The reactions of $\alpha$-amino acids and $\alpha$-amino acid esters with high valent transition metal halides: synthesis of coordination complexes, activation processes and stabilization of $\alpha$-ammonium acylchloride cations†

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Titanium tetrachloride smoothly reacted with a selection of $\alpha$-amino acids (aaH) in CH$_2$Cl$_2$ affording yellow to orange solid coordination compounds, 1a–d, in 70–78% yields. The salts [NHEt$_3$][TiCl$_4$(aa)], 2a–b, were obtained from TiCl$_4$/aaH/NET$_3$ (aa = L-phenylalanine, N,N-dimethylphenylalanine), in 60–65% yields. The complex Nb$_2$Cl$_6$[µ-κ$^2$O,K$^2$N-[CHCH$_2$CH(NH$_2$)CO$_2$Me]$_2$]$_2$ 3, was isolated from the reaction of l-proline with NbCl$_5$/NH$_2$Pr$_2$ in CH$_2$Cl$_2$ at room temperature. The X-ray structure of 3 features a bridging (E)-1,2-bis(3,4-dihydro-2H-pyrrol-5-yl)ethene-1,2-diolato ligand, resulting from the unprecedented C–C coupling between two proline units. Unusually stable $\alpha$-ammonium acyl chlorides were prepared by the reactions of PCl$_5$/MCl$_x$ (MCl$_x$ = NbCl$_5$, WCl$_6$) with l-proline, N,N-dimethylphenylalanine, sarcosine and l-methionine. MX$_5$ (M = Nb, Ta; X = F, Cl) reacted with l-leucine methylester and l-proline ethylester to give ionic coordination compounds, [MX$_4$L$_2$][MX$_6$] (M = Nb, L = Me$_2$CHCH$_2$CH(NH$_2$)CO$_2$Me, X = F, 9; Cl, 11a; M = Nb, X = Cl, L = HNCCH$_2$CHCHCO$_2$Et 11c; Ta, 11d), in moderate to good yields. [NbCl$_5$(Me$_2$CHCH$_2$CH(NH$_2$)CO$_2$Me)][NbCl$_6$, 12] was isolated as a co-product of the reaction of NbCl$_5$ with l-leucine isopropylester, and crystallographically characterized. The reaction of NbCl$_5$ with l-serine isopropylester afforded NbCl$_3$(OCH$_2$CH(NH$_2$)CO$_2$Pr), 13, in 66% yield. The activation of the ester O–R bond was observed in the reactions of l-leucine methyl ester with NbF$_5$ and l-proline ethyl ester with MB$_5$ (M = Nb, Ta), these reactions proceeding with the release of EF and EtBr, respectively. All the metal products were characterized by analytical and spectroscopic methods, while DFT calculations were carried out in order to provide insight into the structural and mechanistic aspects.

Introduction

$\alpha$-Amino acids constitute a class of organic compounds arousing great interest in synthetic chemistry, in view of their easy availability and low toxicity,† the typical presence of a stereogenic centre (making them suitable substrates for asymmetric catalysis)² and the possibility of firmly coordinating metal ions.⁴

The esterification of the carboxylic acid moiety is one of the most viable modifications of the $\alpha$-amino acid skeleton, and indeed a good number of $\alpha$-amino acid esters have been synthesized and employed with reference to several application fields.⁴ Metal complexes containing $\alpha$-amino acid esters as ligands are especially relevant to bio-inorganic chemistry, being useful to the synthesis of peptides,⁵,⁶ as biological models,⁷ and as scaffolds for the development of new drugs.⁸ Furthermore, $\alpha$-amino acids and $\alpha$-amino acid ester metal complexes, being possible chiral sources,⁹ have found increasing attention as privileged, potential catalysts for environmentally friendly asymmetric syntheses.¹⁰,¹¹

It is noteworthy that the large majority of these studies refer to middle to late transition metals, whereas very little is known about the parallel chemistry with early transition metal compounds. In particular, the homoleptic halides of high valent...
elements (oxidation state ≥ 4) belonging to groups 4, 5 and 6, HVTMH, are strongly oxophilic species, usually very air sensitive and incompatible with water. This characteristic has probably discouraged the linking with an “opposite world”, i.e. the exploration of the reactivity with α-amino acids, which in turn exhibit high water affinity, and their simple derivatives such as α-amino acid esters.

As a matter of fact, the coordination chemistry of HVTMH with α-amino acid esters still remains an unexplored field of research, with the exception of a former synthetic study regarding MoCl₅. Similarly, the only information available up to 2014 on the interaction of HVTMH with α-amino acids, in the absence of further reactants, is a note dealing with the reactivity of TiCl₄ with glycine. In all of the cases, the structural characterization of the products relied on limited data.

Recently, in the framework of our interest in the chemistry of HVTMH with naturally occurring compounds, we have found that MoCl₅ and WC₆ behave as chlorinating agents towards natural α-amino acids, affording fairly stable α-ammonium acylchloride salts.

On the other hand, the interaction of MX₅ (M = Nb, Ta; X = Cl, Br) with α-amino acids leads to dinuclear complexes containing bridging α-amino acidato ligands via HX release. Subsequent activation of the coordinated α-amino acidato moiety has been observed in mild conditions in some specific cases, leading to iminium salts.

Herein, we will present an extension of our study on the reactivity between α-amino acids and HVTMH, including the synthesis of TiCl₄ derivatives, the unprecedented metal mediated C–C dimerization of a α-amino acid (l-proline) and the stabilization of otherwise reactive α-ammonium acylchloride cations. We will also describe some reactivity of α-amino acid ester with niobium and tantalum pentahalides. All the reactions were carried out in a weakly coordinating solvent (CH₂Cl₂) by using enantiopure L-organic reactants in case. The metal products were characterized by elemental analysis, IR and NMR spectroscopy, while DFT calculations assisted the structural characterization. A DFT study was performed also in order to shed some light on the NbCl₅-directed unusual l-proline pseudo dimerization.

Results and discussion

Reactivity of MCl₅ with α-amino acids

Titanium tetrachloride. Titanium tetrachloride smoothly reacted with a series of α-amino acids in dichloromethane affording moisture sensitive, yellow to orange solid materials 1a–d, in 70 to 78% yields (Scheme 1). Compounds 1 are coordination adducts: in this respect, the reactivity of TiCl₄ with α-amino acids differs from that of MCl₅ (M = Nb, Ta), featured by HCl release, and from those of MoCl₅ and WC₆, leading to Cl/O interchange products (see Introduction).

Compounds 1a–d were characterized by analytical and spectroscopic methods. The IR spectra (solid state) contain one medium and one strong intensity absorption in the range 1600–1400 cm⁻¹. These two absorptions are due, respectively, to the asymmetric (νₛ) and the symmetric (νₛ) stretching vibrations of the carboxylato group. In general, the wavenumber difference (Δνₛ–s = νₛ – νₛ) is considered as a useful parameter to discriminate between monodentate, chelating, and bridging bidentate carboxylato ligands. Δνₛ–s values within the range 100 to 150 cm⁻¹ are typical of either chelating or bridging bidentate carboxylato ligands. In view of the IR data available for 1a–d, i.e. Δνₛ–s varies between 103 (1a) and 135 (1d) cm⁻¹, and the DFT results (vide infra), we propose a bridging bidentate-coordination fashion. This implies that the amino acid ligand should be coordinated to titanium as a zwitterion. Accordingly, a broad IR absorption is observed at 3091 cm⁻¹ in the IR spectrum of 1d, assigned to ammonium N–H stretching vibration.

The geometry proposed on the basis of spectroscopic data was supported by DFT calculations on the possible isomers of 1b. The dinuclear structure [TiCl₄(α-κ²-O₂CCH(CH₂Ph)NH₃)]₂, depicted in Fig. 1, resulted meaningfully more stable than mononuclear structures (see Fig. S1 given as ESI†).

Compounds 1a–d display low solubility in common organic solvents. The NMR spectra were recorded in CD₃CN, displaying single sets of resonances. The ¹H NMR spectra exhibit broad...
resonances in the 7.7–7.0 ppm range, related to the uncoordinated ammonium group. The $^{13}$C-NMR spectra of the more soluble 1a–b show the resonance of the carboxylate carbon at 176.1 and 170.0 ppm, respectively. These values are similar to those reported for O,O-coordinated $\alpha$-amino acids in NbCl$_5$ derivatives.

The coordination of organic species to high valent transition metal chlorides represents, in a number of cases, the preliminary step of some activation process. The activation is favoured by the strong Lewis acidity of the metal centre, and may be triggered by the addition of a Brønsted base. For instance, Peryshkov and coworkers recently described a C–H bond activation reaction of nitriles by means of NEt$_3$ upon coordination to TaCl$_5$.

Thus, the reaction of 1b with NEt$_3$ proceeded with selective deprotonation of the ammonium group; analogous result was achieved by treatment of a TiCl$_4$–N$_2$N-dimethylphenylalanine mixture with NEt$_3$ (Scheme 2). The reactions of 1a,c,d with NEt$_3$ were not straightforward, leading to non identified compounds; the solid isolated from 1a/NEt$_3$ revealed to be paramagnetic.

