Structural Studies of Titanium(IV) Picolinamide Alkoxide and Oxide Derivatives

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Dedicated to Prof. M. L. H. Green, a fearless innovator.

Abstract

Reactions have been carried out using the titanium(IV) precursors $TiCl_4$ and $Ti(OiPr)_4$, with addition of two equivalents of a functionalized picolinamide ligand. The reactions with $TiCl_4$ led to the formation of either a mononuclear titanium species, $[Ti(N,O)Cl_2X_2]$ or a dinuclear titanium species $[Ti(N,O)X_3]_2[\mu\text{-}O]$ (X = OMe or Cl), with incorporation of one picolinamide ligand. The ligand is bound to the titanium centre as the protonated amide. The reactions with $Ti(OiPr)_4$ resulted in the formation of mononuclear titanium *bis*-picolinamide species $[Ti(N,O)_2(OiPr)_2]$, and also dinuclear and trinuclear products, $[(N,O)Ti(OiPr)_2][\mu\text{-}OiPr]_2$ and $[(N,O)Ti(OiPr)_2]_2[\mu\text{-}OiPr]_2[(OiPr)_2Ti]$ $[\mu_3\text{-}O]$ respectively. In these cases the picolinamide ligand was found to be deprotonated and bound to the titanium as the iminolate. These possible intermediates have been characterized by X-ray crystallographic analysis and structural characteristics are discussed.

Keywords: Titanium; Amides; Iminolates; Isopropoxide; Catalysis

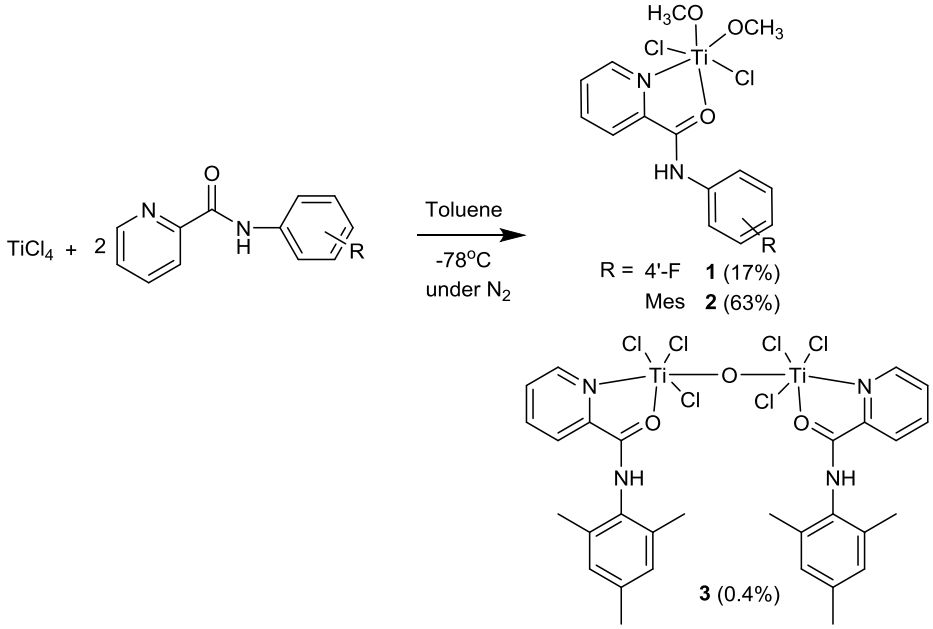
Introduction

The cost-effectiveness and biocompatibility of titanium means it has been widely used in many applications, including medicine,[1] nuclear waste storage[2,3] and as effective catalysts.[4-8] More importantly for this research, titanium salts have been shown to be effective catalysts in the reduction of amides, showing high conversions to either the aldehyde, carbinol or the amine.[9] Lemaire *et al.* have developed and reported the use of 1,1,3,3-tetramethyldisiloxane (TMDS) activated by titanium(IV) isopropoxide for the reduction of phosphine oxides to phosphines,[10-12] nitriles to amines[13] and the reduction of aromatic and aliphatic tertiary amides.[9] They report the use of mild reaction conditions for the reduction of amides to aldehydes,[9] with up to 90% isolated yields. However, further analysis showed the product to be a mixture of the aldehyde and carbinol products. More recently, Luo *et al.* have shown low-valent titanium, prepared *in situ* from $TiCl_4$/Mg, is effective in the reduction of amides to amines, with up to 93% isolated yield of the amine.[14] A study by Iversen in 1970, explored the possible electrochemical reduction of picolinamide and isonicotinamide to the corresponding aldehydes.[15] However, there was no attempt to investigate the utility of this reaction past the aldehyde stage. Toomey Jr. published a patent in 1987 on the electrochemical reduction of pyridine carboxamide bases,[16] and found that in the absence of a titanium salt the reduction gives high yields of the carbinol. In contrast, the addition of a titanium salt gave high isolated yields of the amine, suggesting a titanium complex intermediate is present in this conversion.

Our research has been aimed at both early and late transition metal organometallic and coordination complexes incorporating picolinamide ligands. We have previously reported ruthenium, rhodium and iridium picolinamide complexes in the development of anti-cancer drugs, with high cytotoxicities against a range of tumours.[17-19] We have also reported the use of aluminium picolinamides for the ring-opening polymerisation of *rac*-lactide in the preparation of coloured polymeric materials[20] and picolinamide ligands as effective ligands for copper-catalysed aryl ether formation.[21] Herein, we report the reactions of picolinamide ligands with titanium(IV) precursors and discuss the structural properties of the potential intermediates. The reactions give titanium complexes with the ligand bound as either the amide or iminolate, in which the ligand is exclusively bound *N,O*. The intermediates are not easily predicted and give either mononuclear, dinuclear or trinuclear titanium species. The products obtained are analytically pure and fully characterized by NMR, mass spectrometry and elemental analysis, and their structures have been confirmed by X-ray crystallographic analysis.

Results and Discussion

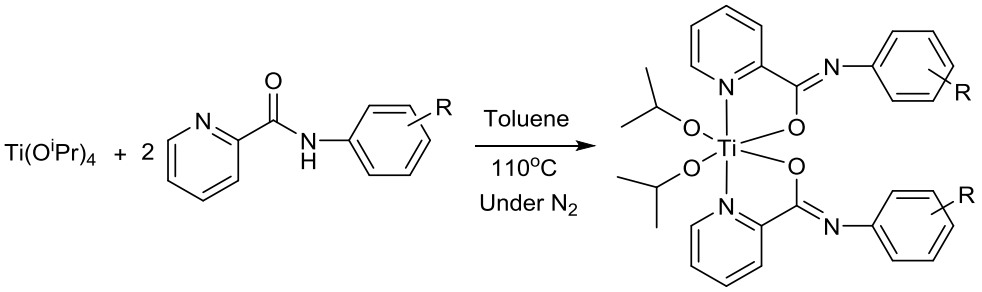
In attempts to synthesis titanium complexes of the type TiL_2X_2, two equivalents of L (picolinamide ligand) were reacted with one equivalent of a titanium salt. Reactions were carried out with $TiCl_4$ and addition of either i) an electron-withdrawing ligand, picolinyl-(4'-fluorophenyl)amide, or ii) an electron donating ligand, picolinyl-(Mes-trimethylphenyl)amide. Two equivalents of ligand in toluene were added to a solution of $TiCl_4$ in toluene at -78 °C (**Scheme 1**).The mixtures were warmed to room temperature and stirred for 16 hours, the suspension filtered and the product recrystallized from methanol. Single crystals of complexes **1** and **2** were obtained in low to moderate yields from a concentrated methanol solution at -20 °C. The X-ray crystallographic data proves the connectivity of these structures; however, the data could not be solved to a publishable quality. The dimeric product **3** was obtained when the crude product of complex **2** was recrystallized from acetonitrile at -20 °C and only obtained in trace amounts.



