triflate or silver hexafluoroantiminate in wet acetone resulted in clean conversion to the corresponding cationic complexes **19** and **20** (Scheme 6). The triflate salt was stored for several weeks

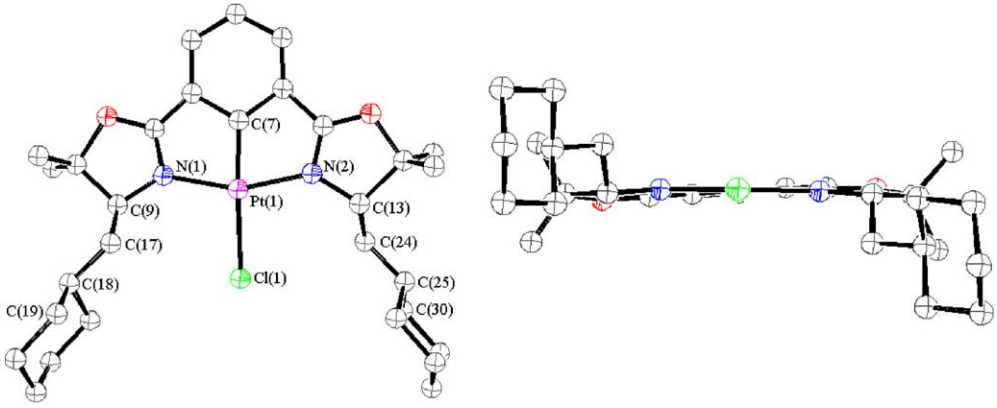


Figure 1. Representations of the two independent crystal structures of **5**.

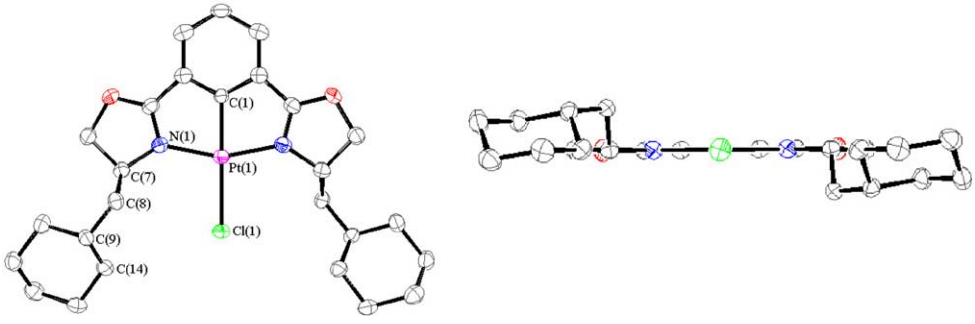


Figure 2. Representations of the crystal structure of **6**.

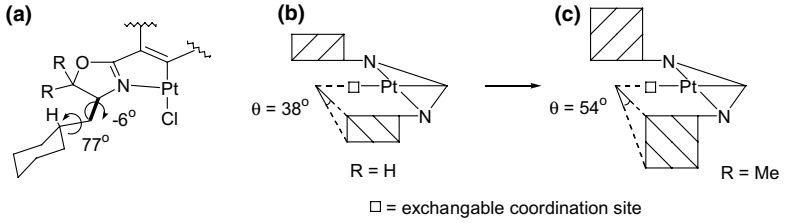
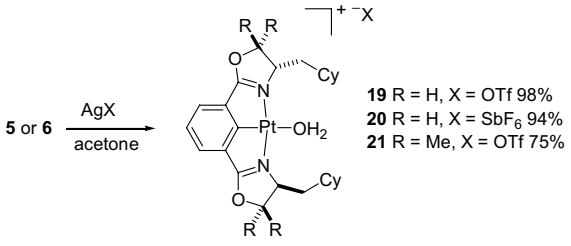


Figure 3. (a) Average changes in the conformation of the methylenecyclohexyl groups on changing from R = H to R = Me, and a cartoon of the environment about the exchangeable coordination site in (b) **6** and (c) **5**.