The CH$_2$Cl$_2$ soluble compounds 2a–b (Scheme 2) were isolated by addition of hexane to the respective reaction mixtures.

The $^1$H NMR spectra of 2a–b display a low field resonance accounting for the triethylammonium proton (e.g. at 9.09 ppm in the case of 2a); the resonances of the N-bound protons within the anion undergo significant upfield shift on going from the amino acid unit in 1b to the amino acidate one in 2b ($\Delta \delta > 3$ ppm). The IR spectra of 2a–b exhibit a strong absorption around 1700 cm$^{-1}$; this evidence suggests O,N-coordination of the aminoacidate moiety, leaving a uncoordinated C=O bond. The geometries of the 2a,b anions were DFT optimized, considering either mononuclear and dinuclear structures as starting points (Fig. S2†). Thus, mononuclear compounds bearing N,O-chelating $\alpha$-aminoacids (Fig. 2) resulted much more stable than dinuclear homologues (see ES† for more details).

Niobium pentachloride. We reported that the 2 : 1 reactions of NbX$_5$ (X = Cl, Br) with a variety of $\alpha$-amino acids afforded dinuclear $\alpha$-aminoacids complexes via HCl release. The addition of a further equivalent of organic reactant resulted in the decarboxylation of one amino acidate moiety, with consequent formation of iminium salts and Nb-formate species (see Scheme 3, showing the specific case of N,N-dimethylphenylalanine).

With the aim of exploring the possibility of further activation pathways, we investigated the reactions of Nb$_2$Cl$_6$($\alpha$-aminoacidate) complexes with NEt$_3$. In general, the amino acidate moiety did not undergo activation under these conditions, with an exception provided by the Nb$_2$Cl$_6$($\alpha$-proline)/NEt$_3$ system. This latter evolved into a complicated mixture of products, including minor amounts of Nb$_2$Cl$_6$($\alpha$-N,N,N,N',N'-pentahydroxy-2,6-dimethylphenylalanine). The use of NH$_3$Pr$_3$ in the place of NEt$_3$ allowed to isolate red crystals of 3 (12% yield), and also yellow crystals of [NH$_3$Pr$_3$][NbCl$_6$], 4 (40% yield), Scheme 4.

Scheme 2 Synthesis of anionic $\alpha$-aminoacidate titanium compounds.

Fig. 2 DFT-optimized geometries of the most stable anions of 2a and 2b (C-PCM/M06 calculations). Selected computed bond lengths for 2a (Å): Ti–O 1.909; Ti–N 2.240; Ti–Cl (trans O) 2.321; Ti–Cl (trans N) 2.263; Ti–Cl (trans Cl) 2.340, 2.353; C–O 1.316; C–O 1.212; N–H 1.018, 1.021. Selected computed angles for 2a ($^\circ$): O–Ti–N 76.0; O–Ti–Cl 87.8, 88.8, 97.6, 160.9; C–O–Ti 127.5. Selected computed bond lengths for 2b (Å): Ti–O 1.893; Ti–N 2.434; Ti–Cl (trans O) 2.309; Ti–Cl (trans N) 2.271; Ti–Cl (trans Cl) 2.333, 2.354; C–O 1.316; C–O 1.212. Selected computed angles for 2b ($^\circ$): O–Ti–N 73.2; O–Ti–Cl 88.6, 89.7, 98.5, 160.3; C–O–Ti 150.2.

Scheme 3 Reaction of NbCl$_6$ with N,N-dimethylphenylalanine.

Scheme 4 Unusual activation of $\alpha$-proline by NbCl$_6$/amine.
The X-ray structure of 3 is shown in Fig. 3, with relevant bonding parameters listed in Table 1; the X-ray structure of 4 is given as ESI (Fig. S3; Tables S1A and S1B†).

Complex 3 displays crystallographic 1 (C1) symmetry with the inversion centre located on the middle of the C(1)–C(1̄) bond. The complex is composed of an unprecedented anionic \( [\text{NbCl}_4]^+ \) cationic fragments. Such anionic ligand is almost perfectly planar (mean deviation from the least squares plane 0.0387 Å) and below this plane. C(1), C(2) and N(1) [sum angles 360.0(9), 360.0(7) and 360.0(6)\(^\circ\), respectively] show a perfect sp\(^2\) hybridization, and the C(1)–C(1̄) [1.357(6) Å] and C(2)–N(1) [1.276(6) Å] distances are typical for double bonds.\(^\text{23}\)

The \( \{\text{C}_2\text{O}_2\} \) core of the \( (E)\text{-1,2-bis(3,4-dihydro-2H-pyrrol-5-yl)ethene-1,2-diolate} \) in 3 is a fully deprotonated 1,2-enediol. In general, 1,2-enediols are quite unstable species,\(^\text{24}\) whose stabilization may be supplied by hydrogen-bonded protons,\(^\text{25}\) or by chelating (N,O) coordination to transition metals.\(^\text{26}\)

![Fig. 3 ORTEP drawing of 3. Displacement ellipsoids are at the 50% probability level.](image)

### Table 1 Selected bond lengths (Å) and angles (\(^\circ\)) for 3

| Bond/Angle | Value (Å/°) |
|-----------|-------------|
| Nb(1)–Cl(1) | 2.3319(13) |
| Nb(1)–Cl(2) | 2.2833(11) |
| Nb(1)–Cl(3) | 2.3453(12) |
| Nb(1)–Cl(4) | 2.3435(12) |
| Nb(1)–O(1) | 1.927(3) |
| C(1)–C(1) | 1.357(6) |
| C(1)–C(2) | 1.471(7) |
| C(1)–C(3) | 1.530(6) |
| N(1)–C(2) | 1.276(6) |
| C(1)–N(1) | 1.337(10) |
| C(2)–C(3) | 1.387(8) |
| C(3)–C(4) | 1.528(6) |
| N(1)–C(2) | 1.477(6) |
| O(1)–N(1) | 1.927(3) |
| Cl(1)–Nb(1)–O(1) | 158.18(10) |
| Cl(3)–Nb(1)–Cl(4) | 170.32(5) |
| Nb(1)–O(1)–C(2) | 117.6(3) |
| Nb(1)–N(1)–C(2) | 114.6(4) |
| C(1)–C(2)–O(1) | 158.18(10) |
| Cl(2)–Nb(1)–N(1) | 167.62(11) |
| O(1)–Nb(1)–N(1) | 73.03(4) |
| N(1)–C(2)–O(1) | 73.03(4) |
| Cl(2)–N(1)–C(5) | 110.4(4) |
| N(1)–C(2)–C(3) | 110.7(4) |
| C(2)–C(3)–C(4) | 102.3(4) |
| C(2)–C(3)–C(5) | 105.3(4) |
| O(1)–C(1)–C(2) | 120.2(6) |
| C(2)–C(1)–C(1̄) | 125.2(6) |

\(^\text{23}\) Symmetry transformation used to generate C(1)̄: –x + 1, –y, –z + 1.

Basically, the process leading to 3 is a C–C bond forming condensation of two proline units (Scheme 5A). Differently, typical \( \alpha \)-amino acid condensation generates a peptide bond (Scheme 5B).\(^\text{27}\)

In order to gain some insight into the mechanism of the low yield formation of 3, a DFT study was undertaken (see Scheme S1 in the ESI†). It seems plausible that the C–C bond forming step consists in the coupling of two acylchloride units, accompanied by the release of HCl and assisted by the amine (see Scheme S1, E → F → G). Indeed the side reactions NH2PF3 + HCl → [NH3PF3]Cl and [NH3PF3]Cl + NbCl5 → 4 should contribute to decrease the \( \Delta G \) variation of the process leading to 3.

The crystals of 3 exhibited insufficient solubility in suitable deuterated solvents, thus preventing the NMR characterization.

