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

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Titanium tetrachloride smoothly reacted with a selection of α-amino acids (aaH) in CH_2Cl_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 $Nb_2Cl_8\{\mu\text{-}\kappa^2O,\kappa^2N\text{-}[\overline{CHCH_2CH_2CH(N)}CH(O)]_2\}$, **3**, was isolated from the reaction of L-proline with $NbCl_5$/NH^iPr_2, performed in CH_2Cl_2 at room temperature. The X-ray structure of **3** features a bridging (*E*)-1,2-bis(3,4-dihydro-2*H*-pyrrol-5-yl)ethene-1,2-diolate ligand, resulting from the unprecedented C–C coupling between two proline units. Unusually stable α-ammonium acyl chlorides were prepared by the reactions of PCl_5/MCl_n (MCl_n = $NbCl_5$, 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, $[MX_4L_2][MX_6]$ (M = Nb, L = $Me_2CHCH_2CH(NH_2)CO_2Me$, X = F, **9**; Cl, **11a**; M = Nb, X = Cl, $L = \overline{HNCH_2CH_2CH_2CH}CO_2Et$, **11c**; Ta, **11d**), in moderate to good yields. $[NbCl_5(Me_2CHCH_2CHNH_3CO_2Me)][NbCl_6]$, **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 $NbCl_3(OCH_2CHNHCO_2{}^iPr)$, **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 MBr_5 (M = Nb, Ta), these reactions proceeding with the release of EtF 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.

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Introduction

α-Amino acids constitute a class of organic compounds arousing great interest in synthetic chemistry, in view of their easy availability and low toxicity,[1] the typical presence of a stereogenic centre (making them suitable substrates for asymmetric catalysis)[2] and the possibility of firmly coordinating metal ions.[3]

The esterification of the carboxylic acid moiety is one of the most viable modifications of the α-amino acid skeleton, and indeed a good number of α-amino acid esters have been synthesized and employed with reference to several application fields.[4] Metal complexes containing α-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, α-amino acids and α-amino acid ester metal complexes, being possible chiral sources,[9] have found increasing attention as privileged, potential catalysts for environmentally friendly asymmetric syntheses.[2h,10]

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

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† Electronic supplementary information (ESI) available: Bond distances and angles and H-bond distances for compound **4** and for $[\mathbf{12}]^-$. The DFT-calculated structures discussed in this paper. CCDC 1041071, 1041072, 1518993 and 1518994 For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ra00073a

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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 $MoCl_5$.[11] 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 $TiCl_4$ with glycine.[12] 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,[13] we have found that $MoCl_5$ and WCl_6 behave as chlorinating agents towards natural α-amino acids, affording fairly stable α-ammonium acylchloride salts.[14]

On the other hand, the interaction of MX_5 (M = Nb, Ta; X = Cl, Br) with α-amino acids leads to dinuclear complexes containing bridging α-amino acidato ligands *via* HX release.[15] Subsequent activation of the coordinated α-amino acidato moiety has been observed in mild conditions in some specific cases, leading to iminium salts.

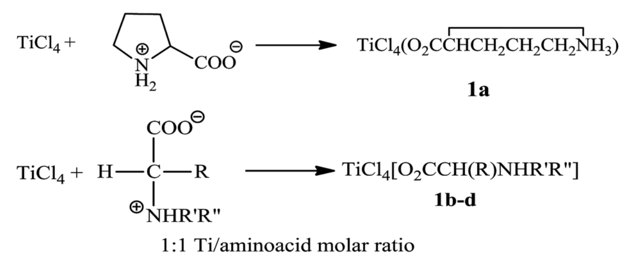
Herein, we will present an extension of our study on the reactivity between α-amino acids and HVTMH, including the synthesis of $TiCl_4$ derivatives, the unprecedented metal mediated C–C dimerization of a α-amino acid (L-proline) and the stabilization of otherwise reactive α-ammonium acylchloride cations. We will also describe some reactivity of α-amino acid ester with niobium and tantalum pentahalides.[16,17] All the reactions were carried out in a weakly coordinating solvent (CH_2Cl_2) 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 $NbCl_5$-directed unusual L-proline pseudo dimerization.