Scheme 1 *Synthetic route to mononuclear and dinuclear titanium picolinamide complexes* ***1-3***

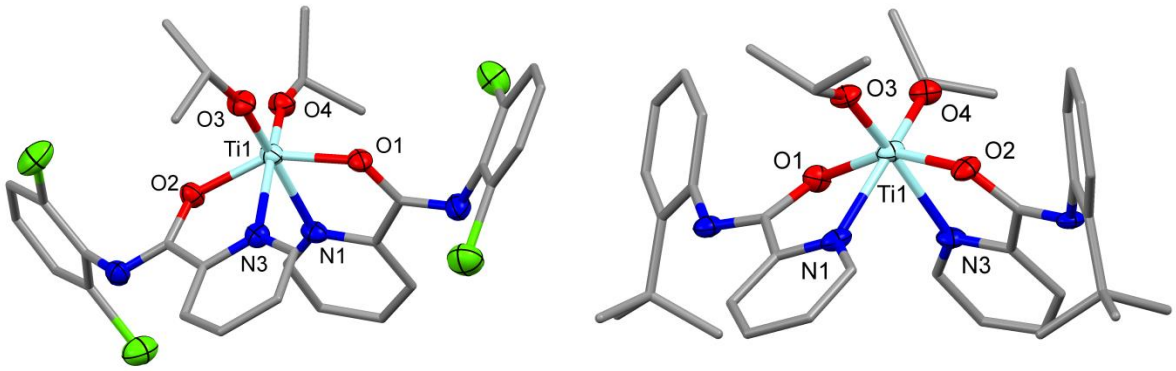
Upon analysis of the ^{1}H NMR spectra for complexes **1** and **2**, a single resonance was observed in the range of 3.35-3.28 ppm. This corresponds to the methoxy groups, which were later confirmed by X-ray crystallographic analysis. The complexes were recrystallized from methanol and due to the titanium having a higher affinity for oxygen, the chloride ligands are hydrolysed by methanol and substituted for methoxy ligands. It is postulated that a dimer similar to complex **3** is formed before recrystallization; however, there was insufficient data to confirm this product. A broad resonance for complexes **1**-**3** is observed in the region of 10.2-10.0 ppm, which was assigned to that of the amide NH proton. The crystal data for complexes **2**-**3** were not fully resolved, but the bond lengths showed the double bond character of the carbonyl C=O (1.255(2)-1.264(4) Å) and the single bond character of the *ipso* C-N (1.316(5)-1.319(3) Å). This evidence suggests that these ligands bind to the titanium centre as the protonated amide, and is one of the possible binding modes observed for these ligands. Other metal picolinamide complexes show the ligand bound as either *N,O* or *N,N*, in which the nitrogen is deprotonated.[17-19]

Further reactions were carried out according to **Scheme 2**, in which two equivalents of a functionalized picolinamide ligand in toluene were added to Ti(O*i*Pr)$_4$ in toluene. After reflux for 16 hours and addition of petroleum ether, the solutions were stored at -20 °C, yielding analytically pure products in yields ranging from 2-97%. The ^{1}H NMR spectra of complexes **4**-**10** show no broad NH resonance in the region of 10.5-10.0 ppm and the iminolate binding mode of the ligand is observed, this was confirmed by X-ray crystallographic analysis.



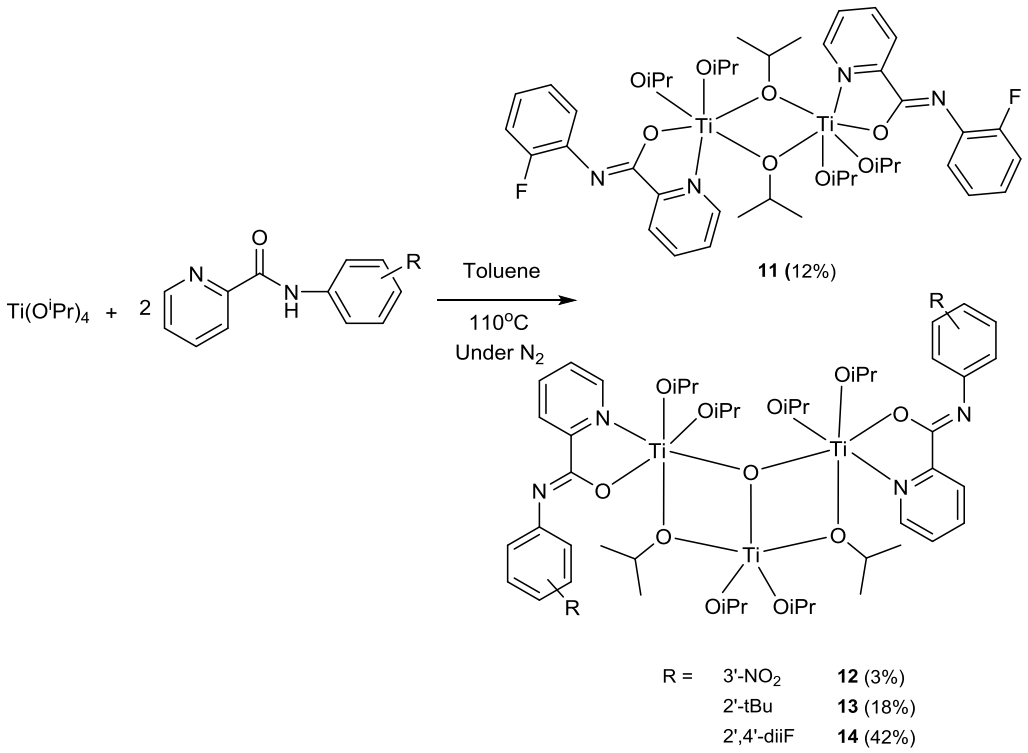
Scheme 2 *Synthetic pathway for the formation of titanium bis-picoliniminolate isopropoxide complexes* ***4***-***10***

Single crystals were obtained for complexes **6** and **9**; the molecular structures are shown in **Figure 1** and selected bond lengths are stated in **Table 1**. Complex **6** crystallized in a monoclinic cell with structural solution performed in the $P2_1/c$ space group, while complex **9** crystallized in a triclinic cell with structural solution performed in the $P\bar{1}$ space group. The titanium centre in both complexes exhibits a distorted *cis*-*cis*-*trans* octahedral arrangement, with the picolinamide oxygen in the *trans* position.[22]



6 **9**

Figure 1 *Molecular structures of complexes **6** and **9**. Hydrogen atoms are omitted for clarity and ellipsoids are at the 50% probability level.*



Scheme 3 *Synthetic pathway for the synthesis of dinuclear titanium picoliniminolate complex **11** and trinuclear titanium picoliniminolate complexes **12**-**14***

The reactions with picolinyl-(2'-fluorophenyl)amide and Ti(O*i*Pr)$_4$, yielded yellow single crystals of complex **11**, which were obtained after recrystallization from toluene (**Scheme 4**). The molecular structure is shown in **Figure 2** and selected bond lengths are stated in **Table 1**. Complex **11** crystallized in a monoclinic cell and structural solution was performed in the $P2_1/c$ space group, with half a molecule in the asymmetric unit.