MCl\(_n\)/phosphorous pentachloride (MCl\(_n\) = NbCl\(_5\), WCl\(_6\)). The carboxylic acid to acyl chloride conversion is an important preliminary step for the subsequent functionalization of \( \alpha \)-amino acids.\(^\text{28}\) PCl\(_3\) has been traditionally employed as CI-source in order to obtain the relevant \( \alpha \)-ammonium acylchloride salts (Fischer procedure); the counterion is Cl\(^-\) or [PCl\(_6\)]\(^-\) depending on the employed PCl\(_3\)/\( \alpha \)-aminoacid molar ratio.\(^\text{29}\) \( \alpha \)-Ammonium acylchloride species stable at room temperature have been obtained only with primary ammonium groups and in the absence of donor atoms in the side chain. On the other hand, in the case of the \( \alpha \)-proline derivative (secondary N), both Cl\(^-\) and [PCl\(_6\)]\(^-\) salts undergo quick degradation at room temperature, due to HCl release and subsequent condensation reactions.\(^\text{29}\) Furthermore, the reactions of PCl\(_3\) with \( \alpha \)-N,N-dimethylphenylalanine (tertiary N), sarcosine (secondary N) and \( \alpha \)-methionine (thioether group), in CH\(_2\)Cl\(_2\), proceed with the formation of complicated mixtures of products (\( ^1\)H and \( ^{31}\)P NMR spectroscopy). Thus, the \( \alpha \)-N,N-dimethylphenylalanine and \( \alpha \)-methionine acylchloride derivatives have not been known heretofore, while the highly moisture sensitive [NH(Me)CH2COCl]\([\text{WOCl}_5]\) has been recently obtained by ourselves from sarcosine/WCl\(_6\).\(^\text{14a}\)

Some of us recently reported\(^\text{13b,29}\) a straightforward and clean route to unusually stable salts of the acylchloride derivative of \( \alpha \)-proline, by combination of the traditional PCl\(_3\)-chlorinating reaction with the considerable stability imparted by the [MCl\(_6\)]\(^{-}\) (M = Nb, Ta) anions, Scheme 6.\(^\text{13b,29}\)

We reckoned that the easily available [NbCl\(_5\)]\(^{-}\) anion could provide stability also to other unstable/unknown \( \alpha \)-ammonium acylchloride cations (see above). Therefore, we tried to optimize
and generalize the synthetic procedure shown in Scheme 6. When a dichloromethane 1 : 1 molar mixture of PCl5 and NbCl5 was treated with L-N,N-dimethylphenylalanine or sarcosine,21 the subsequent 31P NMR analysis on the reaction solution evidenced the presence of POCl1 as prevalent phosphorus species [singlet at 6.2 ppm (from PCl5/NbCl5/L-N,N-dimethylphenylalanine) and 5.6 ppm (from PCl5/NbCl5/sarcosine), respectively].13b,29,32 The corresponding [NbCl6]− α-ammonium acylchlorides, 5a–b, were isolated at room temperature in 40–50% yields (Scheme 7). The presence of [NbCl6]− in 5a–b was unambiguously detected by a typical 93Nb NMR resonance around 0 ppm.13a,34 The structure of 5a was determined by X-ray diffraction (Fig. 4, Table 2). It contains the [PhCH2CH(NMe2)COCl]− cation, which has never been reported heretofore. Within crystals of 5a, some intermolecular N–H···Cl hydrogen bonds are present involving the ammonium group of the cation as donor and the chloride ligands of the anion as an acceptor. The bonding parameters of the cation are comparable to those around 0 ppm.13a,34 The C(1)−O(1) distance [1.178(5) Å] corresponds to an almost pure double bond, whereas all the other contacts are typical for single bonds.34 The C(2) atoms displays an absolute S configuration with refined Flack parameter 0.03(2).35

The iminium salt [PhCH2＝NMe2][NbCl6] (see Scheme 3) and the adduct NbCl5(O＝PCl3), 6, identified by comparison of the crystal cell data with those reported in the literature,26 were obtained as minor products from NbCl5/L-N,N-dimethylphenylalanine and NbCl5/sarcosine, respectively.

The synthetic approach leading to 5a–b exploits the M–Cl (M = P, Nb) bond energy scale,13b,37 making PCl5 a preferential chlorinating agent respect to NbCl5, and the stability of the [NbCl6]− anion. Similar considerations led us to test the PCl5/WCl6 mixture; it should be noted that anionic simple derivatives of WCl6 (i.e., WCl6, WOC15−) have recently proposed as effective partners for the stabilization of otherwise reactive cations.14a,38

Hence, the reactions of PCl5/WCl6 (1 : 1 mixture) with L-proline, L-N,N-dimethylphenylalanine, sarcosine and L-methionine proceeded with PCl5 to POCl3 conversion (31P NMR), and straightforwardly afforded the respective α-ammonium acylchloride cations (Scheme 7). According to elemental analyses and magnetic measurements,28 the cations were isolated in good yields as [WCl6]− salts, 7a–b, respectively from PCl5/WCl6/L-proline and PCl5/WCl6/L-N,N-dimethylphenylalanine. Otherwise, different anions were presumably associated with sarcosine and methionine derivatives, including [WOCl5]− (few crystals of [MeNH2CH2CH(Cl)＝O][WOCl5] were isolated and X-ray characterized) and W[ν] species.

The characterization of the 1 : 1 mixture WCl6/PCl5 suggested that both chlorides remained intact when mixed together (see Experimental for details). This implies that the WCl6 to WCl6− reduction, as clearly observed in 7a–b, is promoted by the α-amino acid. Analogous WCl6 reduction has

![Scheme 6 Stable pyrrolidinium-2-carboxylic chloride salts from L-proline and MC5 (M = Nb, Ta).](image)

![Scheme 7 Formation of otherwise unstable α-ammonium acylchloride cations from α-amino acids and niobium and tungsten chlorides.](image)

![Fig. 4 ORTEP drawing of 5a. Displacement ellipsoids are at the 50% probability level.](image)

| Table 2 Selected bond lengths (Å) and angles (°) for 5a |
|---------------------------------|---------------------------------|---------------------------------|
| Nb(1)−Cl(1) 2.3305(11)           | Nb(1)−Cl(2) 2.3344(11)          |
| Nb(1)−Cl(3) 2.2921(11)           | Nb(1)−Cl(4) 2.3475(11)          |
| Nb(1)−Cl(5) 2.3844(11)           | Nb(1)−Cl(6) 2.4206(11)          |
| C(1)−Cl(7) 1.758(5)              | C(1)−O(1) 1.718(5)              |
| C(1)−C(2) 1.516(7)               | C(2)−C(3) 1.553(6)              |
| N(1)−C(4) 1.500(6)               | N(1)−C(5) 1.499(5)              |
| C(3)−Cl(7) 1.501(6)              | C(3)−C(6) 1.516(5)              |
| Cl(3)−Nb(1)−Cl(4) 176.12(5)     | Cl(2)−Nb(1)−Cl(5) 174.23(5)    |
| Cl(3)−Nb(1)−Cl(6) 179.14(4)     | O(1)−C(1)−Cl(7) 120.6(4)       |
| O(1)−C(1)−C(2) 125.4(4)         | Cl(7)−C(1)−Cl(2) 113.9(3)      |
| C(1)−C(2)−C(3) 115.1(4)         | C(1)−C(2)−N(1) 107.3(4)        |
| C(2)−C(3)−C(6) 115.1(4)         | C(2)−N(1)−C(4) 111.4(3)        |
| C(2)−N(1)−C(3) 114.9(3)         | C(4)−N(1)−C(5) 111.4(4)        |
been previously observed in a number of cases by interaction with organic compounds.\textsuperscript{36,39}

All the $\alpha$-ammonium acyl chloride cations produced from PCl$_5$/NbCl$_5$ and PCl$_5$/WCl$_6$ were fully characterized by IR and NMR spectroscopy, and those cations derived from $\alpha$-N,N-dimethylphenylalanine and $\alpha$-methionine are reported here for the first time. The chloro-acyl moiety manifests itself by a strong IR absorption in the region 1765–1783 cm$^{-1}$, other than the $^{13}$C NMR resonance in the range 169.0–171.7 ppm.

**Reactivity of MCl$_n$ with $\alpha$-amino acid esters**

**Preparation of $\alpha$-amino acid ester hydrochlorides and $\alpha$-amino acid esters.** The $\alpha$-amino acid ester derivatives, 8, were prepared from the corresponding hydrochlorides, 8-HCl, which were in general isolated (Scheme 8). Although most of the compounds 8 and 8-HCl have been already appeared in the literature,\textsuperscript{40} we decided to collect their preparations and IR and NMR data in this paper, in view of possible modifications to the reported procedures or additional spectroscopic data.

**Reactions with niobium and tantalum pentahalides.** The reactions of $\alpha$-amino acid esters with NbF$_5$ are often non selective, affording in most cases mixtures of products where the only recognizable compounds are the scarcely soluble ammonium ester salts [RCH(NH$_3$)COOR][NbF$_6$]. These might be formed as a consequence of some activation reaction or the adventitious presence of water.\textsuperscript{41} We were able to isolate satisfactory yields of well defined coordination compounds only in two cases (Scheme 9).

Compound 9 can be viewed as a coordination compound resulting from the unsymmetrical rupture of the structure of NbF$_5$ (a tetramer in the solid state).\textsuperscript{17a,42} The IR spectrum shows a strong absorption at 1648 cm$^{-1}$, attributed to the stretching vibration of the C=O bond belonging to the ester function. The ca. 100 cm$^{-1}$ shift to lower wavenumbers is in agreement with the coordination of the carbonyl moiety to niobium. The shift of the absorptions due to the stretching of the amino group from 3380 cm$^{-1}$ (in 8k) to 3232 cm$^{-1}$ (in 9) suggests that also the nitrogen atom is involved in the coordination to the metal centre. Accordingly, two low field $^1$H NMR resonances have been found for the NH$_2$ group in 9 ($\delta = 8.6$ and 7.0 ppm, CDCl$_3$ solution). On the other hand, the same group
gives rise to a singlet at 1.65 ppm in the $^1$H NMR spectrum of 8k.