Results and discussion

Reactivity of MCl_n 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 $TiCl_4$ with α-amino acids differs from that of MCl_5 (M = Nb, Ta), featured by HCl release,[15] and from those of $MoCl_5$ and WCl_6, leading to Cl/O interchange products (see Introduction).[14]

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 (ν_a) and the symmetric (ν_s) stretching vibrations of the carboxylato group. In general, the wavenumber difference ($\Delta\nu_{a-s} = \nu_a - \nu_s$) is considered as a useful parameter to discriminate between monodentate, chelating, and bridging bidentate carboxylato ligands. $\Delta\nu_{a-s}$ values within the range 100 to 150 cm^{-1} are typical of either chelating or bridging bidentate carboxylates.[18] In view of the IR data available for **1a–d**, *i.e.* $\Delta\nu_{a-s}$ 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.



R	R'	R"	
CH_2Ph	H	H	**1b**
H	CH_3	H	**1c**
H	CH_3	CH_3	**1d**

Scheme 1 Synthesis of titanium tetrachloride α-amino acid complexes.

The geometry proposed on the basis of spectroscopic data was supported by DFT calculations on the possible isomers of **1b**. The dinuclear structure $[TiCl_4(\mu\text{-}\kappa^2O\text{–}O_2CCH(CH_2Ph)NH_3)]_2$, 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 CD_3CN, displaying single sets of resonances. The ^1H NMR spectra exhibit broad

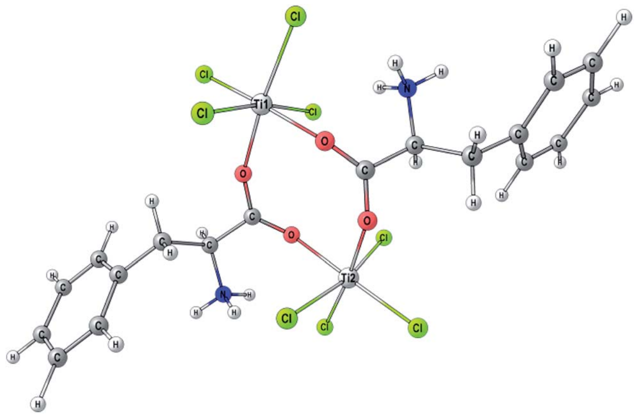
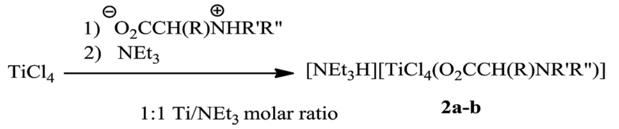


Fig. 1 DFT-optimized geometry of the most stable isomer of **1b** (C-PCM/M06 calculations). Selected computed bond lengths (Å): Ti1–O 2.020, 2.081; Ti2–O 1.990, 2.080; Ti1–Cl (*trans* O) 2.295, 2.232; Ti2–Cl (*trans* O) 2.232, 2.304; Ti1–Cl (*cis* O) 2.266, 2.392; Ti2–Cl (*cis* O) 2.291, 2.394; C–O 1.244, 1.261, 1.251, 1.252; N–H 1.025, 1.028, 1.038, 1.027, 1.028, 1.037. Selected computed angles (°): O–Ti1–O 86.1; O–Ti2–O 84.6; Ti1–O–C 149.8, 151.4; Ti2–O–C 139.2, 151.3; O–C–O 124.9, 126.4.



$$TiCl_4 \xrightarrow[\text{1:1 Ti/NEt}_3\text{ molar ratio}]{\text{1) } {}^{\ominus}O_2CCH(R)\overset{\oplus}{N}HR'R'' \quad \text{2) } NEt_3} [NEt_3H][TiCl_4(O_2CCH(R)NR'R'')]$$

2a-b

R	R'	R''	
$PhCH_2$	H	H	**2a**
$PhCH_2$	Me	Me	**2b**

Scheme 2 Synthesis of anionic α-aminoacidate titanium compounds.

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 α-amino acids in $NbCl_5$ derivatives.[15]

The coordination of organic species to high valent transition metal chlorides represents, in a number of cases, the preliminary step of some activation process.[13c,19] The activation is favoured by the strong Lewis acidity of the metal centre, and may be triggered by the addition of a Brönsted base. For instance, Peryshkov and coworkers recently described a C–H bond activation reaction of nitriles by means of NEt_3 upon coordination to $TaCl_5$.[20]

Thus, the reaction of **1b** with NEt_3 proceeded with selective deprotonation of the ammonium group; analogous result was achieved by treatment of a $TiCl_4$/L-*N*,*N*-dimethylphenylalanine mixture with NEt_3 (Scheme 2).[21] 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_2Cl_2 soluble compounds **2a–b** (Scheme 2) were isolated by addition of hexane to the respective reaction mixtures.[22]

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, on considering either mononuclear and dinuclear structures as starting points (Fig. S2†). Thus, mononuclear compounds bearing N,O-chelating α-aminoacidates (Fig. 2) resulted much more stable than dinuclear homologues (see ESI† for more details).