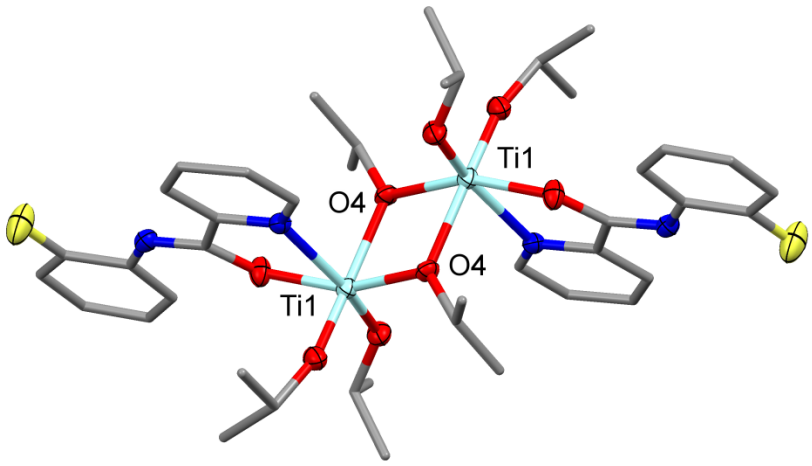


Figure 2 *Molecular structure of complex* ***11****. Hydrogen atoms are omitted for clarity and ellipsoids are at the 50% probability level.*

There are very few analogous complexes of this type and no crystal data to allow comparisons to be made.[23-26] The complex that closest resembles **11** is that of the dimeric methoxyethyl titanium structure $Ti_2(OCH_2CH_2OCH_3)_8$.[23] However, this structure was proposed based only on mass spectrometry data. It was synthesized as part of an investigation of solution routes to perovskite-phase mixed-metal oxides, in which bimetallic cluster complexes are a common product.[24-26]

Colourless single crystals were obtained from the reactions of $Ti(O\textit{i}Pr)_4$ with picolinyl-(3-nitrophenyl)amide and picolinyl-(2-*t*butylphenyl)amide ligands (**Scheme 3**). These were recrystallized from either petroleum ether at -20 °C or from toluene at room temperature, yielding complexes **12** and **13** respectively. Complex **14** was synthesized according to **Scheme 4** and recrystallized from petroleum ether at -20 °C. These complexes all yield trinuclear titanium complexes, with one triply bridging μ-O and two doubly bridging μ-O*i*Pr groups. Two of the metal centres are bound to one picoliniminolate ligand each, whereas the third centre only binds two O*i*Pr substituents.

Complex **12** crystallized in a triclinic cell and structural solution was performed in the $P\ \bar{1}$ space group. The asymmetric unit contained two molecules and the molecular structure is shown in **Figure 3** and selected bond lengths are stated in **Table 1**. This structure also contains 0.1 equivalents of ethyl acetate in the asymmetric unit cell, which was present from the recrystallization of the picolinyl-(3'-nitrophenyl)amide ligand.

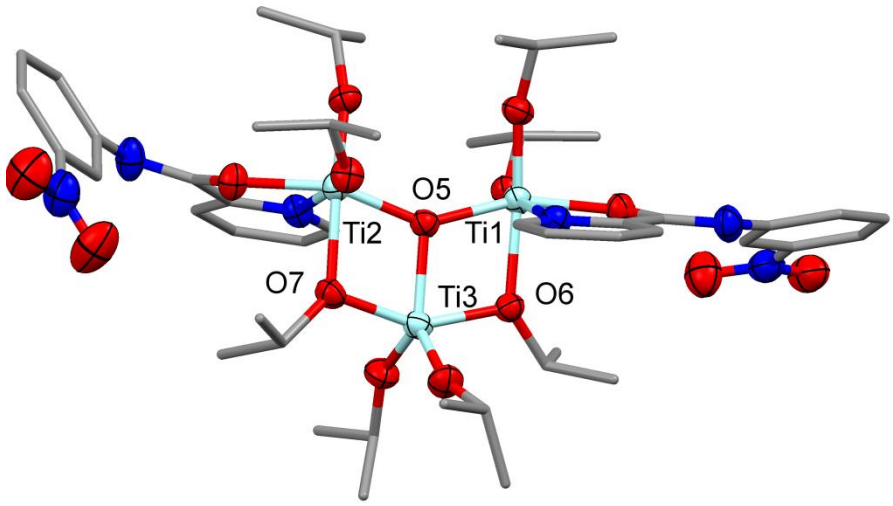


Figure 3 *Molecular structure of complex* ***12****. Hydrogen atoms and solvent are omitted for clarity and ellipsoids are at the 50% probability level.*

Multi-centre titanium alkoxide compounds have been shown to have applications in catalysis and supramolecular chemistry, for example, in the sol-gel process of preparing ceramic materials, where the hydrolysis and condensation of titanium(IV) alkoxides produces titanium(IV)-oxides.[27,28] Henry *et al.* have characterized various trinuclear titanium compounds using different alkyl and aryl ligands in a range of stoichiometries.[29,30] It was deduced from the studies that a co-solvent was required in order to produce crystals in which the ligand is bound to the metal centre.

The ^{1}H NMR spectra of complex **12** suggests multiple picoliniminolate ligand environments, as seen between 9.87-6.24 ppm, but only one septet present for the O*i*Pr groups. However, the solid state crystal structure confirms a possibility of three environments for these O*i*Pr groups. Variable temperature NMR (**Figure S2**) was recorded in order to calculate the coalescence rate of the methyl groups (OCH(C$\underline{H}_3$)$_2$). At 223 K the protons are observable as two separate resonances at 1.23 and 1.16 ppm. Upon warming to 323 K, the methyl groups now appear as a broad doublet; and raising the temperature further to 333 K shows the methyl groups as one broad signal; this is the temperature of coalescence. The Gibbs energy for coalescence was calculated to be 74.8 kJ.mol^{-1}; the NMRs and calculations are shown in the *Supplementary Information* (**Figure S3**).

X-ray crystallographic data confirmed complex **14** has a trinuclear structure and is isostructural with complex **12**. The structure could not be solved to a publishable quality, however, the X-ray crystallographic data and molecular structure is shown in the *Supplementary Information* (**Figure S1** and **Table S1**). Comparison of the dinuclear complex **11** and trinuclear titanium complex **12**, with the mononuclear titanium complexes **6** and **9**, shows similar Ti-O bond lengths for the picoliniminolate ligands, but a slightly longer Ti-N bond length is observed for complexes **11** and **12**. On comparison of the crystal data for the free picolinamide ligand and these titanium complexes, the average C=O bond length of 1.21 Å, is significantly elongated upon complexation, showing a C-O bond length ranging from 1.300(4)-1.343(3) Å. Consequently the average *ipso* C-N bond length of 1.36 Å in the free ligand is shortened upon complexation to a bond length ranging from

1.287(4)-1.355(3) Å. This type of iminolate binding motif has previously been observed for aluminium and copper picolamide complexes.[20,21] Here we show this binding mode is observed for the first time when the picolinamide ligands are bound to titanium, showing the Ti(O*i*Pr)$_4$ is a strong enough base to remove the acidic amide NH proton.