In addition, the $^{19}$F and $^{93}$Nb NMR spectra (decet at 103 ppm and septet at $-1553$ ppm, respectively) are unequivocal fingerprints for the presence of the [NbF$_6$]$^-$ anion in solution.$^{13e,42,43}$

In conclusion, on considering the tendency of NbF$_5$ to the unsymmetrical breaking of the Nb–F bridges, with formation of [NbF$_4$]$^+$ cations and [NbF$_6$]$^-$ anions,$^{42}$ analytical and spectroscopic data suggest that 9 is a salt containing an octacoordinate [NbF$_4$(Me$_2$CHCH$_2$CHNH$_2$CO$_2$Me)]$^+$ cation, comprising two O,N-ligated $\alpha$-amino acid esters, and a [NbF$_6$]$^-$ anion. The coordination number of the cation was confirmed by DFT calculations, being six-coordinate geometries less stable by more than 30 kcal mol$^{-1}$. The optimized geometry is shown in Fig. 5. DFT calculations with dichloromethane as implicit solvent also indicated that the [NbF$_4$(Me$_2$CHCH$_2$CHNH$_2$CO$_2$Me)]$^+$ salt is slightly more stable compared to its neutral isomer NbF$_4$(Me$_2$CHCH$_2$CHNH$_2$CO$_2$Me). The metal centre in this last species should be eight-coordinated, the $\alpha$-amino acid ester behaving as N,O-donor chelating ligand (Fig. S4†).

It worth noting that the majority of coordination complexes containing $\alpha$-amino acid ester ligands are based on late transition metals (Ru, Os, Co, Rh, Pt, Zn).$^{44}$ Only few examples are known with group 6 elements$^{45}$ and also derivatives of group 4 and group 5 metals are very rare.

The reaction of NbF$_5$ with $\alpha$-proline ethyl ester, 8b, revealed a different outcome, and 10 was obtained under the same conditions employed for NbF$_5$/8k. The use of Nb/8b molar ratio $= 2$ afforded 10 with the best yield (Scheme 9). Ethyl fluoride was NMR identified as a co-product of the reaction performed in CD$_2$Cl$_2$ in a closed tube, while $\alpha$-proline was recovered after hydrolysis of the reaction mixture. These experimental facts support the presence in 10 of a carboxylato moiety originated from the cleavage of the ester function.

Compound 10 is a colourless solid whose salient spectroscopic features are two IR bands at 3381 cm$^{-1}$ (N–H) and 1636 cm$^{-1}$ (C=O), and $^1$H and $^{19}$F NMR resonances at 11.77 ppm (NH) and 100.9 ppm ([NbF$_6$]$^-$), respectively. These data suggest a bidentate N,O-coordination of the $\alpha$-amino carboxylate ligand. Dinuclear geometries with the $\alpha$-amino acidate as bridging ligand were ruled out by DFT calculations. The optimized geometry of the cation of 10 is depicted in Fig. 6 (see also Fig. S5 given as ES†).

We extended the present study to the interaction of $\alpha$-amino acid esters with the heavier niobium pentahalides. These reactions led to complicated mixtures of metal products, with presumable activation of the organic substrates. Only in a few cases, all involving the metal pentachlorides, a clean reaction pathway was observed (Scheme 10).

All the identified products, 11a–d and 12, are colourless to pale yellow solids, being scarcely soluble in organic solvents. Spectroscopic considerations discussed for 10 are valid also for 11a–d, thus suggesting the bidentate N,O coordination of two $\alpha$-amino acid ester ligands to the same metal centre within a cation. The presence of the [NbCl$_6$]$^-$ anion in 11a–e is the consequence of unsymmetrical cleavage of the dinuclear NbCl$_5$, structure,$^{13e,35,46}$ and was unambiguously evidenced by a sharp $^9$Nb NMR resonance occurring in the interval 4–13 ppm.$^{13e,21}$

DFT calculations were carried out on the cation of 11a, considering either one or two $\alpha$-amino acid esters in the niobium sphere. The coordination of another equivalent of the $\alpha$-amino acid ester to [NbCl$_4$(Me$_2$CHCH$_2$CHNH$_2$CO$_2$Me)]$^+$ resulted a favourable process, being the associated $\Delta G$ variation

![Fig. 5 DFT-optimized geometry of the cation of 9 (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 2.273, 2.273; Nb–N 2.364, 2.364; Nb–F 1.900, 1.900, 1.900, 1.900; C–O(Nb) 1.234, 1.234; C–O(Me) 1.303, 1.303; N–H 1.019, 1.019, 1.019, 1.020. Selected computed angles (°): O–Nb–N 68.3, 68.3; O–Nb–O 135.0; N–Nb–N 132.3; C–O–Nb 123.3, 123.3.](image)

![Scheme 10 Synthesis of niobium pentachloride derivatives of $\alpha$-amino acid esters.](image)
around $-25$ kcal mol$^{-1}$. The DFT-optimized geometry of $\text{[NbCl}_4(\text{Me}_2\text{CHCH}_2\text{CHNH}_2\text{CO}_2\text{Me})_2]^{+}$ is represented in Fig. 7.

A crop of X-ray quality crystals of 12 was obtained directly from the reaction mixture after separation from 11a. Compound 12 differs from the previous compounds as far as the solubility is concerned. Once isolated in the solid state, it does not dissolve again in common organic solvents.

Compound 12 consists of an ionic packing of $\text{[NbCl}_5(\text{CH}_3\text{CH}_2\text{CHNH}_2\text{CO}_2\text{Me})\text{]+}$ cations and $\text{[NbCl}_6]^{-}$ anions. The cation is represented in Fig. 8, and the related bonding parameters are reported in Table 3. A view of the structure of the anion is given in Fig. S6,† the relevant bonding parameters being collected in Table S2A.† H-bonds between the NH$_2$-group of the cation and the chlorides of $\text{[NbCl}_6]^{−}$ are present within the crystals (see Table S2B† for details). Compound 12 crystallizes in the chiral space group $P2_1$, and the C(2) atom of the $\alpha$-amino acid ester ligand displays $S$ absolute configuration.

The source of protonation leading to 12 is not clear, being possibly the result of some activation of the organic reactant promoted by the strongly acidic niobium chloride. Nevertheless, the occurrence of fortuitous hydrolysis might play some role and should not be ruled out.

12 represents the second crystallographically characterized example where a cationic $\alpha$-amino acid ester is coordinated to any metal centre, and the first one where the coordination occurs via oxygen. In fact, previous to this work, only the structure of a Ru(ii) complex containing a $\eta^6$-bonded $\alpha$-phenylalaninium methyl ester was reported.

More commonly, $\alpha$-amino acid esters act as ligands in the neutral form RCHNH$_2$CO$_2$R', via the N-atom or both N and O.

We moved to study the reaction of NbCl$_5$ with $\alpha$-serine isopropylester, 8h, i.e. a $\alpha$-amino acid ester bearing a peripheral OH group and potentially acting as a pincer ligand. The 1:1 reaction of NbCl$_5$ and 8h in refluxing chloroform led to the formation of $\text{[NbCl}_5(\text{OCHCH}_2\text{NHCOOiPr})]$,

A crop of X-ray quality crystals of 12a was obtained directly from the reaction mixture a

Table 3 Selected bond distances (Å) and angles (°) for the $\text{[NbCl}_6(\text{CH}_3\text{CH}_2\text{CHCH}_2\text{CHNH}_2\text{CO}_2\text{Me})\text{]+}$ cation in 12. The data relative to the $\text{[NbCl}_6]^{-}$ anion are reported in Tables S2A and S2B

| Bond/Geometry | Value |
|---------------|-------|
| Nb(2)–Cl(7)   | 2.3555(9) |
| Nb(2)–Cl(9)   | 2.3318(10) |
| Nb(2)–Cl(11)  | 2.2918(9)  |
| C(1)–O(1)     | 1.231(4)   |
| C(7)–O(2)     | 1.473(3)   |
| C(2)–N(1)     | 1.506(4)   |
| C(7)–Nb(2)–Cl(10) | 174.26(3) |
| Cl(8)–Nb(2)–O(1) | 177.18(6) |
| O(1)–C(1)–C(2) | 112.3(3)   |
| O(1)–C(1)–C(2) | 113.5(3)   |
| N(1)–C(2)–N(1) | 109.4(2)   |

Fig. 7 DFT-optimized geometry of the cation of 11a (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 2.261, 2.266; Nb–N 2.377, 2.381; Nb–Cl 2.390, 2.382, 2.413, 2.414; C–O(Nb) 1.236, 1.237; C–O(Me) 1.294, 1.294; N–H 1.020, 1.021, 1.020, 1.021. Selected computed angles (°): O–Nb–O 68.4, 68.4; O–Nb–O 136.2; N–Nb–N 132.9; O–C–O 123.7, 123.8.

Fig. 8 ORTEP drawing of the $\text{[NbCl}_4(\text{CH}_3\text{CH}_2\text{CHCH}_2\text{CHNH}_2\text{CO}_2\text{Me})_2]^{+}$ cation in 12. The $\text{[NbCl}_4]^{−}$ anion is reported in Fig. S6.† Displacement ellipsoids are at the 50% probability level.