Niobium pentachloride. We reported that the 2 : 1 reactions of NbX_5 (X = Cl, Br) with a variety of α-amino acids afforded dinuclear α-aminoacidate 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).[15]

With the aim of exploring the possibility of further activation pathways, we investigated the reactions of Nb_2Cl_9(α-amino acidate) complexes with NEt_3. In general, the amino acidate moiety did not undergo activation under these conditions, with an exception provided by the Nb_2Cl_9(L-prolinate)/NEt_3 system. This latter evolved into a complicated mixture of products, including minor amounts of $Nb_2Cl_8\{\mu\text{-}\kappa^2O,\kappa^2N\text{-}[\overline{CH_2CH_2CH_2C(N)}C(O)]\}_2$, **3**. The use of NH^iPr_2 in the place of NEt_3 allowed to isolate red crystals of **3** (12% yield), and also yellow crystals of $[NH_2{}^iPr_2][NbCl_6]$, 4 (40% yield), Scheme 4.

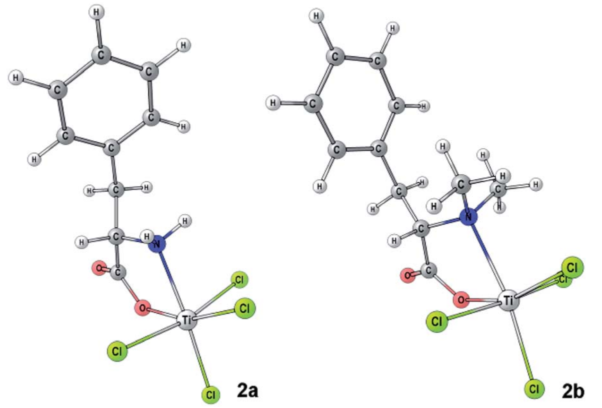
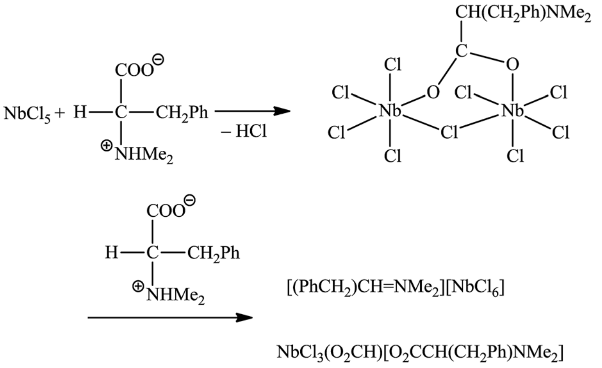
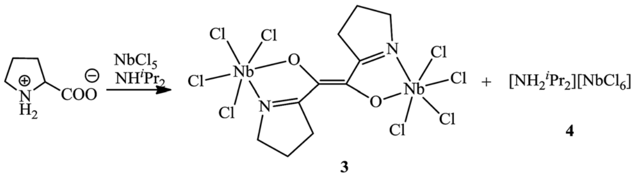


Fig. 2 DFT-optimized geometries of the most stable anions of **2a** and **2b** (C-PCM/M06 calculations). Selected computed bond lengths for **2a** (Å): Ti–O 1.909; Ti–N 2.240; Ti–Cl (*trans* O) 2.321; Ti–Cl (*trans* N) 2.263; Ti–Cl (*trans* Cl) 2.340, 2.353; C–O 1.316; C=O 1.212; N–H 1.018, 1.021. Selected computed angles for **2a** (°): 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** (°): O–Ti–N 73.2; O–Ti–Cl 88.6, 89.7, 98.5, 160.3; C–O–Ti 130.2.



Scheme 3 Reaction of $NbCl_5$ with *N*,*N*-dimethylphenylalanine.



Scheme 4 Unusual activation of L-proline by $NbCl_5$/amine.