Table 1 *Selected bond lengths (Å) for complexes* ***6, 9, 11*** *and* ***12***

	Mononuclear		**Dinuclear**	**Trinuclear**
Bond Length (Å)	**6**	**9**	**11**	**12**
Ti-O(lig)	2.001(3)/ 1.992(3)	1.988(2)/ 1.963(2)	2.006(2)	2.0854(19)/ 1.995(2)
Ti-N(lig)	2.253(3)/ 2.268(3)	2.283(3)/ 2.281(2)	2.316(2)	2.290(2)/ 2.291(2)
Ti-OiPr	1.791(3)/ 1.795(3)	1.805(2)/ 1.813(2)	1.829(2)/ 1.795(2)	1.772(2)/ 1.812(2) 1.772(2)/ 1.809(2) 1.771(2)/ 1.781(2)
Ti-μ-O*i*Pr	-	-	1.9986(19)	2.0854(19)/ 1.964(2) 2.087(2)/ 1.964(2)
Ti-μ-O	-	-	-	1.9612(19)/ 1.9515(19)/ 1.9715(19)
C-O	1.317(4)/ 1.323(4)	1.339(3)/ 1.343(3)	1.324(3)	1.310(4)/ 1.300(4)
C-N	1.287(5)/ 1.298(5)	1.355(3)/ 1.292(3)	1.302(4)	1.287(4)/ 1.291(4)

Table 2 *Crystallographic data for complexes* ***6****,* ***9****,* ***11*** *and* ***12***

Complex	**6**	**9**	**11**	**12**
formula	$C_{30}H_{28}Cl_4N_4O_4Ti$	$C_{38}H_{48}N_4O_4Ti$	$C_{42}H_{58}F_2N_4O_8Ti_2$	$C_{48}H_{72}N_6O_{15}Ti_3{\cdot}0.1(C_4H_8O_2)$
formula wt	698.26	672.7	880.72	1125.54
cryst syst	Monoclinic	Triclinic	Monoclinic	Triclinic
space group	$P2_1/c$	$P\ \bar{1}$	$P2_1/c$	$P\ \bar{1}$
a (Å)	9.8745(9)	8.3863(9)	12.7797(10)	12.4280(10)
b (Å)	24.040(2)	12.9525(14)	17.8904(16)	22.1490(2)
c (Å)	15.6525(13)	18.555(2)	10.1188(7)	23.3800(2)
α (°)	90.00	74.020(6)	90.00	72.7058(9)
β (°)	97.229(5)	80.440(6)	96.728(5)	78.2739(7)
γ (°)	90.00	81.490(6)	90.00	89.9250(6)
V (Å^3)	3686.0(6)	1899.6(4)	2297.6(3)	6004.36(9)
Z	4	2	2	4
density (mg/m^3)	1.489	1.176	1.273	1.245
absorp coeff (mm^{-1})	0.558	0.267	0.407	0.453
λ[Mo−Kα] (Å)	0.71073	0.71073	0.71073	071073
T (K)	123(2)	150(2)	273(2)	173(2)
reflns collected	92516	11910	21087	27453
independent reflns	9612	5953	3609	20384
***R*1**	0.0660	0.0839	0.0438	0.0538
***wR*2**	0.2450	0.2305	0.1191	0.1699
GOOF	1.049	1.031	1.032	1.043

Summary

This work reports new titanium picolinamide complexes from the reactions of picolinamide ligands with the titanium precursors, TiX_4 and $Ti(OiPr)_4$. X-ray crystallographic analysis has been obtained for mononuclear (**6**, **9**), dinuclear (**11**) and trinuclear (**12**) titanium picolinamide isopropoxide complexes. They provide insight into the possible intermediates formed in the reduction of amides using titanium precursors. Results show these reactions give multiple products, with variable control over the structural properties of the products obtained. The reactions with TiX_4 yield titanium complexes in which the picolinamide ligand is bound datively to the metal centre and the *ipso* nitrogen remains protonated. When using the basic $Ti(OiPr)_4$, the picolinamide NH proton is removed and the ligand binds in a anionic fashion, which is the first time this has been observed for this ligand when bound to titanium. These modes of binding have been confirmed by ^{1}H NMR and X-ray crystallographic analysis, in which no NH is observed and the bond lengths of the carbonyl C-O and *ispo* C-N can be seen to lengthen and shorten respectively. Research is being undertaken to optimize the conditions for these reactions, in order to provide higher yields and allow catalytic reactions to be studied.

Experimental

Materials

All ligand preparation were conducted using standard air-stable techniques, whilst all complex preparations were conducted using standard Schlenk line techniques under an inert atmosphere of dry N_2 using a dual vacuum/N_2 line or in a Braun Labmaster 100 glove box. Dry N_2 was obtained by passing N_2 gas through a double column of self-indicating phosphorus pentoxide and activated 4 Å molecular sieves. Solvents were pre-dried over the appropriate drying agent and distilled under an inert atmosphere of dry N_2. Chemicals were obtained from Sigma-Aldrich Chemical Co., Lancaster Synthesis Ltd., Acros Organics, Strem Chemical Co. and BOC gases. Unless otherwise stated these were used as received. Deuterated NMR solvents were purchased from GOSS Scientific Ltd. or Apollo Scientific Ltd. and were used as purchased or dried using the appropriate drying agent.

Analysis

All NMR spectra were recorded on a Bruker ARX 250 spectrometer, a Bruker DPX 300 spectrometer, a Bruker DRX 500 spectrometer or a Bruker DRX 500 spectrometer. Microanalyses were recorded at the University of Leeds Microanalytical Service. Mass Spectra were recorded on a Micromass ZMD spectrometer with electrospray ionisation and photoiodide array analyser at the University of Leeds Mass Spectrometry Service.

X-ray Crystallography

A suitable single crystal was selected and immersed in an inert oil. The crystal was then mounted on a glass capillary or nylon loop and attached to a goniometer head on a Nonius KappaCCD area detector diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073Å), using 1.0° ϕ-rotation frames. The crystal was cooled to between 123(2)-273(2) K by an Oxford Cryostream low temperature device.[31] The full data sets were recorded and the images processed using DENZO and SCALEPACK programs.[32]

Structure solution by direct methods was achieved through the use of SHELXS programs,[33] and the structural model refined by full matrix least squares on F^2 using SHELX97. Unless otherwise stated, hydrogen atoms were placed using idealized geometric positions (with free rotation for methyl groups), allowed to move in a "riding model" along with the atoms to which they were attached, and refined isotropically. Molecular graphics were plotted using Mercury[34] and Olex2.[35] Editing of CIFs and construction of tables of bond lengths and angles were achieved using PLATON.[36]

Synthetic Procedures

Further reactions have been carried out using titanium(IV) precursors, these are discussed in the *Supplementary Information*.