Table 1. Key bond distances (Å), angles (°) and torsions (°) for complexes **5** and **6**

Complex **5**		Complex **6**	
Space group	*P*21	Space group	*C*2
Pt(1)–C(7)	1.843(4) [1.893(4)][a]	Pt(1)–C(1)	1.947(9)
Pt(1)–Cl(1)	2.3834(11) [2.3846(10)]	Pt(1)–Cl(1)	2.381(2)
Pt(1)–N(1)	2.057(4) [2.017(3)]	Pt(1)–N(1)	2.022(4)
Pt(1)–N(2)	2.023(4) [2.023(3)]	—	—
C(7)–Pt(1)–N(1)	80.29(18) [78.29(15)]	C(1)–Pt(1)–N(1)	79.22(10)
C(7)–Pt(1)–N(2)	77.25(17) [81.18(16)]	—	—
N(1)–C(9)–C(17)	109.6(4) [109.2(3)]	N(1)–C(7)–C(8)	110.9(4)
N(2)–C(13)–C(24)	109.8(4) [109.2(4)]		
N(1)–C(9)–C(17)–C(18)	−168.4 [166.6]	N(1)–C(7)–C(8)–C(9)	−160.8
N(2)–C(13)–C(24)–C(25)	−167.6 [−163.6]	—	—
C(9)–C(17)–C(18)–C(19)	−167.1 [−179.8]	C(7)–C(8)–C(9)–C(14)	69.9
C(13)–C(24)–C(25)–C(30)	−177.5 [−167.8]	—	—

[a] For complex **5** the corresponding values of the second structure are given in parenthesis.



Scheme 6.

exposed to the atmosphere without noticeable decomposition. In contrast, the hexafluoroantiminate salt discoloured after several hours exposure. Thus **5** was treated with only silver triflate resulting in the isolation of **21** as a pale yellow crystalline solid that darkened on prolonged exposure to the atmosphere. This may be avoided by storage under a nitrogen atmosphere.

3. Conclusions

Direct platination of 1,3-bisoxazolines provides a convenient route to C_2-symmetric bisoxazoline pincer complexes. Systems unsubstituted at the 5-position of the oxazolines are available in two- or three-steps from commercially available starting materials. The platination method is also applicable to the synthesis of novel complex **5** containing *gem*-dimethyl substituents at position 5. The changes in the conformational properties of **5**, compared to its unsubstituted analogue **6**, were determined by X-ray crystal structure analyses. The major change, an average 77° rotation about the CH_2–cyclohexyl bond, significantly increases the height of the 'walls' of **5** that define the C_2-symmetric cleft about the exchangeable coordination site. That substitution reactions can be performed at this position was confirmed by chloride abstraction from both **5** and **6** to provide isolable cationic complexes in excellent yield. The application of these as catalysts in asymmetric synthesis will be reported shortly.

4. Experimental

Tetrahydrofuran was distilled from sodium benzophenone ketal; dichloromethane was distilled from calcium hydride and glacial acetic acid was distilled from P_2O_5 and acetic anhydride, all under a nitrogen atmosphere. Petroleum ether refers to the fraction boiling in the 40–60 °C range and column chromatography was performed on SiO_2 (40–63 μm). (*S*)-2-Amino-3-cyclohexanepropionic acid hydrate was obtained from Aldrich.

4.1. (*S*)-Methyl 2-amino-3-cyclohexylpropanoate hydrochloride 7[7]

To a suspension of (*S*)-2-amino-3-cyclohexanepropanoic acid hydrate (5.44 g, 28.7 mmol) in dry methanol (100 mL) was added TMSCl (17.26 g, 0.16 mol) and the mixture heated at reflux overnight. After removal of the solvent in vacuo **7** was isolated as a colourless solid (6.20 g, 97%). ν_{max}/cm^{-1} 1749 (C=O); δ_H ($CDCl_3$) 0.83 (13H, m, CH_2Cy), 3.75 (3H, s, CH_3), 4.00–4.04 (1H, m, CHN), 8.79 (3H, br s, NH_3).