Fig. 9 DFT-optimized geometry of 13 (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 1.873; Nb–N 1.943; Nb–Cl 2.359, 2.368, 2.389; N–H 1.019. Selected computed angles (°): O–Nb–N 76.0; O–Nb–Cl 93.3, 96.7, 157.8; N–Nb–Cl 82.0, 109.3, 110.0.
Compound 13 showed a single set of signals in $^1$H and $^{13}$C NMR spectra (in CD$_3$CN); $^1$H resonances are shifted to higher ppm values with respect to 8h [most notably $\delta$(NH) from 2.6 ppm in 8h to 7.0 ppm in 13], while $^{13}$C resonances are shifted to lower ppm values [e.g., $\delta$(CO) from 175 ppm in 8h to 167 ppm in 13].

At variance to the other $\alpha$-amino acid ester complexes of niobium in this work, compound 13 is a neutral species in solution with a single $^{93}$Nb resonance at $-493$ ppm. DFT calculations suggest a mononuclear structure (Fig. 9) as the most probable geometry. A positive Gibbs energy variation (about 3.5 kcal mol$^{-1}$) is accompanied to the dimerization of this species to the dinuclear form (see Fig. S7 and S8 for more details).

We could not cleanly isolate metal products from MBr$_5$/$\alpha$-amino acid ester (M = Nb, Ta). However, NMR investigations outlined the release of ethyl bromide from $\gamma$-proline ethylester, in the presence of MBr$_5$ (see Experimental for details).

Conclusions

The reactions of TiCl$_4$ with a series of $\alpha$-amino acids do not proceed with HCl release, in spite of the Lewis acidic character of the metal centre, and afford dinuclear coordination compounds containing zwitterionic ligands. Deprotonation of the ammonium function may be easily promoted by the addition of triethylamine, resulting in a modification of the coordination fashion of the $\alpha$-amino acid frame. On the other hand, the interaction of $\gamma$-proline with NbCl$_5$/NEt$_2$ has provided the first example of C–C bond forming self-condensation of a $\alpha$-amino acid, although in modest yield. The overall transformation may be regarded as a Lewis acid–base addition of triethylamine, resulting in a modification of the coordination fashion of the $\alpha$-amino acid frame. On the other hand, the interaction of $\gamma$-proline with NbCl$_5$/NEt$_2$ has provided the first example of C–C bond forming self-condensation of a $\alpha$-amino acid, although in modest yield. The overall transformation may be regarded as a Lewis acid–base addition of triethylamine, resulting in a modification of the coordination fashion of the $\alpha$-amino acid frame. On the other hand, the interaction of $\gamma$-proline with NbCl$_5$/NEt$_2$ has provided the first example of C–C bond forming self-condensation of a $\alpha$-amino acid, although in modest yield.

Experimental

General

**Warning:** all the metal products reported in this paper are highly moisture-sensitive, thus rigorously anhydrous conditions were required for the reaction and crystallization procedures. The reaction vessels were oven dried at 140 ºC prior to use, evacuated (10$^{-2}$ mmHg) and then filled with argon. TiCl$_4$, NbX$_5$ (X = F, Cl), PCl$_3$ and WCl$_6$ were purchased from Strem (>98% purity) and stored in sealed tubes under argon atmosphere. NbBr$_3$ and TaBr$_3$ were prepared according to literature procedures and stored under argon atmosphere. Once isolated, the metal products were conserved in sealed glass tubes under argon. The organic reactants were commercial products (Sigma-Aldrich) stored under argon atmosphere as received.

Solvents (Sigma-Aldrich) were distilled before use from appropriate drying agents. Chromatographic purification of organic products was carried out on columns of deactivated alumina (4% w/w water). Infrared spectra were recorded at 298 K on a FT IR-Perkin Elmer Spectrometer, equipped with a UATR sampling accessory. NMR spectra were recorded at 293 K on a Bruker Avance II DRX400 instrument equipped with a BBFO broadband probe. The chemical shifts for $^1$H and $^{13}$C were referenced to the non-deuterated aliquot of the solvent; the chemical shifts for $^{93}$Nb were referenced to external [NEt$_4$][NbCl$_6$]; the chemical shifts for $^{19}$F were referenced to external CFCl$_3$. Conductivity measurements was carry out using an Eutech Con 700 instrument (cell constant = 1.0 cm$^{-1}$). Magnetic susceptibilities (reported per W atom) were measured on solid samples at 298 K with a Magway MSB Mk1 magnetic susceptibility balance (Sherwood Scientific Ltd). Diamagnetic corrections were introduced according to König. Carbon, hydrogen and nitrogen analyses were performed on a Carlo Erba mod. 1106 instrument. The chloride/bromide content was determined by the Mohr method on solutions prepared by dissolution of the solids in aqueous KOH and heated at boiling temperature for 72 hours, followed by cooling to room temperature and addition of HNO$_3$ up to neutralization. Titanium, niobium and tantalum were analyzed, respectively, as TiO$_2$ and M$_2$O$_5$ (M = Nb, Ta), obtained by hydrolysis of the samples followed by calcination in a platinum crucible.

Reactions of TiCl$_4$ with $\alpha$-amino acids: synthesis of TiCl$_4$(aa)

(aa = $\gamma$-proline, 1a; $\gamma$-phenylalanine, 1b; sarcosine, 1c; N,N-dimethylglycine, 1d)

**General procedure.** A suspension of the appropriate $\alpha$-amino acid (1.50 mmol) in CH$_2$Cl$_2$ (ca. 15 mL) was treated with a solution (100 mg mL$^{-1}$) of TiCl$_4$ (1.50 mmol) in heptane. The mixture was stirred at room temperature overnight, then hexane (ca. 30 mL) was added. The precipitate was separated and dried in vacuo.

**TiCl$_4$(aa)*** (1a). Yellow solid, yield 321 mg (70%). Anal. calcd for C$_7$H$_7$Cl$_4$NO$_2$Ti: C, 19.70; H, 2.98; N, 4.60; Cl, 46.52; Ti, 15.70. Found: C, 19.39; H, 3.09; N, 4.52; Cl, 45.88; Ti, 15.89. IR (solid state): $\nu$ = 3219 mw, 2962 w, 1570 m, 1544 vs, 1441 vs, 1367 m, 1331 ms, 1260 m, 1081 m, 1031 ms, 798 s cm$^{-1}$. $^1$H NMR (CD$_3$CN): $\delta$ = 7.46, 7.15 (br, 2H, NH$_2$); 4.53 (br, 1H, NCH); 3.54, 3.45, 2.42, 2.20, 2.06 (br, 6H, CH$_2$) ppm. $^{13}$C NMR (CD$_3$CN): $\delta$ = 176.1 (OCO); 61.6 (CH); 47.6, 28.6, 23.7 (CH$_2$) ppm.

**TiCl$_4$(1b)*** (1b). Light orange solid, yield 388 mg (73%). Anal. calcd for C$_9$H$_{10}$Cl$_4$NO$_2$Ti: C, 30.46; H, 3.12; N, 3.95; Cl, 39.96; Ti, 13.49. Found: C, 30.60; H, 3.02; N, 4.13; Cl, 39.40; Ti, 13.28. IR (solid state): $\nu$ = 3030 m-br, 1600 m, 1558 w, 1445 vs-br, 1336 m, 1331 ms, 1260 m, 1081 m, 1031 ms, 798 s cm$^{-1}$. $^1$H NMR (CD$_3$CN): $\delta$ = 7.39–7.30, 6.98 (8H, Ph + NH$_3$); 4.46 (m, 1H, CH); 3.28 (m, 2H, CH$_2$) ppm. $^{13}$C NMR (CD$_3$CN): $\delta$ = 170.0 (OCO); 134.1 (ipso-PH); 129.8, 129.2, 127.9 (C$_6$H$_5$); 61.8 (CH); 35.3 (CH$_2$) ppm.

**TiCl$_4$(1c)*** (1c). Yellow solid, yield 448 mg (78%). Anal. calcd for C$_{15}$H$_{15}$Cl$_4$NO$_2$Ti: C, 45.14; H, 3.70; N, 3.60; Cl, 38.56; Ti, 17.73. Found: C, 45.61; H, 3.74; N, 3.69; Cl, 38.49; Ti, 17.73. IR (solid state): $\nu$ = 3185 m, 2930 vw, 2810 vw, 1575 ms, 1561 vs,
Reactions of TiCl₄ with ω-aminophenol/NEt₃: synthesis of
[NNH₂][TiCl₄(aa)] (aa = 1-phenylnalanine, 2a; N,N-dimethylphenylalanine, 2b)

General procedure. A suspension of the appropriate ω-aminophenol acid (1.00 mmol) in CH₂Cl₂ (ca. 10 mL) was treated with a solution (100 mg mL⁻¹) of TiCl₄ (1.00 mmol) in heptane. The mixture was stirred at room temperature overnight, then hexane (ca. 30 mL) was added. The lipids were evaporated with a syringe, then CH₂Cl₂ (20 mL) and NEt₃ (1.00 mmol) were added in the order given. The mixture was allowed to stir for 5 h, then hexane (30 mL) was added. The resulting precipitate was separated and dried in vacuo.