Synthesis of $Ti(C_{12}H_9N_2OF)Cl_2(OCH_3)_2$ (1). To $TiCl_4$ (0.10 mL, 0.91 mmol) in toluene at -78°C was added picolinyl-(4-fluorophenyl)amide (0.45 g, 2.09 mmol) in toluene drop-wise. The mixture was warmed to room temperature and stirred for 16 hours. The suspension was filtered and the orange solid dried *in vacuo* and recrystallized from dry methanol at -20°C. **Yield:** 60.0 mg, 0.15 mmol, 17%. **ES MS (+):** m/z 354.9 [M-

2OMe+Na]$^+$. **Anal. Found:** C 42.4; H 3.6; N 7.2%. **Anal. Calculated for $C_{14}H_{15}Cl_2FN_2O_3Ti$:** C 42.4; H 3.8; N 7.0%. **^{1}H NMR** (MeOD, 300.13 MHz, 300K) δ 8.86 [s, 1H], 8.47 [d, 1H, $^3J(^1H\text{-}^1H)$ = 7.8 Hz], 8.35 [m, 1H], 7.86 [m, 3H], 7.18 [m, 2H], 3.35 [m, 6H]. **^{13}C{^{1}H} NMR** (MeOD, 75.48 MHz, 300K) δ 163.3 [Q, d, $^2J(^{13}C\text{-}^{19}F)$ = 18.1 Hz], 160.0 [Q], 148.8 [CH], 142.0 [CH], 135.6 [Q], 129.2 [CH], 124.6 [CH], 124.3 [CH], 124.1 [CH], 117.1 [CH], 116.8 [CH].

Synthesis of 2 and 3. To $TiCl_4$ (1.00 mL, 9.12 mmol) in toluene at -78°C was added picolinyl-(2',4',6'-trimethylphenyl)amide (4.35 g, 18.4 mmol) in toluene drop-wise. The mixture was warmed to room temperature and stirred for 16 hours. The suspension was filtered and the yellow solid dried *in vacuo* and recrystallized from dry methanol. Pale blue crystals of **2** were obtained from vapour diffusion with ether and methanol at -20°C. The crude product was recrystallized from acetonitrile at -20°C yielding yellow crystals of the dimeric complex **3**.

$Ti(C_{15}H_{16}N_2O)Cl_2(OCH_3)_2$ (2). Yield: 2.58 g, 5.73 mmol, 63%. **ES MS (+):** m/z 375.1 [M^{2+}-2Cl$^-$+Na]$^+$, 381.1 [M^{2+}-2OMe+Na]$^+$. **Anal. Found:** C 48.3; H 5.0; N 6.8%. **Anal. Calculated for $C_{17}H_{22}Cl_2N_2O_3Ti$:** C 48.5; H 5.3; N 6.7%. **^{1}H NMR** (MeOD, 300.13 MHz, 300K) δ 8.75 [br. s, 1H], 8.28 [d, 1H, $^3J(^1H\text{-}^1H)$ = 7.5 Hz], 8.18 [d, 1H, $^3J(^1H\text{-}^1H)$ = 6.9 Hz], 7.74 [m, 1H], 6.96 [m, 2H], 3.35-3.28 [m, 6H, OC$\underline{H}_3$], 2.23 [d, 9H, $^2J(^1H\text{-}^1H)$ = 23.1 Hz, CH(C$\underline{H}_3$)$_3$]. **^{13}C{^{1}H} NMR** (MeOD, 75.48 MHz, 300K) δ 164.2 [Q, C-O], 149.7 [Q], 148.8 [CH], 140.9 [CH], 138.4 [Q], 131.4 [Q], 130.2 [CH], 129.8 [CH], 128.5 [CH], 123.9 [CH], 49.9 [O$\underline{C}H_3$], 21.0 [CH($\underline{C}H_3$)$_3$], 18.3 [CH($\underline{C}H_3$)$_3$].

$[Ti(C_{15}H_{16}Cl_3N_2O)]_2[\mu\text{-}O]$ (3). Yield: 16.3 mg, 0.02 mmol, 0.4%. **ES MS (+):** m/z 805.0 [MH]$^+$. **Anal. Found:** C 45.7; H 4.1; N 6.2%. **Anal. Calculated for $C_{30}H_{32}Cl_6N_4O_3Ti_2$:** C 44.8; H 4.0; N 6.7%. **^{1}H NMR** (d^6-DMSO, 300.13MHz, 300K) δ 10.12 [s, 2H, N$\underline{H}$], 8.74[m, 2H], 8.21 [m, 2H], 8.00 [m, 2H], 7.61 [m, 2H], 6.92 [s, 4H], 2.26 [d, 6H, $^3J(^1H\text{-}^1H)$ = 3.6 Hz, CH(C$\underline{H}_3$)$_3$], 2.19 [d, 6H, $^3J(^1H\text{-}^1H)$ = 3.6 Hz, CH(C$\underline{H}_3$)$_3$]. **^{13}C{^{1}H} NMR** (d^6-DMSO, 75.48MHz, 300K) δ 173.3 [Q, C-O], 148.1 [CH], 137.4 [CH], 126.2 [CH], 121.9 [CH(CH$_3$)$_3$], 20.1 [CH($\underline{C}H_3$)$_3$], 17.7 [CH($\underline{C}H_3$)$_3$].

Syntheis of $Ti(C_{12}H_9N_2O)_2(OC_3H_7)_2$ (4). To Ti(^{i}OPr)$_4$ (0.37 mL, 1.25 mmol) in toluene was added picolinyl-phenyl amide (0.5 g, 2.52 mmol) in toluene drop-wise. The mixture was heated under reflux for 16 hours and the solvent removed *in vacuo*. Petroleum ether was added and the mixture heated, cooled and then filtered. The resulting crude product was recrystallized from acetonitrile and stored at -20°C to yield colourless crystals of complex **4**. **Yield:** 15.0 mg, 0.03 mmol, 2%. **ES MS (+):** m/z 561.2 [MH]$^+$. **Anal. Found:** C 64.3; H 5.2; N 11.1%. **Anal. Calculated for $C_{30}H_{32}N_4O_4Ti$:** C 64.3; H 5.8; N 10.2%. **^{1}H NMR** (C_6D_6, 300.13 MHz, 300K) δ 8.47 [m, 2H], 8.34 [m, 4H], 7.58 [m, 4H], 7.25 [m, 4H], 6.79 [m, 2H], 6.28 [m, 2H], 4.78 [m, 2H, C$\underline{H}$(CH$_3$)$_2$], 1.36 [s, 6H, CH(C$\underline{H}_3$)$_3$], 1.29 [s, 6H, CH(C$\underline{H}_3$)$_3$]. **^{13}C{^{1}H} NMR** (C_6D_6, 125.76 MHz, 300K) δ 161.4 [Q, C-O], 155.7 [Q], 145.6 [CH], 138.5 [CH], 137.2 [CH], 129.1 [CH], 128.8 [CH], 127.7 [CH], 126.3 [CH], 126.2 [CH], 125.9 [CH], 124.4 [CH], 123.8 [CH], 119.5 [CH], 79.5 [CH(CH$_3$)$_2$], 25.3 [CH($\underline{C}H_3$)$_2$].

Synthesis of 5 and 11. To Ti(^{i}OPr)$_4$ (0.34 mL, 1.15 mmol) in toluene was added picolinyl-(2-fluorophenyl)amide (0.50 g, 2.31 mmol) in toluene drop-wise. The mixture was heated under reflux for 16 hours and the solvent removed *in vacuo*. Petroleum ether was added and the mixture heated, cooled and then filtered. The crude

product was recrystallized from acetonitrile and stored -20°C to give yellow crystalline product of complex **5**. The remaining residue was recrystallized from toluene to give colourless crystals of complex **11**.