4.2. (*S*)-Methyl 2-(trifluoroacetyl)amino-3-cyclohexylpropanoate 8

Trifluoroacetic anhydride (5.69 g, 27.1 mmol) was added dropwise to a suspension/solution of **7** (5.00 g, 22.6 mmol) and triethylamine (5.02 g, 49.6 mmol) in dry dichloromethane (100 mL) at −78 °C, with stirring continued at this temperature for 2.5 h. The reaction mixture was then allowed to warm to room temperature and stirred for a further 2 h. The resulting mixture was washed with 0.1 M HCl (2 × 20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The resulting pale yellow oil was then purified by column chromatography (EtOAc) to give **8** as a pale yellow oil, which solidified on standing (5.96 g, 94%). Mp 64–65 °C (Found: C, 51.23; H, 6.50; N, 4.74. $C_{12}H_{18}F_3NO_3$ requires C, 51.25; H, 6.45; N, 4.98%); $[\alpha]_D^{20} = +35$ (*c* 0.99, $CHCl_3$); ν_{max}/cm^{-1} (Nujol) 1750 (C=O), 1704 (C=O), 1567; δ_H ($CDCl_3$) 0.85–1.80 (13H, m, CH_2*Cy*), 3.79 (3H, s, CH_3), 4.69 (1H, td, *J* 8.5, 5.4, C*H*N), 6.84 (1H, d, *J* 7.3, N*H*); δ_C ($CDCl_3$){^{1}H} 26.2 (*C*H_2), 26.3 (*C*H_2), 26.5 (*C*H_2), 32.8 (*C*H_2), 33.6 (*C*H_2), 34.3 (CH$_2$*C*H), 40.2 (*C*H$_2$Cy), 50.9 (*C*HN), 53.2 (O*C*H$_3$), 116.0 (q, *J* 286, *C*F$_3$), 157.1 (q, *J* 37, *C*=O), 172.4 (*C*O$_2$CH$_3$); *m*/*z* (EI) 282 (MH$^+$, 37), 222 (57), 109 (56), 69 (100).

4.3. (*S*)-4-Cyclohexyl-2-methyl-3-(trifluoroacetyl)aminobutan-2-ol 9

A solution of **8** (8.20 g, 29.2 mmol) in dry THF (100 mL) was cooled under an atmosphere of nitrogen to −78 °C and to this was added dropwise an Et_2O solution of methylmagnesium bromide (48.7 mL, 146 mmol). The reaction mixture was then allowed to warm to room temperature, stirred for 3 h and quenched by careful dropwise addition of satd $NH_4Cl_{(aq)}$ (40 mL). The organic layer was separated, dried over $MgSO_4$, filtered and the solvent removed in vacuo to give **9** as a colourless crystalline solid (5.99 g, 73%). Mp 73–75 °C (Found: C, 55.30; H, 7.92; N, 4.80. $C_{13}H_{22}F_3NO_2$ requires C, 55.50; H, 7.88; N, 4.98%); $[\alpha]_D^{20} = -39$ (*c* 0.89, $CHCl_3$); ν_{max}/cm^{-1} (Nujol) 3415 (OH, NH), 1705 (C=O); δ_H ($CDCl_3$) 0.77–1.90 (13H, m, CH_2*Cy*), 1.21 (3H, s, CH_3), 1.24 (3H, s, CH_3), 3.91–3.97 (1H, m, C*H*N), 6.47 (1H, d, *J* 9.5, N*H*); δ_C ($CDCl_3$){^{1}H} 26.4 (*C*H_2), 26.8 (*C*H_2), 26.9 (*C*H_2), 27.1 (*C*H_3), 28.1 (*C*H_3), 32.6 (*C*H_2), 34.8 (*C*H_2), 35.0 (CH$_2$*C*H), 37.3 (*C*H$_2$Cy), 55.9 (*C*HN), 73.2 (*C*(CH$_3$)$_2$OH), 116.6 (q, *J* 290, *C*F$_3$), 158.0 (q, *J* 40, *C*=O); *m*/*z* (APCI) 282 (MH$^+$, 13), 264 (100), 112 (87), 87 (52).

4.4. (*S*)-3-Amino-4-cyclohexyl-2-methylbutan-2-ol 10

Potassium hydroxide (4.27 g, 76.1 mmol) was added to a solution of **9** (10.70 g, 38.0 mmol) in dry methanol (100 mL) and the resulting solution stirred overnight. The solvent was then removed in vacuo and the resultant yellow oil purified by Kugelrohr distillation to give **10** as fine colourless needles (5.00 g, 71%): Mp 61–63 °C (Found: C, 71.23; H, 12.17; N, 7.30. $C_{11}H_{23}NO$ requires C, 71.30; H, 12.51; N, 7.56%); $[\alpha]_D^{20} = -35$ (*c* 0.32, $CDCl_3$); ν_{max}/cm^{-1} (liquid film) 3423 (OH/NH); δ_H ($CDCl_3$) 0.78–1.79 (13H, m, CH_2*Cy*), 1.04 (3H, s, CH_3), 1.16 (3H, s, CH_3), 2.57 (1H, dd, *J* 11, 2, C*H*N); δ_C ($CDCl_3$){^{1}H} 23.4 (*C*H$_3$), 26.5 (*C*H$_2$), 26.8 (*C*H$_2$), 26.9 (*C*H$_2$), 27.2 (*C*H$_3$), 32.4 (*C*H$_2$), 35.1 (*C*H$_2$), 35.4 (CH$_2$*C*H), 41.3 (*C*H$_2$Cy), 57.4 (*C*HN), 72.0 (*C*(CH$_3$)$_2$OH); *m*/*z* (EI) 186 (MH$^+$, 6), 170 (3), 126 (71), 55 (100).