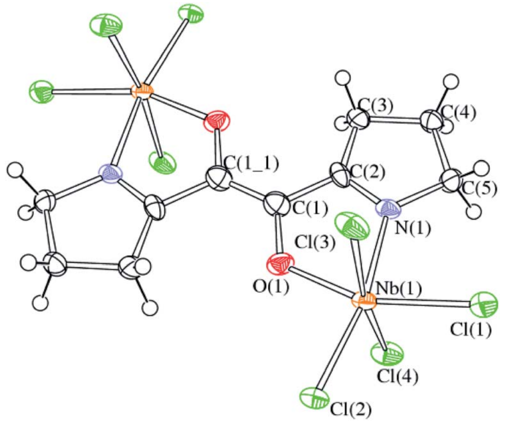


Fig. 3 ORTEP drawing of **3**. Displacement ellipsoids are at the 50% probability level.

Table 1 Selected bond lengths (Å) and angles (°) for **3**^{a}

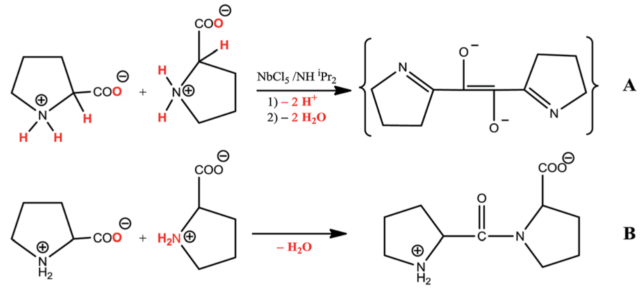
Nb(1)–Cl(1)	2.3319(13)	Nb(1)–Cl(2)	2.2833(11)
Nb(1)–Cl(3)	2.3454(12)	Nb(1)–Cl(4)	2.3453(12)
Nb(1)–O(1)	1.927(3)	Nb(1)–N(1)	2.235(4)
C(1)–O(1)	1.357(6)	C(1)–C(1_1)	1.337(10)
C(1)–C(2)	1.471(7)	C(2)–C(3)	1.488(7)
C(3)–C(4)	1.530(6)	C(4)–C(5)	1.528(6)
N(1)–C(2)	1.276(6)	N(1)–C(5)	1.477(6)
Cl(1)–Nb(1)–O(1)	158.18(10)	Cl(2)–Nb(1)–N(1)	167.62(11)
Cl(3)–Nb(1)–Cl(4)	170.32(5)	O(1)–Nb(1)–N(1)	73.03(14)
Nb(1)–O(1)–C(1)	122.9(3)	Nb(1)–N(1)–C(2)	117.6(3)
Nb(1)–N(1)–C(5)	132.0(3)	C(2)–N(1)–C(5)	110.4(4)
N(1)–C(2)–C(3)	115.8(4)	N(1)–C(2)–C(1)	110.7(4)
C(1)–C(2)–C(3)	133.5(4)	C(2)–C(3)–C(4)	102.3(4)
C(3)–C(4)–C(5)	105.8(4)	C(4)–C(5)–N(1)	105.7(4)
O(1)–C(1)–C(2)	114.6(4)	O(1)–C(1)–C(1_1)	120.2(6)
C(2)–C(1)–C(1_1)	125.2(6)		

[a] Symmetry transformation used to generate C(1_1): $-x + 1, -y, -z + 1$.

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 $\bar{1}$ (C_i) symmetry with the inversion centre located on the middle of the C(1)–C(1_1) bond. The complex is composed of an unprecedented anionic $[\overline{CH_2CH_2CH_2CH(N)}CH(O)]_2^{2-}$ ligand (*E*-1,2-bis(3,4-dihydro-2*H*-pyrrol-5-yl)ethene-1,2-diolate) that is μ-κ^{2}O,κ ^{2}N-coordinated over two $[NbCl_4]^+$ cationic fragments. Such anionic ligand is almost perfectly planar (mean deviation from the least squares plane 0.0387 Å), being the two Nb atoms respectively 0.1879 Å above and below this plane. C(1), C(2) and N(1) [sum angles 360.0(9), 360.0(7) and 360.0(6)°, respectively] show a perfect sp^2 hybridization, and the C(1)–C(1_1) [1.357(6) Å] and C(2)–N(1) [1.276(6) Å] distances are typical for double bonds.[23]

The $\{C_2O_2\}$ core of the (*E*)-1,2-bis(3,4-dihydro-2*H*-pyrrol-5-yl)ethene-1,2-diolate ligand in **3** is a fully deprotonated 1,2-enediol. In general, 1,2-enediols are quite unstable species,[24] whose stabilization may be supplied by hydrogen-bonded protons,[25] or by chelating (N,O) coordination to transition metals.[26]



Scheme 5 NbCl$_5$-promoted C–C pseudo-dimerization of L-proline (**A**); peptide bond formation from two L-proline units (**B**).