$Ti(C_{12}H_8FN_2O)_2(OC_3H_7)_2$ (5). **Yield:** 390 mg, 0.65 mmol, 57%. **ES MS (+):** m/z 597.16 [MH^+]. **Anal. Found:** C 61.3; H 4.5; N 11.1%. **Anal. Calculated for $C_{30}H_{30}F_2N_4O_4Ti\cdot(C_2H_3N)$:** C 60.7; H 5.3; N 10.8%. **^{1}H NMR** (C_6D_6, 300.13 MHz, 300K) δ 10.66 [br. s, 1H] 9.16 [m, 1H], 8.65 [d, 1H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz], 8.30 [m, 2H], 8.17 [m, 1H], 8.06 [m, 1H], 7.18 [m, 1H], 7.09 [m, 1H], 7.03-6.69 [m, 5H], 6.67 [m, 1H], 6.45 [m, 1H], 4.68 [m, 2H, C<u>H</u>$(CH_3)_2$], 1.23 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.1 Hz, CH(C<u>H</u>$_3)_2$], 1.19 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.1 Hz, CH(C<u>H</u>$_3)_2$]. **$^{13}C\{^1H\}$ NMR** (C_6D_6, 125.76 MHz, 300K) δ 162.0 [Q, <u>C</u>-O], 160.5 [Q], 156.5 [Q, <u>C</u>-F, d, $^1J(^{13}C\text{-}^{19}F)$ = 175.9 Hz], 155.1 [Q], 153.2 [Q, <u>C</u>-F, d, $^1J(^{13}C\text{-}^{19}F)$ = 238.8 Hz], 150.2 [<u>C</u>H], 148.1 [<u>C</u>H], 138.9 [<u>C</u>H], 137.3 [<u>C</u>H], 126.3 [<u>C</u>H], 125.7 [<u>C</u>H], 125.0 [<u>C</u>H], 124.2 [<u>C</u>H], 122.4 [<u>C</u>H], 121.4 [<u>C</u>H], 116.2 [<u>C</u>H, d, $^2J(^{13}C\text{-}^{19}F)$ = 18.8 Hz], 114.9 [<u>C</u>H, d, $^2J(^{13}C\text{-}^{19}F)$ = 18.9 Hz], 80.0 [<u>C</u>H$(CH_3)_2$], 25.2 [CH(<u>C</u>H$_3)_2$]

$[(C_{12}H_9FN_2O)Ti(OC_3H_7)_2]_2[\mu\text{-}OC_3H_7]_2$ (11). **Yield:** 60.7 mg, 0.07 mmol, 12%. **ES MS (+):** 883.34 m/z [MH^+]. **Anal. Found:** C 57.0; H 6.8; N 6.5%. **Anal. Calculated for $C_{42}H_{60}F_2N_4O_8Ti$:** C 57.2; H 6.9; N 6.4%. **^{1}H NMR** (C_6D_6, 300.13 MHz, 300K) δ 8.39 [d, 2H, $^3J(^1H\text{-}^1H)$ = 6.0Hz] 8.23 [m, 6H], 7.21 [m, 2H], 6.82 [m, 2H], 6.28 [m, 2H], 4.74 [m, 2H, C<u>H</u>$(CH_3)_2$], 1.31 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz, CH(C<u>H</u>$_3)_2$], 1.22 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz, CH(C<u>H</u>$_3)_2$]. **$^{13}C\{^1H\}$ NMR** (C_6D_6, 75.47 MHz, 300K) δ 160.3 [Q, <u>C</u>-O], 155.9 [Q], 146.0 [<u>C</u>H], 139.1 [<u>C</u>H], 125.7 [<u>C</u>H], 124.0 [<u>C</u>H], 115.8 [<u>C</u>H, d, $^2J(^{13}C\text{-}^{19}F)$ = 15.1 Hz], 80.1 [<u>C</u>H$(CH_3)_2$], 25.8 [CH(<u>C</u>H$_3)_2$]

Synthesis of $Ti(C_{12}H_7Cl_2N_2O)_2(OC_3H_7)_2$ (6). To Ti(^{i}OPr)$_4$ (0.11 mL, 0.37 mmol) in toluene was added picolinyl-(2',5'-dichlorophenyl)amide (0.20 g, 0.75 mmol) in toluene drop-wise. The mixture was heated under reflux for 16 hours and the solvent removed *in vacuo*. Petroleum ether was added and the mixture heated, cooled and then filtered. The resulting petroleum ether mixture was stored at -20°C to give crystals suitable for X-ray crystallography. **Yield:** 251 mg, 0.36 mmol, 97%. **ES MS (+):** m/z 698.05 $[MH]^+$. **Anal. Found:** C 51.6; H 4.8; N 7.8%. **Anal. Calculated for $C_{30}H_{28}Cl_4N_4O_4Ti$:** C 51.6; H 4.1; N 8.0%. **^{1}H NMR** (C_6D_6, 300.13 MHz, 300K) δ 8.87 [d, 2H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz] 8.32 [d, 2H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz], 7.35 [d, 4H, $^3J(^1H\text{-}^1H)$ = 9.0 Hz], 6.81 [m, 2H], 6.68-6.58 [m, 4H], 4.53 [m, 2H, C<u>H</u>$(CH_3)_2$], 1.12 [d, 12H, $^3J(^1H\text{-}^1H)$ = 6.1 Hz, CH(C<u>H</u>$_3)_2$]. **$^{13}C\{^1H\}$ NMR** (C_6D_6, 125.76 MHz, 300K) δ 161.6 [Q, <u>C</u>-O] 153.5 [Q], 146.5 [<u>C</u>H], 146.1 [<u>C</u>H], 139.3 [<u>C</u>H], 137.3 [Q], 127.6 [<u>C</u>H$(CH_3)_2$], 126.3 [<u>C</u>H], 124.3 [<u>C</u>H], 123.6 [<u>C</u>H], 122.9 [<u>C</u>H], 80.4 [<u>C</u>H], 22.8 [CH(<u>C</u>H$_3)_2$]

Synthesis of 7 and 12. To Ti(^{i}OPr)$_4$ (0.31 mL, 1.05 mmol) in toluene was added picolinyl-(3'-nitrophenyl)amide (0.50 g, 2.06 mmol) in toluene drop-wise. The mixture was heated under reflux for 16 hours and the solvent removed *in vacuo*. Petroleum ether was added and the mixture heated, cooled and then filtered. The resulting petroleum ether mixture was stored at -20°C to give yellow crystals of complex **7**. The remaining residue was recrystallized from toluene to give a colourless crystals of complex **12**.