4.5. (*S*,*S*)-1,3-Bis(4′-cyclohexylmethyl-5′,5′-dimethyl-2′-oxazolinyl)benzene 13

To a solution of 1,3-bis(ethyl carboximidate)benzene dihydrochloride **12**[4] (0.12 g, 0.41 mmol) in CH_2Cl_2 (10 mL) was added satd $K_2CO_{3(aq)}$ (5 mL) and the biphasic mixture stirred vigorously for 10 min. The organic layer was separated, dried over Na_2SO_4, filtered and the solvent removed in vacuo. The resultant material combined directly with **10** (0.23 g, 1.2 mmol) in chlorobenzene (10 mL) and the mixture heated at reflux under a nitrogen atmosphere for 16 h. After cooling, the solvent was removed in vacuo and the residue purified by column chromatography (1:1 petroleum ether/EtOAc) to yield **13** as a waxy orange solid (0.10 g, 53%): $[\alpha]_D^{20} = -12$ (*c* 0.54, $CHCl_3$); ν_{max}/cm^{-1} (liquid film) 1643 (C=N); δ_H ($CDCl_3$) 0.81–1.87 (26H, m, CH_2*Cy*), 1.24 (6H, s, CH_3), 1.41 (6H, s, CH_3), 3.82 (2H, dd, *J* 9.8, 5.0, C*H*N), 7.41 (1H, t, *J* 7.8, 5-H), 8.05 (2H, d, *J* 7.8, 4- & 6-H), 8.40 (1H, s, 2-H); δ_C ($CDCl_3$){^{1}H} 26.3 (*C*H$_3$), 26.5 (*C*H$_2$), 26.7 (*C*H$_2$), 26.9 (*C*H$_2$), 28.0 (*C*H$_3$), 32.6 (*C*H$_2$), 33.2 (*C*H$_2$), 34.8 (CH$_2$*C*H), 37.4 (*C*H$_2$Cy), 56.0 (*C*HN), 73.6 (O*C*(CH$_3$)$_2$), 126.1 (Ar, 2-C), 128.9 (Ar, 5-C), 130.3 (Ar, 4- & 6-C), 135.0 (Ar, 1- & 3-C), 167.9 (*C*=N); *m*/*z* (APCI) 465 (M$^+$, 100). HRMS (APCI) *m*/*z* found 465.3475; calcd for $C_{30}H_{45}N_2O_2$ 465.3481.

4.6. (*S*,*S*)-Chloro[2,6-bis(4′-dimethylethyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) 17[1f]

(*S*,*S*)-1,3-Bis(4′-dimethylethyl-2′-oxazolinyl)benzene **14**[1e] (0.045 g, 0.14 mmol) and K_2PtCl_4 (0.187 g, 0.45 mmol) were heated at reflux in distilled acetic acid (15 mL) under a nitrogen atmosphere for 48 h. The solvent was removed in vacuo and the residue triturated with petroleum ether and purified by column chromatography (CH_2Cl_2). Removal of the solvent in vacuo gave **16** as a yellow crystalline solid (0.027 g, 35% yield, based on **14**): ν_{max}/cm^{-1} (CH_2Cl_2) 1607 (C=N); δ_H ($CDCl_3$) 0.98 (18H, s, CH_3), 4.05 (2H, dd, *J* 8.3, 2.2, NC*H*), 4.61 (2H, t, *J* 8.8, OCH*H*), 4.89 (2H, dd, *J* 9.2, 2.2, OC*H*H), 7.12 (1H, t, *J* 7.6, Ar 4-H), 7.31 (2H, (66%) d, *J* 7.8, (34%) app t, $^4J_{PtH}$ 7.1, Ar 3- & 5-H); δ_C ($CDCl_3$){^{1}H} 26.4 (*C*H$_3$), 35.4 (*C*CH$_3$), 70.2 ((34%) d, $^2J_{PtC}$ 25.3, N*C*H), 122.1 (Ar, 4-C), 127.3 ((34%) d, $^3J_{PtC}$ 45.6, 3- & 5-C), 1-, 2- & 6-C not observed; *m*/*z* (FAB) 557 (M$^+$, 6), 522 (M$^+$−Cl, 100).