Basically, the process leading to **3** is a C–C bond forming condensation of two proline units (Scheme 5A). Differently, typical α-amino acid condensation generates a peptide bond (Scheme 5B).[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 $NH^iPr_2 + HCl \rightarrow [NH_2{}^iPr_2]Cl$ and $[NH_2{}^iPr_2]Cl + NbCl_5 \rightarrow$ **4** should contribute to decrease the ΔG 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 α-amino acids.[28] PCl$_5$ has been traditionally employed as Cl-source in order to obtain the relevant α-ammonium acylchloride salts (*Fischer procedure*); the counterion is Cl$^-$ or $[PCl_6]^-$ depending on the employed PCl$_5$/α-aminoacid molar ratio.[29] α-Ammonium acylchloride species stable at room temperature have been obtained only with primary ammonium groups and in the absence of donor atoms within the side chain. On the other hand, in the case of the L-proline derivative (secondary N), both Cl$^-$ and $[PCl_6]^-$ salts undergo quick degradation at room temperature, due to HCl release and subsequent condensation reactions.[29] Furthermore, the reactions of PCl$_5$ with L-*N*,*N*-dimethylphenylalanine (tertiary N), sarcosine (secondary N) and L-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 L-*N*,*N*-dimethylphenylalanine and L-methionine acylchloride derivatives have not been known heretofore, while the highly moisture sensitive $[NH(Me)CH_2COCl][WOCl_5]$ has been recently obtained by ourselves from sarcosine/WCl$_6$.[14a]

Some of us recently reported[13b,29] a straightforward and clean route to unusually stable salts of the acylchloride derivative of L-proline, by combination of the *traditional* PCl$_5$-chlorinating reaction with the considerable stability imparted by the $[MCl_6]^-$ (M = Nb, Ta) anions, Scheme 6.[13b–c,30]

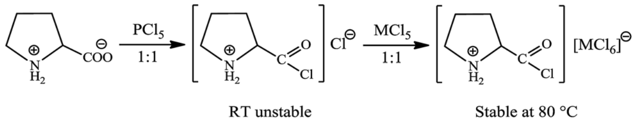
We reckoned that the easily available $[NbCl_6]^-$ anion could provide stability also to other unstable/unknown α-ammonium acylchloride cations (see above). Therefore, we tried to optimize and generalize the synthetic procedure shown in Scheme 6. When a dichloromethane 1 : 1 molar mixture of PCl_5 and $NbCl_5$ was treated with L-*N*,*N*-dimethylphenylalanine or sarcosine,[31] the subsequent ^{31}P NMR analysis on the reaction solution evidenced the presence of $POCl_3$ as prevalent phosphorous species [singlet at 6.2 ppm (from $PCl_5/NbCl_5$/L-*N*,*N*-dimethylphenylalanine) and 5.6 ppm (from $PCl_5/NbCl_5$/sarcosine), respectively].[13b,29,32] The corresponding $[NbCl_6]^-$ α-ammonium acylchloride salts, **5a–b**, were isolated at room temperature in 40–50% yields (Scheme 7). The presence of $[NbCl_6]^-$ in **5a–b** was unambiguously detected by a typical ^{93}Nb NMR resonance around 0 ppm.[13c,33] The structure of **5a** was determined by X-ray diffraction (Fig. 4, Table 2). It contains the $[PhCH_2CH(NHMe_2)COCl]^+$ 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 previously reported for other α-ammonium acylchloride salts.[13b,14,29] Thus, 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 $[PhCH_2{=}NMe_2][NbCl_6]$ (see Scheme 3) and the adduct $NbCl_5(O{=}PCl_3)$, **6**, identified by comparison of the crystal cell data with those reported in the literature,[36] were obtained as minor products from $NbCl_5$/L-*N*,*N*-dimethylphenylalanine and $NbCl_5$/sarcosine, respectively.