$Ti(C_{12}H_8N_3O_3)_2(OC_3H_7)_2$ (7). **Yield:** 92.0 mg, 0.14 mmol, 13%. **Anal. Found:** C 54.3; H 4.5; N 13.0%. **Anal. Calculated $C_{30}H_{30}N_6O_8Ti$:** C 55.4; H 4.7; N 12.9%. **^{1}H NMR** (C_6D_6, 300.13 MHz, 300K) δ 9.29 [d, 2H, $^3J(^1H\text{-}^1H)$ = 2.1 Hz] 8.39 [d, 2H, $^3J(^1H\text{-}^1H)$ = 5.2 Hz], 8.23 [d, 2H, $^3J(^1H\text{-}^1H)$ = 7.9 Hz], 8.09 [m, 2H], 7.91 [m, 2H], 7.20 [m, 2H], 6.79

[m, 2H], 6.33 [m, 2H], 4.81 [m, 2H, C<u>H</u>(CH$_3$)$_2$], 1.32 [d, 6H, ^3J(^{1}H-^{1}H) = 6.1 Hz, CH(C<u>H</u>$_3$)$_2$], 1.24 [d, 6H, ^3J(^{1}H-^{1}H) = 6.1 Hz, CH(C<u>H</u>$_3$)$_2$]. **^{13}C{^{1}H} NMR** (C_6D_6, 125.76 MHz, 300K) δ 161.8 [Q, <u>C</u>-O], 154.8 [C Q], 149.7 [Q], 145.7 [<u>C</u>H], 139.1 [<u>C</u>H], 132.2 [<u>C</u>H], 129.2 [<u>C</u>H], 127.6 [<u>C</u>H], 126.0 [<u>C</u>H], 120.4 [<u>C</u>H], 119.0 [<u>C</u>H], 80.9 [<u>C</u>H(CH$_3$)$_2$], 25.3 [CH(<u>C</u>H$_3$)$_2$]

[($C_{12}H_8N_3O_3$)Ti(OC_3H_7)]$_2$[OC_3H_7][(OC_3H_7)$_2$Ti][μ-O] (12). **Yield:** 10.6 mg, 0.01 mmol, 3%. **ES MS (+):** m/z 1069.4 [MH]$^+$. **Anal. Found:** C 55.2; H 6.9; N 7.5%. **Anal. Calculated for $C_{48}H_{72}N_6O_{11}Ti_3$:** C 54.8; H 6.9; N 8.0%. **^{1}H NMR** (C_6D_6, 500.13 MHz, 300K) δ 9.21 [m, 1H] 8.39 [m, 1H], 8.01 [m, 1H], 7.84 [m, 1H], 7.57 [m, 3H], 6.24 [m, 1H], 4.72 [m, 1H, C<u>H</u>(CH$_3$)$_2$], 1.23 [d, 3H, ^3J(^{1}H-^{1}H) = 6.1 Hz, CH(C<u>H</u>$_3$)$_2$], 1.16 [d, 3H, ^3J(^{1}H-^{1}H) = 6.1 Hz, CH(C<u>H</u>$_3$)$_2$]. **^{13}C{^{1}H} NMR** (C_6D_6, 125.76 MHz, 300K) δ 162.6 [Q, <u>C</u>-O], 155.9 [Q], 149.6 [Q], 146.2 [<u>C</u>H], 132.7 [<u>C</u>H], 127.0 [<u>C</u>H], 125.2 [<u>C</u>H], 123.3 [<u>C</u>H], 119.1 [<u>C</u>H], 81.4 [<u>C</u>H(CH$_3$)$_2$], 25.9 [CH(<u>C</u>H$_3$)$_2$].

Synthesis of Ti($C_{12}H_8FN_2O$)$_2$(OC_3H_7)$_2$ (8). To Ti(^{i}OPr)$_4$ (0.34 mL, 1.15 mmol) in toluene was added picolinyl-(4-fluorophenyl)amide (0.5 g, 2.31 mmol) in toluene drop-wise. The mixture was heated under reflux for 16 hours and the solvent removed *in vacuo* and petroleum ether added. The mixture was heated until dissolution, cooled and then filtered. The resulting petroleum ether mixture was stored at -20°C to give only ligand. The residue was recrystallized from toluene at -20°C to yield complex **8**. **Yield:** 398 mg, 0.67 mmol, 58%. **ES MS (+):** 597.17m/z [MH$^+$]. **Anal. Found:** C 59.9; H 4.8; N 9.5%. **Anal. Calculated for $C_{30}H_{30}F_2N_4O_4Ti$:** C 60.4; H 5.1; N 9.4%. **^{1}H NMR** (C_6D_6, 300.13MHz, 300K) δ 8.38 [d, 2H, ^{3}J(^{1}H-^{1}H) = 6.0Hz, CH of C_5<u>H</u>$_4$N] 8.24 [m, 6H, CH of C_6<u>H</u>$_4$F & C_5<u>H</u>$_4$N], 7.21 [t of d, CH of C_6<u>H</u>$_4$F], 6.82 [t of d, 2H, CH of C_5<u>H</u>$_4$N], 6.28 [t of d, 2H, CH of C_5<u>H</u>$_4$N], 4.74 [sept., 2H, CH of OC<u>H</u>(CH$_3$)$_2$], 1.31 [d, 6H, ^{2}J(^{1}H-^{1}H) = 6.0Hz, CH of OCH(C<u>H</u>$_3$)$_2$], 1.22 [d, 6H, ^{2}J(^{1}H-^{1}H) = 6.0Hz, CH of OCH(C<u>H</u>$_3$)$_2$]. **^{13}C NMR** (C_6D_6, 75.47MHz, 300K) δ 160.3 [C of <u>C</u>ON], 155.9 [C of <u>C</u>$_5$H$_4$N], 146.0 [CH of <u>C</u>$_5$H$_4$N], 139.1 [CH of <u>C</u>$_6$H$_4$F], 125.7 [CH of <u>C</u>$_5$H$_4$N], 124.0 [CH of <u>C</u>$_5$H$_4$N], 115.9-115.7 [d, ^{2}J(^{13}C-^{19}F) = 15.1Hz, CH of <u>C</u>$_6$H$_4$F], 80.1 [CH of O<u>C</u>H(CH$_3$)$_2$], 25.8 [CH of OCH(<u>C</u>H$_3$)$_2$]

Synthesis of 9 and 13. To Ti(^{i}OPr)$_4$ (0.29 mL, 0.98 mmol) in toluene was added picolinyl-(2-tbutylphenyl)amide (0.50 g, 1.97 mol) in toluene drop-wise. The mixture heated under reflux for 16 hours under nitrogen and the solvent removed *in vacuo*. The crude product was recrystallized from acetonitrile and stored at -20°C to yield colourless crystals of complex **9**. The filtrate of these crystals also yielded colourless crystals of complex **13**.

Ti($C_{16}H_{17}N_2O$)$_2$(OC_3H_7)$_2$ (9). Yield: 138 mg, 0.21 mmol, 21%. **ES MS (+):** m/z 673.3 [MH]$^+$. **Anal. Found:** C 65.7; H 6.7; N 9.5%. **Anal. Calculated for $C_{32}H_{48}N_4O_4Ti$·0.5(C_2H_3N):** C 65.2; H 7.7; N 9.8%. **^{1}H NMR** (C_6D_6, 300.13 MHz, 300K) δ 8.56 [d, 2H, ^3J(^{1}H-^{1}H) = 5.1 Hz], 8.23 [m, 4H], 7.69 [m, 2H], 7.48 [m, 2H], 7.26 [m, 2H], 6.86 [m, 2H], 6.45 [m., 2H], 4.71 [m, 2H, C<u>H</u>(CH$_3$)$_2$], 1.86 [s, 18H, CH(C<u>H</u>$_3$)$_3$], 1.30 [d, 6H, ^3J(^{1}H-^{1}H) = 6.0 Hz, CH(C<u>H</u>$_3$)$_2$], 1.20 [d, 6H, ^3J(^{1}H-^{1}H) = 6.0 Hz, CH(C<u>H</u>$_3$)$_2$]. **^{13}C{^{1}H} NMR** (C_6D_6, 125.76 MHz, 300K) δ 158.6 [Q, <u>C</u>-O], 156.0 [Q], 147.5 [<u>C</u>H], 146.4 [Q], 143.7 [<u>C</u>H], 139.3 [Q], 126.8 [<u>C</u>H], 126.3 [<u>C</u>H], 125.4 [<u>C</u>H], 124.4 [<u>C</u>H], 123.8 [<u>C</u>H], 79.9 [<u>C</u>H(CH$_3$)$_2$], 36.4 [Q, <u>C</u>(CH$_3$)$_3$)], 31.1 [C(<u>C</u>H$_3$)$_3$], 25.7 [<u>C</u>H(CH$_3$)$_2$].