[NNH₂][TiCl₄(1-phenylalanine)], 2a. Light brown solid, yield 297 mg (65%). Anal. calcld for C₁₇H₁₈Cl₂O₅N₃Ti: C, 39.50; H, 5.75; N, 6.14; Cl, 39.50; Ti, 10.50. Found: C, 39.33; H, 5.87; N, 6.16; Cl, 39.19; Ti, 10.61. IR (solid state): ν = 3306 w, 3240 w, 2928 w-br, 2984 w-br, 2675 w-br, 2488 w-br, 1691 vs, 1652 vs, 1568 s, 1545 s, 1228 m, 1099 m-s, 1070 m-s, 749 vs, 702 s cm⁻¹. ¹H NMR (CD₂Cl₂): δ = 7.09 (s, 1H, NH); 7.39-7.50 (5H, Ph); 3.48 (m, 1H, CH₃); 4.13-4.36 (2H, NH₂); 3.26 (m, 6H, NCH₃); 3.40; 3.17 (dd, 2H, CH₂Ph); 1.40 (t, 3JHH = 7.34 Hz, 9H, NCH₂CH₃) ppm. ¹³C NMR (CD₂Cl₂): δ = 179.5 (OCO); 135.9 (ipso-Ph); 129.4, 129.2, 127.5 (Ph); 61.7 (CH); 47.1 (NCH₃); 38.6 (CH₂Ph); 9.0 (NCH₂CH₃) ppm.

[NNH₂][TiCl₄(1-N,N-dimethylphenylalanine)], 2b. Yellow solid, yield 290 mg (60%). Anal. calcld for C₁₇H₁₉Cl₂O₅N₃Ti: C, 42.18; H, 6.25; N, 5.79; Cl, 32.99; Ti, 9.89. Found: C, 42.36; H, 6.08; N, 5.65; Cl, 32.91; Ti, 9.72. IR (solid state): ν = 3260 w-br, 2963 w, 2679 w-br, 1702 s, 1660 vs, 1518 vs, 1454 s, 1228 m, 1098 m-s, 1070 m-s, 749 vs, 702 s cm⁻¹. ¹H NMR (CD₂Cl₂): δ = 7.09 (s, 1H, NH); 7.36-7.25 (6H, Ph); 4.47 (m, 1H, CH₃); 3.32 (m, 6H, NCH₃); 3.19, 3.07 (m, 2H, CH₂Ph); 2.95, 2.73 (s, 6H, NEt₃); 1.42 (t, 3JHH = 7.34 Hz, 9H, NCH₂CH₃) ppm. ¹³C NMR (CD₂Cl₂): δ = 178.8 (OCO); 138.9 (ipso-Ph); 129.9, 129.2, 128.6, 126.6 (Ph); 75.6 (CH); 50.9, 47.6 (NEt₃); 47.5 (NCH₃); 30.8 (CH₂Ph); 8.9 (NCH₂CH₃) ppm.

Reaction of NbCl₅ with ω-proline/NEt₃: synthesis and isolation of
[NbCl₅(κ-ωH₂κ-ωN,N-CH₂CH₂CH₂CONCO₅)], 3, and [NH₄⁺][Pr₃][NbCl₅], 4

NbCl₅ (0.358 g, 1.42 mmol) and ω-proline (0.163 g, 1.42 mmol) were allowed to react in CH₂Cl₂ (20 mL). The solution was repetitively purged with nitrogen gas in order to remove released HCl. After six hours, the yellowish mixture was treated with NH₄Cl (0.203 mL, 1.45 mmol), then the stirring was prolonged for additional 20 min. The final dark-red mixture was filtered off in order to remove a minor amount of solid, layered with hexane and settled aside at −30 °C. Red crystals of 3 were recovered after 48 h. Yield 56 mg, 12%. Anal. calcld for C₁₉H₁₉Cl₂N₅O₅Nb: C, 31.12; H, 2.67; N, 12.66; Cl, 27.93; Nb, 16.92. Found: C, 31.0; H, 2.67; N, 12.66; Cl, 27.93; Nb, 16.92.

The mother liquors were dried in vacuo, hence the residue was dissolved into CHCl₃ (10 mL). The solution was layered with pentane and settled aside at −30 °C, thus 4 was isolated as a yellow-orange crystals after 48 h. Yield 238 mg, 40%. Anal. calcld for C₁₉H₁₉Cl₂N₅O₅Nb: C, 31.12; H, 2.67; N, 12.66; Cl, 27.93; Nb, 16.92. Found: C, 31.0; H, 2.67; N, 12.66; Cl, 27.93; Nb, 16.92.

Reactions of ω-aminocids with PCl₅/NbCl₅: synthesis of
[(R)MeNHC(OC)(O)Cl][NbCl₅] (R = Me, R′ = CH₂Ph, 5a; R = R′ = H, 5b)

General procedure. A suspension of PCl₅ (169 mg, 0.81 mmol) and NbCl₅ (220 mg, 0.81 mmol) in CH₂Cl₂ (10 mL) was stirred at room temperature for 2–3 h. Then the appropriate ω-aminophenol acid (0.81 mmol) was added. The resulting mixture was stirred at room temperature for 2 h. The solution was concentrated to 3–5 mL, then it was layered with pentane and stored in the freezer (−30 °C) for one week. A crop of crystalline material was collected and then stored at −30 °C. By slow evaporation of the crystallization solutions under inert atmosphere, few crystals of [PhCH₂NEt₂] [NBCl₅] and [NBCl₅(O-PCL₅)], 6, were obtained from PCl₅/NbCl₅/i-Pr₃/N,N-dimethylphenylalanine and PCl₅/NbCl₅/sarcosine, respectively.

[Me₂NHCH(PhCH₂Ph)C(O)Cl][NbCl₅], 5a. Orange solid, yield 214 mg (47%) from PCl₅/NbCl₅/i-Pr₃/N,N-dimethylphenylalanine. Anal. calcld for C₁₉H₁₉Cl₂N₅O₅Nb: C, 31.12; H, 2.67; N, 12.66; Cl, 27.93; Nb, 16.92. Found: C, 31.0; H, 2.67; N, 12.66; Cl, 27.93; Nb, 16.92. ¹H NMR (CD₂Cl₂): δ = 8.0 (br, 1H, NH); 7.36-7.25 (6H, Ph); 4.47 (m, 1H, CH₂); 3.32 (m, 6H, NCH₃); 3.19, 3.07 (m, 2H, CH₂Ph); 2.95, 2.73 (s, 6H, NEt₃); 1.42 (t, 3JHH = 7.34 Hz, 9H, NCH₂CH₃) ppm. ¹³C NMR (CD₂Cl₂): δ = 178.8 (OCO); 138.9 (ipso-Ph); 129.9, 129.2, 128.6, 126.6 (Ph); 75.6 (CH); 50.9, 47.6 (NEt₃); 47.5 (NCH₃); 30.8 (CH₂Ph); 8.9 (NCH₂CH₃) ppm.
Reactions of z-amino acids with PCl5/WCl6: synthesis of [NH2(CH2)4CH(CH2)3]Cl [WCl6], 7a, [Me2NHCH(CH2Ph)C(O)Cl] [WCl6], 7b, and [(R)NH2CH(R')C(O)Cl] (R = Me, R' = H; R = H, R' = CH2CH2SMe)

General procedure. A suspension of PCl5 (163 mg, 0.78 mmol) and WCl6 (310 mg, 0.78 mmol) in CD2Cl2 (4 mL) was stirred at room temperature overnight. Then the appropriate z-amino acid (0.78 mmol) was added. The resulting mixture was stirred at room temperature for 3 h. Thus 31P NMR analyses revealed the presence of POCl3 as unique phosphorous species. In addition, 1H and 13C NMR analyses on PCl5/WCl6/3-N,N-dimethylphenylalanine and PCl5/WCl6/sarcosine solutions pointed out the clean formation of 7a and [MeNH2(CH2)4CH(CH2)3]Cl. These solutions were layered with hexane and stored at −30 °C for a few days, thus resulting in the isolation of 7a and a mixture of [MeNH2(CH2)4CH(CH2)3]Cl. The reaction of PCl5/WCl6-methionine and PCl5/WCl6-proline, dark solid materials precipitated, which were isolated from the respective yellow solutions and dried in vacuo.

In a different experiment, a 1:1 PCl5/WCl6 mixture obtained in CD2Cl2 (3 mL) was analyzed. δ (CD2Cl2) = 0.3 S cm−1 mol−1. 31P NMR (CD2Cl2): δ = −81.1 (POCl3) ppm. Analysis was carried out on the solid residue obtained by removal of the volatiles in vacuo. Anal. calc. for Cl3PW: Cl, 64.48. Found: Cl, 63.91.

Magnetic measurement: diamagnetic.