4.7. (*S*,*S*)-Chloro[2,6-bis(4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) 6

(*S*,*S*)-1,3-Bis(4′-methylenecyclohexyl-2′-oxazolinyl)benzene **15**[1e] (2.1 g, 5.14 mmol) and K_2PtCl_4 (2.6 g, 6.26 mmol) were heated at reflux in distilled acetic acid

(180 mL) under a nitrogen atmosphere for 48 h. The solvent was removed in vacuo and the residue passed through silica eluting with 5% ethyl acetate/CH_2Cl_2. Slow evaporation of the yellow fraction gave **6** as a yellow crystalline solid (0.29 g, 9% yield based on **15**). Mp 279 °C (decomp.); $[\alpha]_D^{20} = +136$ (*c* 0.03, $CHCl_3$); ν_{max}/cm^{-1} (thin film) 1610 (C=N); δ_H ($CDCl_3$) 0.98–1.41 (12H, m, Cy), 1.46–1.80 (10H, m, Cy), 2.55 (2H, app t, *J* 9.8, C*H*HCy), 3.72 (2H, app t, *J* 9.8, CH*H*Cy), 4.38–4.40 (2H, m, NC*H*), 4.58 (2H, dd *J* 8.5, 6.1, OC*H*H), 4.94 (2H, app t, *J* 9.0, OCH*H*), 7.08 (1H, t, *J* 7.6, Ar 4-H), 7.28 (2H, (66%) d, *J* 7.7, (34%) app t, $^4J_{PtH}$ 7.2, Ar 3- & 5-H); δ_C ($CDCl_3$){^{1}H} 26.0 (CH_2), 26.2 (CH_2), 26.4 (CH_2), 32.2, 34.2, 34.9, 42.3 (CH_2Cy), 60.9 ((34%) d, $^2J_{PtC}$ 36.2, *C*HN), 77.4 (OCH_2), 122.0 (Ar, 4-C), 126.8 ((34%) d, $^3J_{PtC}$ 40.0, Ar, 3- & 5-C), 128.0 ((34%) d, $^2J_{PtC}$ 38.1, Ar, 2- & 6-C), 161.4 (Ar, 1-C, $^1J_{PtC}$ not observed), 178.7 ((34%) d, $^2J_{PtC}$ 170.0, *C*=N); *m*/*z* (FAB) 602 (M^+-Cl, 100). HRMS (FAB) *m*/*z* found for M^+-Cl 602.2330; calcd for $C_{26}H_{35}N_2O_2Pt$ 602.2346.

4.8. (*S*,*S*)-1,3-Bis(4′-methylethyl-2′-oxazolinyl)-5-nitrobenzene 16

A solution of 5-nitroisophthaloyl dichloride (3.00 g, 12.1 mmol—prepared from commercially available 5-nitro-1,3-benzenedicarboxylic acid) in $CHCl_3$ (15 mL) was added to a solution of (*S*)-2-amino-3-methylbutan-1-ol (5.00 g, 48 mmol) in $CHCl_3$ (125 mL) cooled to 0 °C. The reaction mixture was allowed to warm to room temperature and stirring continued for 24 h. Isolation of the resulting solid by filtration, washing with $CHCl_3$ (3×100 mL) and recrystallisation from MeOH gave (*S*,*S*)-*N*,*N*′-di(1-hydroxy-3-methyl-2-butyl)-5-nitro-1,3-benzenedicarboxamide as a colourless powder (3.79 g, 82%). Mp 230–232 °C (Found: C, 56.42; H, 7.31; N, 11.27. $C_{18}H_{27}N_3O_6$ requires C, 56.68; H, 7.13; N, 11.02%); $[\alpha]_D^{20} = -12$ (*c* 0.1, EtOH); ν_{max}/cm^{-1} (Nujol) 3299, 3264 (NH), 3085 (OH), 1645 (C=O); δ_H (d_6-DMSO) 0.93 (6H, d, *J* 6.8, CH_3), 0.97 (6H, d, *J* 6.8, CH_3), 1.93–2.02 (2H, m, C*H*(CH_3)$_2$), 3.54–3.63 (4H, m, C*H*N & OC*H*H), 3.85–3.92 (2H, m, OCH*H*), 4.70 (2H, t, *J* 5.5, O*H*), 8.60 (2H, d, *J* 8.8, N*H*), 8.80 (1H, s, Ar 2-H), 8.86 (2H, s, Ar 4- & 6-H); δ_C (d_6-DMSO){^{1}H} 19.7 (CH_3), 20.5 (CH_3), 29.5 (*C*H(CH_3)$_2$), 58.2 (*C*HN), 62.0 (OCH_2), 125.0 (Ar 4- & 6-C), 133.7 (Ar 2-C), 137.5 (Ar 1- & 3-C), 148.4 (Ar 5-C), 165.0 (*C*=O); *m*/*z* (CI) 382 (MH^+, 15), 147 (100).