[($C_{16}H_{17}N_2O$)Ti(OC_3H_7)$_2$]$_2$[μ-OC_3H_7][(OC_3H_7)$_2$Ti][μ-O) (13). Yield: 66.6 mg, 0.06 mmol, 18%. **ES MS (+):** m/z 1138.5 [MH]$^+$. **Anal. Found:** C 58.7; H 6.7; N 6.7%. **Anal. Calculated for $C_{44}H_{62}N_4O_{11}Ti_3$:** C 58.5; H 6.9; N 6.2%. **^{1}H**

NMR (C_6D_6, 500.13 MHz, 300K) δ 8.93 [m, 1H], 8.57 [m, 1H], 8.44 [m, 1H], 8.25 [m, 3H], 7.69 [m, 1H] 7.45 [m, 2H], 7.30 [m, 2H], 7.13 [m, 2H], 6.85 [m, 1H], 6.70 [m, 1H], 6.44 [m, 1H], 4.71 [m, 2H, C<u>H</u>$(CH_3)_2$], 1.86 [s, 9H, C$(C\underline{H}_3)_3$], 1.55 [s, 9H, C$(C\underline{H}_3)_3$], 1.30 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz, CH$(C\underline{H}_3)_2$], 1.21 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.0 Hz, CH$(C\underline{H}_3)_2$]. **$^{13}C\{^1H\}$ NMR** (C_6D_6, 125.76 MHz, 300K) δ 147.7 [<u>C</u>H], 137.2 [<u>C</u>H], 127.0 [<u>C</u>H], 126.3 [<u>C</u>H], 125..6 [<u>C</u>H], 124.8 [<u>C</u>H], 122.5 [<u>C</u>H], 63.6 [<u>C</u>H$(CH_3)_2$], 30.3 [Q, <u>C</u>$(CH_3)_3$], 25.2 [C$(\underline{C}H_3)_3$].

Synthesis of $Ti(C_{15}H_{15}N_2O)_2(OC_3H_7)_2$ (10). To Ti(^{i}OPr)$_4$ (0.31 mL, 1.04 mmol) in toluene was added picolinyl-(2',4',6'-trimethylphenyl)amide (0.50 g, 2.08 mmol) in toluene drop-wise. The mixture was heated under reflux for 16 hours and the solvent removed *in vacuo*. Petroleum ether was added and the mixture heated, cooled and then filtered. The resulting petroleum ether mixture was stored at -20°C to yield complex **13**. **Yield:** 115 mg, 0.18 mmol, 17%. **ES MS (+):** m/z 668.3 [M+Na]. **Anal. Found:** C 68.7; H 5.9; N 8.3%. **Anal. Calculated for $C_{36}H_{44}N_4O_4Ti\cdot0.2(C_7H_8)$:** C 67.8; H 6.9; N 8.5%. **^{1}H NMR** (C_6D_6, 500.13 MHz, 300K) δ 9.33 [br. s, 2H], 8.32 [d, 2H, $^3J(^1H\text{-}^1H)$ = 4.7 Hz], 8.27 [m, 2H], 7.03 [m, 2H], 6.78 [m, 4H], 3.66 [m, 2H, C<u>H</u>$(CH_3)_2$], 2.23 [s, 12H, C$(C\underline{H}_3)_3$], 2.13 [s, 6H, C$(C\underline{H}_3)_3$], 0.95 [d, 12H, $^4J(^1H\text{-}^1H)$ = 3.7 Hz, CH$(C\underline{H}_3)_3$]. **$^{13}C\{^1H\}$ NMR** (C_6D_6, 125.76MHz, 300K) δ 147.7 [<u>C</u>H], 137.0 [<u>C</u>H], 128.9 [<u>C</u>H], 127.6 [<u>C</u>H], 125.6 [<u>C</u>H], 122.4 [<u>C</u>H], 63.6 [<u>C</u>H$(CH_3)_2$], 25.2 [CH$(\underline{C}H_3)_2$], 20.7 [C$(\underline{C}H_3)_3$], 18.4 [C$(\underline{C}H_3)_3$].

Synthesis $[(C_{12}H_7F_2N_2O)Ti(OC_3H_7)_2]_2[\mu\text{-}OC_3H_7]_2[(OC_3H_7)_2Ti][\mu\text{-}O]$ (14). To Ti(^{i}OPr)$_4$ (0.32 mL, 1.08 mmol) in toluene was added picolinyl-(2',4'-difluorophenyl)amide (0.50 g, 1.98 mmol) in toluene drop-wise and the mixture heated under reflux for 16 hours and the solvent removed *in vacuo*. Petroleum ether was added and the mixture heated, cooled and then filtered. The resulting crude product was recrystallized from acetonitrile and stored at -20°C to give yellow crystals of complex **14**. **Yield:** 133 mg, 0.15 mmol, 42%. **Anal. Found:** C 55.0; H 5.9; H 7.9%. **Anal. Calculated for $C_{54}H_{70}F_2N_4O_{11}Ti_3\cdot3(C_2H_3N)$:** C 55.7; H 6.2; N 7.6%**ES MS (+):** m/z 1098.3 $[M+2H]^{+\cdot}$. **^{1}H NMR** (C_6D_6, 300.13MHz, 300K) δ 8.55 [d, 1H, $^3J(^1H\text{-}^1H)$ = 5.4 Hz] 8.30 [d, 1H, $^3J(^1H\text{-}^1H)$ = 7.8 Hz], 8.04 [m, 1H], 7.02-6.81 [m, 3H], 6.78 [m, 1H], 4.67 [m, 1H, C<u>H</u>$(CH_3)_2$], 1.19 [d, 6H, $^3J(^1H\text{-}^1H)$ = 6.1 Hz, CH$(C\underline{H}_3)_2$]. **$^{13}C\{^1H\}$ NMR** (C_6D_6, 125.76 MHz, 300K) δ 161.4 [Q, <u>C</u>-O], 160.5 [Q], 156.7 [Q, <u>C</u>-F, d, $^1J(^{13}C\text{-}^{19}F)$ = 260.3 Hz], 154.6 [Q], 150.0 [<u>C</u>H], 145.8 [<u>C</u>H], 139.0 [<u>C</u>H], 133.7 [<u>C</u>H, d, $^3J(^{13}C\text{-}^{19}F)$ = 3.7 Hz], 126.7 [<u>C</u>H], 126.2 [<u>C</u>H], 125.7 [<u>C</u>H], 124.1 [<u>C</u>H], 122.4 [<u>C</u>H], 111.2 [<u>C</u>H, d, $^2J(^{13}C\text{-}^{19}F)$ = 90.5 Hz], 104.3 [<u>C</u>H], 80.1 [<u>C</u>H$(CH_3)_2$], 25.2 [CH$(\underline{C}H_3)_2$].

Appendix A. Supplementary data

CCDC 1455810, 1455812, 1455809 and 1455814 contains the supplementary crystallographic data for complexes **6**, **9**, **11** and **12**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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