2-[Me2NHCH(CH2Ph)C(O)Cl] [WCl6], 7b. Dark yellow - brown solid, yield 302 mg (73%) from PCl5/WCl6-proline. Anal. calc. for C31H33Cl5NO: C, 45.2; H, 3.63; Cl, 34.2; N, 3.11. Found: C, 45.0; H, 3.7; Cl, 34.2; N, 3.3. IR (solid state): ν = 3133 cm−1 (s, νas POCl3), 3073 cm−1 (m), 2955 w, 1768 vs (νCH=CH), 1708 m, 1306 m, 1070 w, 1015 m cm−1.

Magnetic measurement: aFe300 cm−1 = 0.360 × 10−2 cgsu, μeff = 0.93 BM.

2-[Me2NHCH(CH2Ph)C(O)Cl] [WCl6], 7b. Green solid, yield 302 mg (73%) from PCl5/WCl6-proline. Anal. calc. for C31H33Cl5NO: C, 45.2; H, 3.63; Cl, 34.2; N, 3.11. Found: C, 45.0; H, 3.7; Cl, 34.2; N, 3.3. IR (solid state): ν = 3133 cm−1 (s, νas POCl3), 3073 cm−1 (m), 2955 w, 1768 vs (νCH=CH), 1708 m, 1306 m, 1070 w, 1015 m cm−1.

Magnetic measurement: aFe300 cm−1 = 0.360 × 10−2 cgsu, μeff = 0.93 BM.

Synthesis of z-amino acid ester hydrochlorides

These compounds were obtained by a slight modification of the literature procedures.

Procedure A (compounds 8a-d-HCl). A 250 mL flask was charged with the appropriate alcohol (120 mL)/z-amino acid (ca. 35 mmol) combination. SOCl2 (12 mL, 170 mmol) was slowly added (3 h) to the suspension under vigorous stirring at room temperature. After 24 h stirring, volatiles were removed in vacuo at room temperature. The residue was suspended in Et2O (50 mL) for 4 h. The suspension was filtered and the resulting solid was dried in vacuo at 40 °C.

Procedure B (compounds 8e-i-HCl). SOCl2 (10 mL, 138 mmol) was slowly added (30 minutes) at 0 °C to the alcohol (80 mL) in a 500 mL Schlenk tube. The solution was then allowed to reach room temperature and the z-amino acid (24 mmol) was introduced. The mixture was refluxed for 8 h and a pale yellow solution was obtained. Afterwards, the volatiles were removed in vacuo and the residue was suspended in Et2O (50 mL) for 2 h. The suspension was filtered and the resulting solid was dried in vacuo at 40 °C.
mmol) was dissolved into CH$_2$Cl$_2$ (100 mL) and the solution was treated with a 28% w/w NH$_3$ aqueous solution until neutrality. This journal is © The Royal Society of Chemistry 2017 RSC Adv. Glycine isopropylester hydrochloride, 8c.$^{19}$ Colourless solid, yield 98%. H NMR (DMSO-$d_6$): $\delta$ = 8.51 (br, 3H, NH$_3$); 7.51–7.55 (m, 1H, OH); 6.44–6.94 (m, 1H, CH$_2$); 4.03–4.98 (m, 1H, CH$_2$); 3.38–3.78 (s, 2H, CH$_2$O + CH$_2$N); 1.56–1.61 (m, 6H, CH$_2$Me$_2$) ppm. $^{13}$C($^1$H) NMR (DMSO-$d_6$): $\delta$ = 172.6 (CO); 69.6 (CH$_2$); 59.5 (CH$_2$N); 54.9 (CH$_2$O) ppm.

Serine isopropylester hydrochloride, 8h.$^{21}$ Colourless solid, 71% yield. H NMR (DMSO-$d_6$): $\delta$ = 8.49 (s, 1H, OH); 8.49 (br, 3H, NH$_3$); 7.01 (d, $^3$J$_{HH}$ = 8.2 Hz, 2H, Ar); 6.67 (d, $^3$J$_{HH}$ = 8.2 Hz, 2H, Ar); 4.88 (sept, $^1$J$_{HH}$ = 5.9 Hz, 1H, OCH$_2$); 4.07 (t, $^1$J$_{HH}$ = 6.6 Hz, 1H, NCH$_2$); 3.17–2.83 (m, 2H, CH$_2$); 1.16 (d, $^3$J$_{HH}$ = 6.2 Hz, 3H) and 1.06 (d, $^3$J$_{HH}$ = 6.2 Hz, 3H, CH$_2$Me) ppm.

Synthesis of $\alpha$-amino acid esters. Three different procedures were adopted. Compounds 8a–g were prepared by treating the appropriate $\alpha$-amino acid ester hydrochloride with NH$_3$($aq$) as described in detail for 8a. Compounds 8h–j were prepared by treating the appropriate $\alpha$-amino acid ester hydrochloride with NaOH($aq$) as described in detail for 8h. Compounds 8k–l were obtained directly from the appropriate alcohol/$\alpha$-amino acid (ca. 50 mmol) combination, followed by treatment with NH$_3$($aq$); attempts to isolate (8k–l)·HCl led to mixtures of products.

Proline methylster, 8a.$^{20}$ Compound 8a·HCl (10.2 g, 60.4 mmol) was dissolved into CH$_2$Cl$_2$ (100 mL) and the solution was treated with a 28% w/w NH$_3$ aqueous solution until neutrality. The mixture was left stirring at room temperature for 24 h. The phases were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 50 mL). The organic phase was filtered and the solvent was removed by distillation at 40 °C and $p$ = 700 mbar. The product was obtained as a colourless liquid, which was stored under argon. Yield 4.71 g (60%). H NMR (CDCl$_3$): $\delta$ = 3.54 (s, 3H, CH$_2$); 2.92 (m, 1H, CH); 2.48 (m, 2H, CH$_2$N); 1.99, 1.64 (m, 4H, CH$_2$) ppm.

Proline ethylster, 8b.$^{20}$ Pale yellow liquid, yield 65%. IR (liquid film): $\nu$ = 1730 vs (H$_2$O) cm$^{-1}$. H NMR (CDCl$_3$): $\delta$ = 4.12 (q, $^3$J$_{HH}$ = 6.85 Hz, 2H, OCH$_2$); 3.73 (m, 1H, CH$_3$); 3.03, 2.90 (m, 2H, NCH$_2$); 2.07, 1.81, 1.73 (m, 4H, CH$_2$); 1.22 (t, $^3$J$_{HH}$ = 6.85 Hz, 3H, OCH$_2$CH$_3$) ppm. $^{13}$C($^1$H) NMR (CDCl$_3$): $\delta$ = 173.9 (C–O); 61.0 (OCH$_2$); 59.7 (CH); 46.9 (NCH$_3$); 30.2, 25.4 (CH$_2$); 14.2 (OCH$_2$CH$_3$) ppm.

Proline isopropylester, 8c.$^{20}$ Pale orange liquid, yield 60%. H NMR (CDCl$_3$): $\delta$ = 5.03 (sept, $^3$J$_{HH}$ = 6.3 Hz, 1H, OCH$_3$); 3.71 (dd, $^3$J$_{HH}$ = 8.3 Hz, 5.6 Hz, 1H, CH$_3$); 3.12–3.04 (m, 1H, NCH$_2$); 2.94–2.85 (m, 1H, NCH$_2$F); 2.28 (br, 2H, NH$_2$); 2.18–2.06 (m, 1H) and 1.86–1.67 (m, 3H, 3H, CH$_2$CH$_3$); 1.25 (d, $^3$J$_{HH}$ = 3.5 Hz, 3H, CHMe$_2$) ppm. $^{13}$C($^1$H) NMR (CDCl$_3$): $\delta$ = 174.6 (C–O); 68.0 (OCH$_2$); 59.6 (CH); 46.8 (NCH$_3$); 30.1, 25.2 (CH$_2$); 21.5 (OCH$_2$CH$_3$) ppm.

Phenylalanine methylster, 8d.$^{20}$ Pale orange liquid, yield 63%. IR (liquid film): $\nu$ = 3381 w (H$_2$O), 3062 w, 3028 w, 2951 w, 1732 vs (C=C–O), 1603 w, 1496 m, 1454 m, 1366 m, 1266 m, 1195 s, 1172 s, 1111 m, 1076 m, 1009 m, 826 m, 812 m, 744 m, 699 vs cm$^{-1}$. H NMR (CDCl$_3$): $\delta$ = 7.24–7.12 (5H, Ph); 3.66 (m, 1H, CH$_3$); 3.63 (s, 3H, OMe$_3$); 3.01, 2.80 (m, 2H, CH$_2$) ppm. $^{13}$C($^1$H) NMR (CDCl$_3$): $\delta$ = 175.3 (C–O); 137.3 (ips-ipo); 129.3, 128.5, 126.7 (Ph); 55.8 (OMe); 51.8 (CH); 41.0 (CH$_2$) ppm.
concentration of the solution was determined by $^1$H NMR, using CH$_3$Br$_2$ as internal standard.