To a suspension of (*S*,*S*)-*N*,*N*′-di(1-hydroxy-3-methyl-2-butyl)-5-nitro-1,3-benzenedicarboxamide (0.550 g, 1.44 mmol) in CH_3CN (22 mL) containing NEt_3 (1.03 g, 10.2 mmol) and CCl_4 (1.55 g, 10.08 mmol) was added, dropwise at room temperature, a solution of PPh_3 (2.27 g, 8.65 mmol) in pyridine (25 mL) and acetonitrile (25 mL). The resulting yellow solution was stirred at room temperature overnight after which time it darkened to brown. After concentration in vacuo, the resulting mixture was redissolved in EtOAc (100 mL), washed with water (2×75 mL) and the organic phase dried over $MgSO_4$, filtered and the solvent removed in vacuo. Purification by column chromatography (20% EtOAc/CH_2Cl_2) gave **16** as a colourless crystalline solid (0.240 g, 48%). Mp 66–68 °C (Found: C, 62.59; H, 6.53; N, 12.39. $C_{18}H_{23}N_3O_4$ requires C, 62.59, H, 6.71; N, 12.17%); $[\alpha]_D^{21} = -112$ (*c* 0.1, EtOH); ν_{max}/cm^{-1} (Nujol) 1659 (C=N); δ_H ($CDCl_3$) 0.98 (6H, d, *J* 6.9, CH_3), 1.03 (6H, d, *J* 6.8, CH_3), 1.76–1.85 (2H, m, C*H*(CH_3)$_2$), 4.04–4.16 (4H, m, C*H*N & OC*H*H); 4.40 (2H, app t, *J* 7.9, OCH*H*), 8.75 (1H, s, Ar 2-H), 8.79 (2H, s, Ar 4- & 6-H); δ_C (d_6-acetone){^{1}H} 18.3 (CH_3), 18.5 (CH_3), 33.2. (*C*H(CH_3)$_2$), 71.4 (OCH_2), 73.3 (*C*HN), 124.9 (Ar 4- & 6-C), 130.6 (Ar 1- & 3-C), 132.8 (Ar 2-C), 148.8 (Ar 5-C), 160.6 (*C*=N); *m*/*z* (EI) 345 (M^+, 1), 302 (100), 258 (8), 214 (5), 189 (26), 149 (58), 57 (35).

4.9. (*S*,*S*)-Chloro[2,6-bis(4′-methylethyl-2′-oxazolinyl)-4-nitrophenyl-*N*,*C*^{1},*N*′]platinum(II) 18

(*S*,*S*)-1,3-Bis(4′-methylethyl-2′-oxazolinyl)-5-nitrobenzene **16** (0.028 g, 0.081 mmol) and K_2PtCl_4 (0.06 g, 0.14 mmol) were refluxed in glacial acetic acid (35 mL) under nitrogen for 48 h. Following removal of the solvent in vacuo, the resulting dark brown residue was purified by column chromatography (CH_2Cl_2) to give **18** as a yellow crystalline solid (0.0096 g, 0.017 mmol, 21%, based on **16**. Mp 252 °C (decomp.); $[\alpha]_D^{20} = +72$ (*c* 0.1, $CHCl_3$); ν_{max}/cm^{-1} (thin film) 1611 (C=N) cm^{-1}; δ_H ($CDCl_3$) 0.77 (6H, d, *J* 6.9, CH_3), 0.97 (6H, d, *J* 7.1, CH_3), 2.88–2.90 (2H, m, C*H*(CH_3)$_2$), 4.47–4.50 (2H, m, C*H*N), 4.82 (4H, app d, *J* 8.3, OCH_2), 8.28 (2H (66%) s, (34%) d, $^4J_{PtH}$ 6.9, Ar 3- & 5-H); δ_C ($CDCl_3$){^{1}H} 13.9 (CH_3), 18.8 (CH_3), 29.0 (*C*H(CH_3)$_2$), 67.4 ((34%) d, $^2J_{PtC}$ 33.3, *C*HN), 72.6 ((34%) d, $^3J_{PtC}$ 29.1, OCH_2), 123.1 ((34%) d, $^3J_{PtC}$ 42.6, Ar 3- & 5-C), 128.1 ((34%) d, $^2J_{PtC}$ 42.8, Ar 2- & 6-C), 143.3 (Ar 4-C), 168.7 (Ar, 1-C, $^1J_{PtC}$ coupling not observed), 178.0 ((34%) d, $^3J_{PtC}$ 171.2, *C*=N); *m*/*z* (TOF ES) 574.2 (M^+, 18), 571 ($M^+-Cl+MeOH$, 100), 539 (M^+-Cl, 83); HRMS (TOF ES) *m*/*z* found for M^+ 574.1552; calcd for $C_{18}H_{22}ClN_3O_4Pt$ 574.0947.

4.10. (*S*,*S*)-Chloro[2,6-bis(5′,5′-dimethyl-4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) 5

(*S*,*S*)-1,3-Bis(4′-cyclohexylmethyl-5′,5′-dimethyl-2′-oxazolinyl)benzene **13** (0.387 g, 0.83 mmol) and K_2PtCl_4 (0.311 g, 0.75 mmol) were heated at reflux in distilled acetic acid (20 mL) under a nitrogen atmosphere for 48 h. The solvent was removed in vacuo and the residue dissolved in CH_2Cl_2, filtered through Celite, and column chromatographed (CH_2Cl_2) to give **5** as a bright yellow crystalline solid (0.13 g, 22%). Mp >250 °C; $[\alpha]_D^{22} = +150$ (*c* 0.1, CH_2Cl_2); ν_{max}/cm^{-1} ($CDCl_3$) 1609 (C=N); δ_H ($CDCl_3$) 1.00–1.80 (22H, m, Cy), 1.56 (12H, s, CH_3), 1.90–1.97 (2H, m, C*H*HCy), 2.35–2.46 (2H, m, CH*H*Cy), 4.02 (2H, d, *J* 11, C*H*N), 7.10 (1H, t, *J* 7, Ar 4-H), 7.25–7.30 (2H, m, Ar 3- & 5-H); δ_C ($CDCl_3$){^{1}H} 22.4, 26.2, 26.4, 26.6, 29.6, 32.1, 34.6, 35.6, 37.8, 67.9 (*C*HN), 93.0 (O*C*(CH_3)$_2$), 121.9, 126.7, 128.7, 176.9

(C=N); HRMS (ES) m/z found for M^+-Cl 657.2939; calcd for $C_{30}H_{43}N_2O_2\ ^{194}Pt$ 657.2946.

4.11. (*S*,*S*)-Aqua[2,6-bis(4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) triflate 19

In a flask protected from light, (*S*,*S*)-chloro[2,6-bis(4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) **6** (0.130 g, 0.20 mmol) and silver triflate (0.051 g, 0.20 mmol) were stirred in acetone (10 mL) for 24 h. The resulting grey precipitate of silver chloride was removed by filtration through Celite, eluting with acetone. Removal of the solvent in vacuo gave **18** as a dark yellow sticky solid (0.154 g, 0.20 mmol, 98% yield). Mp 78 °C; $[\alpha]_D^{20} = +97$ (*c* 0.01, acetone); ν_{max}/cm^{-1} (thin film) 1610 (C=N); δ_H (d_6-acetone) 0.80–2.20 (26H, m, CH_2Cy), 3.85 (2H, br s, OH_2) 4.47–4.48 (2H, m, C*H*N), 4.85 (2H, dd, *J* 8.0, 6.0, OC*H*H), 5.24 (2H, dd, *J* 8.5, 6.9, OCH*H*), 7.32 (1H, t, *J* 6.4, Ar 4-H), 7.44 (2H, d, *J* 6.4, Ar 3- & 5-H) no ^{195}Pt coupling observed; δ_C (d_6-acetone) {^{1}H} 24.3 (*C*H$_2$), 27.2 (*C*H$_2$), 33.9 (*C*H$_2$), 35.1 (*C*H$_2$), 44.9 (*C*H$_2$), 61.8 ((34%) d, $^2J_{PtC}$ 27, *C*HN), 79.0 ((34%) d, $^3J_{PtC}$ 20, O*C*H$_2$), 124.9 (Ar 4-C), 129.0 (Ar 3- & 5-C), 130.1 (Ar 2- & 6-C), 131.2 (Ar 1-C), 177.2 ((34%) d, $^2J_{PtC}$ 169, *C*=N); m/z; (TOF ES) 602.2 (M^+-OH_2-OTf, 100). HRMS (TOF ES) m/z: found for M^+-OH_2-OTf 602.2349; calcd for $C_{26}H_{35}N_2O_2Pt$ 602.2346.