**1-Tyrosine isopropylester, 8i.** Colourless solid, yield 83%. $^1$H NMR (CDCl$_3$): $\delta = 7.02$ (d, $^3J_{HH} = 8.3$ Hz, 2H, Ph); 6.68 (d, $^3J_{HH} = 8.3$ Hz, 2H, Ph); 5.05 (sept, $^3J_{HH} = 6.5$ Hz, 1H, OCH$_2$); 3.73–3.63 (m, 6H, NCH$_3$); 3.23 (br, 3H, NH$_2$ + NH); 3.04 (dd, $^3J_{HH} = 13.8$ Hz, $^3J_{HH} = 5.0$ Hz, 1H, CHF$^\beta$); 2.81 (dd, $^3J_{HH} = 13.7$ Hz, $^3J_{HH} = 7.7$ Hz, 1H, CH$^\beta$H$^\gamma$); 1.29–1.22 (m, 6H, CH$_2$Me$_2$) ppm.

**1-Alanine ethylester, 8j.** Prepared from commercial l-alanine ethylester hydrochloride (Fluka). Pale yellow viscous liquid, yield 60%. $^1$H NMR (CDCl$_3$): $\delta = 4.01$ (q, $^3J_{HH} = 6.6$ Hz, 2H, OCH$_2$); 3.37 (q, $^3J_{HH} = 6.6$ Hz, 1H, NCH); 1.54 (br, 2H, NH$_2$); 1.17 (d, $^3J_{HH} = 6.9$ Hz, 3H, CH$_3$CH$_2$); 1.13 (t, $^3J_{HH} = 7.1$ Hz, 3H, CH$_3$CH$_2$O) ppm.

**1-Leucine methylester, 8k.** Pale yellow liquid, yield 42%. IR (liquid film): $\nu = 3380$ w, 2965 m, 1553 (septet, $^3J_{HH} = 140$ Hz, 2H, Me), 1409 m, 1374 m, 1328 m, 1290 w, 1152 w, 1011 w-m, 922 w-m, 860 vs, 744 m-s cm$^{-1}$. $^1$H NMR (CDCl$_3$): $\delta = 7.17$ (br, 2H, NH$_2$); 4.44 (s, 3H, OMe); 4.40 (m, 1H, CH$_2$); 1.96 (m, 1H, CH$_2$Me); 1.51 (m, 2H, CH$_2$); 1.10 (m, 6H, CH$_2$Me$_2$) ppm.

**Reactions of NbF$_5$ with z-amino acid esters**

**Synthesis of [NbF$_5$(Me$_2$CHCH$_2$CHNH$_2$CO$_2$Me)$_2$][NbCl$_6$], 11a.**[1] A suspension of NbCl$_5$ (199 mg, 0.736 mmol) in CH$_2$Cl$_2$ (15 mL) was treated with 8k (97 mg, 0.74 mmol). After 24 h stirring at room temperature, a pale orange solution was obtained. By addition of hexane, 11a was obtained as a colourless solid. Yield 130 mg (44% based on Nb). Anal. calc. for C$_{14}$H$_{26}$Cl$_{10}$N$_2$NbO$_4$: C, 20.34; H, 3.64; N, 3.37; Cl, 42.68; Nb, 23.27. Found: C, 20.5; H, 3.18; N, 3.27; Cl, 42.98; Nb, 23.13. IR (solid state): $\nu = 3292$ w (Ph$_2$), 3243 w, 2959 w-m, 1633 (pca), 1569 m, 1467 m, 1387 m, 1327 m, 1234 w, 1152 w-m, 1015 w-m, 934 m-w, 856 vs, 746 m-s cm$^{-1}$. $^1$H NMR (CDCl$_3$): $\delta = 7.17$ (br, 2H, NH$_2$); 4.44 (s, 3H, OMe); 4.40 (m, 1H, CH$_2$); 1.96 (m, 1H, CH$_2$Me); 1.51 (m, 2H, CH$_2$); 1.10 (m, 6H, CH$_2$Me$_2$) ppm. $^9$Nb NMR (CDCl$_3$): $\delta = 7.8$ (8.3 Hz, NbCl$_2$) ppm.

**Synthesis of [NbCl$_5$(Me$_2$CHCH$_2$CHNH$_2$CO$_2$Et)$_2$][NbCl$_6$], 11b.**[1] Colourless viscous solid, yield 73%. Anal. calc. for C$_{16}$H$_{32}$Cl$_{10}$N$_2$NbO$_4$: C, 21.57; H, 4.02; N, 3.26; Nb, 25.74. Found: C, 22.0; H, 3.07; N, 3.25; Nb, 25.74.

**Synthesis of [NbCl$_5$(Me$_2$CHCH$_2$CHNH$_3$CO$_2$Me)$_2$][NbCl$_6$], 11c.**[1] These products were prepared by a procedure analogous to that described for 11a, from the appropriate niobium pentahalide (ca. 0.70 mmol)/z-amino acid ester combination.

**10.** Compound 10 was prepared by a procedure analogous to that described for the synthesis of 9, from NbF$_5$ (222 mg, 1.18 mmol) and 8b (85 mg, 0.59 mmol). Yield 167 mg (60%). Anal. calc. for C$_{16}$H$_{32}$F$_8$Nb$_2$O$_{12}$N$_2$: C, 12.75; H, 1.71; N, 2.97; Nb, 36.46. Found: C, 12.70; H, 1.61; N, 3.03; Nb, 36.27.

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### Table 4 Crystal data and experimental details for 3, 4, 5a and 12

|   | 3  | 4  | 5a  | 12  |
|---|----|----|-----|-----|
| Formula | C₆H₅Cl₂Cl₃N₂Nb₂O₂ | C₆H₅Cl₂Nb | C₆H₅Cl₂Cl₃N₂Nb₂O₂ | C₆H₅Cl₂Cl₃NNb₂O₂ |
| Fw | 661.64 | 407.81 | 518.30 | 721.98 |
| T, K | 100(2) | 100(2) | 100(2) | 100(2) |
| Crystal system | Monoclinic | Monoclinic | Orthorhombic | Monoclinic |
| Space group | P2₁/c | P2₁/c | P2₂₁,2 | P2₁ |
| a, Å | 6.7734(9) | 8.065(3) | 6.9864(4) | 10.045(2) |
| b, Å | 13.4440(18) | 18.492(7) | 12.7821(7) | 6.9628(17) |
| c, Å | 11.9844(16) | 10.184(4) | 20.9934(11) | 16.994(4) |
| β, ° | 103.854(2) | 94.034(5) | 90 | 106.428(3) |
| Cell volume, Å³ | 1059.6(2) | 1515.1(10) | 1874.73(18) | 1140.2(5) |
| Z | 2 | 4 | 2 | 2 |
| D₀, g cm⁻³ | 2.074 | 1.788 | 1.836 | 2.103 |
| μ, mm⁻¹ | 2.097 | 1.821 | 1.635 | 2.297 |
| F(000) | 640 | 808 | 700 |
| Independent reflections | 2315 [Rint = 0.0261] | 3507 [Rint = 0.0656] | 3338 [Rint = 0.0312] | 4492 [Rint = 0.0312] |
| Data/restraints/parameters | 23150/109 | 35072/137 | 33380/195 | 44924/217 |
| R₁ (I > 2σ(I)) | 0.0406 | 0.0442 | 0.0249 | 0.0217 |
| wR₁ (all data) | 0.0913 | 0.0870 | 0.0575 | 0.0428 |
| Largest diff. peak and hole, e Å⁻³ | 2.092/−1.392 | 0.769/−0.891 | 0.372/−0.692 | 0.286/−0.360 |

Crystal data and collection details for 3, 4, 5a and 12 are reported in Table 4. The surface experiments were carried out on a Bruker APEX II diffractometer equipped with a CCD detector and using Mo-Kα radiation (λ = 0.71073 Å). Data were corrected for Lorentz polarization and absorption effects (empirical absorption correction SADABS). Structures were solved by direct methods and refined by full-matrix least-squares based on all data using SHELXL. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were fixed at calculated positions and refined by a riding model, except hydrogens bonded to N(1) in 4, 5a and 12 which were located in the Fourier map and refined isotropically using the 1.2 fold (for 4 and 5a) and 1.5 fold (for 12) Uiso value of the parent N-atom. The N(1)−H distances were restrained to 0.93 Å (s.u. 0.02).

#### Computational studies

The computational geometry optimizations were carried out without symmetry constrains using the hybrid-GGA EDF2 functional, in combination with the 6-31G** basis set (ECP-based LANL2DZ basis set for elements beyond Kr). The “restricted” formalism was applied in all cases. The software used was Spartan 08. Further computational geometry optimizations were carried out without symmetry constrains, using the hyper-GGA functional M06, in combination with a polarized basis set composed by the 6-31G(d,p) set on the light atoms.
and the ECP-based LANL2TZ(f) on the metal centre. The CPCM implicit solvation model ($\varepsilon = 9.08$) was added to M06 calculations. Gaussian '09 was used as software. All the stationary points were characterized by IR simulations (harmonic approximation), from which zero-point vibrational energies and thermal corrections ($T = 298.15$ K) were obtained. Vibrational simulation supported the interpretation of experimental IR data. Cartesian coordinates of the optimized geometries are collected in a separated .xyz file.

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