4.12. (*S*,*S*)-Aqua[2,6-bis(4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) hexafluoroantimonate 20

In a flask protected from light, (*S*,*S*)-chloro[2,6-bis[4′-methylenecyclohexyl-2′-oxazolinyl]pheny-*N*,*C*^{1},*N*′]platinum(II) **6** (0.034 g, 0.05 mmol) and silver hexafluoroantimonate (0.017 g, 0.05 mmol) were stirred in acetone (10 mL) for 24 h. The resulting grey precipitate of silver chloride was removed by filtration through Celite, eluting with acetone. Removal of the solvent in vacuo gave **19** as a dark yellow solid (0.043 g, 0.05 mmol, 94% yield). Mp 119 °C; $[\alpha]_D^{20} = +61$ (*c* 0.1, acetone); ν_{max}/cm^{-1} (thin film) 1609 (C=N); δ_H (400 MHz, d_6-acetone) 0.62–2.00 (26H, m, Cy), 2.79 (2H, br s, OH_2), 4.24–4.40 (2H, m, C*H*N), 4.87 (2H, dd, *J* 8.0, 6.1, OC*H*H), 5.12 (2H, dd, *J* 8.5, 7.0, OCH*H*), 7.20 (1H, t, *J* 6.9, Ar 4-H), 7.40 (2H, d, *J* 6.9, Ar 3- & 5-H), no ^{195}Pt coupling observed; δ_C (d_6-acetone){^{1}H} 23.2 (*C*H$_2$), 27.3 (*C*H$_2$), 33.7 (*C*H$_2$), 35.2 (*C*H$_2$), 43.5 (*C*H$_2$), 62.0 (*C*HN), 79.1 (O*C*H$_2$), 125.8 (Ar 4-C), 129.0 (Ar 3- & 5-C), 130.0 (Ar 2- & 6-C), 131.5 (Ar 1-C), 179.5 (*C*=N), no ^{195}Pt coupling observed; m/z (ES) 602 ($M^+-SbF_6-H_2O$, 67). HRMS (ES) m/z found for $M^+-SbF_6-H_2O$ 602.2339; calcd for $C_{26}H_{35}N_2O_2Pt$ 602.2346.

4.13. (*S*,*S*)-Aqua[2,6-bis(5′,5′-dimethyl-4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) triflate 21

In a flask protected from light, (*S*,*S*)-chloro[2,6-bis(5′,5′-dimethyl-4′-methylenecyclohexyl-2′-oxazolinyl)phenyl-*N*,*C*^{1},*N*′]platinum(II) **5** (0.100 g, 0.14 mmol) and silver triflate (0.064 g, 0.25 mmol) were stirred in acetone (10 mL) for 24 h. The resulting precipitate of silver chloride was removed by repeated (×4) filtration through Celite, eluting with acetone, followed by removal of the solvent in vacuo to give **21** as a dark yellow solid (0.087, 75% yield). Mp >250 °C; $[\alpha]_D^{20} = +30$ (*c* 0.2, acetone); ν_{max}/cm^{-1} (thin film) 1609 (C=N); δ_H (270 MHz, d_6-acetone) 0.80–01.08 (4H, m, Cy), 1.08–1.48 (6H, m, Cy), 1.52–2.20 (28H, m, Cy, 4 × –CH$_3$, 2× –CH$_2$–), 4.06 (2H, dd, *J* 11.0, 2.6, C*H*N), 7.32 (1H, t, *J* 7, Ar 4-H), 7.42 (2H, d, *J* 7, Ar 3- & 5-H); δ_C (d_6-acetone){^{1}H} 21.7, 25.8, 26.0, 26.1, 32.3, 34.5, 37.3, 67.9 (*C*HN), 94.9 (O*C*(CH$_3$)$_2$), 120.8, 120.9 (q, *J* 319, –*C*F$_3$) 124.1, 127.7, 129.5, 178.9 (*C*=N) HRMS (ES) m/z found for $M^+-OTf-H_2O$ 658.2977; calcd for $C_{30}H_{43}N_2O_2Pt$ 658.2972.

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6. Crystallographic data (excluding structure factors) for the structures in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 238166 (**5**) and 238165 (**6**). 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.com.ac.uk).
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