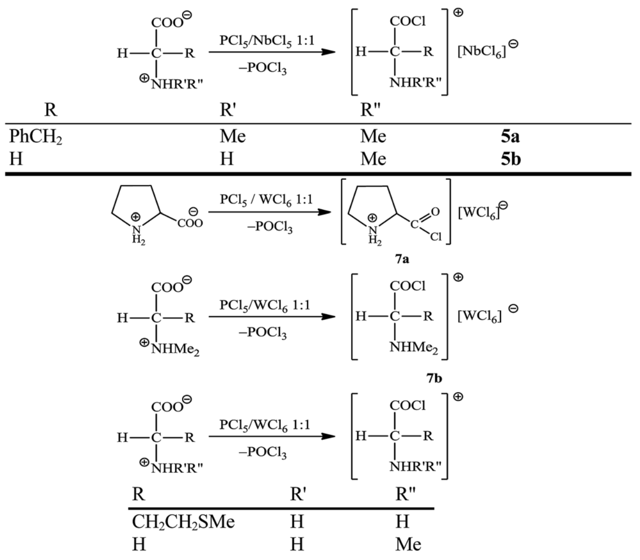
The synthetic approach leading to **5a–b** exploits the M–Cl (M = P, Nb) bond energy scale,[13b,37] making PCl_5 a preferential chlorinating agent respect to $NbCl_5$, and the stability of the $[NbCl_6]^-$ anion. Similar considerations led us to test the PCl_5/WCl_6 mixture; it should be noted that anionic simple derivatives of WCl_6 (*i.e.*, WCl_6, $WOCl_5^-$) have recently proposed as effective partners for the stabilization of otherwise reactive cations.[14a,38]

Hence, the reactions of PCl_5/WCl_6 (1 : 1 mixture) with L-proline, L-*N*,*N*-dimethylphenylalanine, sarcosine and L-methionine proceeded with PCl_5 to $POCl_3$ conversion (^{31}P NMR), and straightforwardly afforded the respective α-ammonium acylchloride cations (Scheme 7). According to elemental analyses and magnetic measurements,[38] the cations were isolated in good yields as $[WCl_6]^-$ salts, **7a–b**, respectively from PCl_5/WCl_6/L-proline and PCl_5/WCl_6/L-*N*,*N*-dimethylphenylalanine. Otherwise, different anions were presumably associated with sarcosine and methionine derivatives, including $[WOCl_5]^-$ (few crystals of $[MeNH_2CH_2C({=}O)Cl][WOCl_5]$ were isolated and X-ray characterized) and W(IV) species.

The characterization of the 1 : 1 mixture WCl_6/PCl_5 suggested that both chlorides remained intact when mixed together (see Experimental for details). This implies that the WCl_6 to WCl_6^- reduction, as clearly observed in **7a–b**, is promoted by the α-amino acid. Analogous WCl_6 reduction has



Scheme 6 Stable pyrrolidinium-2-carbonylchloride salts from L-proline and MCl_5 (M = Nb, Ta).



Scheme 7 Formation of otherwise unstable α-ammonium acylchloride cations from α-amino acids and niobium and tungsten chlorides.

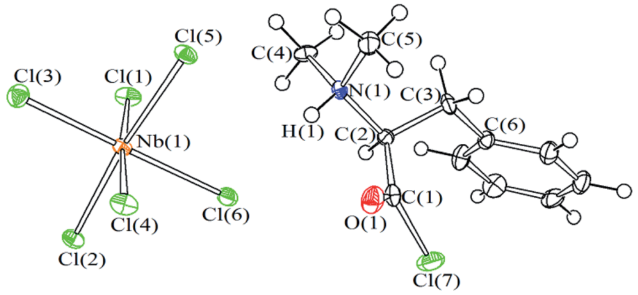


Fig. 4 ORTEP drawing of **5a**. Displacement ellipsoids are at the 50% probability level.

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)	1.178(5)
C(1)–C(2)	1.516(7)	C(2)–C(3)	1.553(6)
C(2)–N(1)	1.500(6)	N(1)–C(4)	1.499(5)
N(1)–C(5)	1.501(6)	C(3)–C(6)	1.516(6)
Cl(1)–Nb(1)–Cl(4)	176.12(5)	Cl(2)–Nb(1)–Cl(5)	174.25(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)–C(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(5)	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.[38,39]

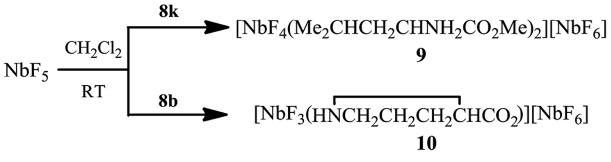
All the α-ammonium acylchloride cations produced from $PCl_5/NbCl_5$ and PCl_5/WCl_6 were fully characterized by IR and NMR spectroscopy, and those cations derived from L-*N*,*N*-dimethylphenylalanine and L-methionine are reported here for the first time. The chloro-acyl moiety manifests itself by a 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 α-amino acid esters

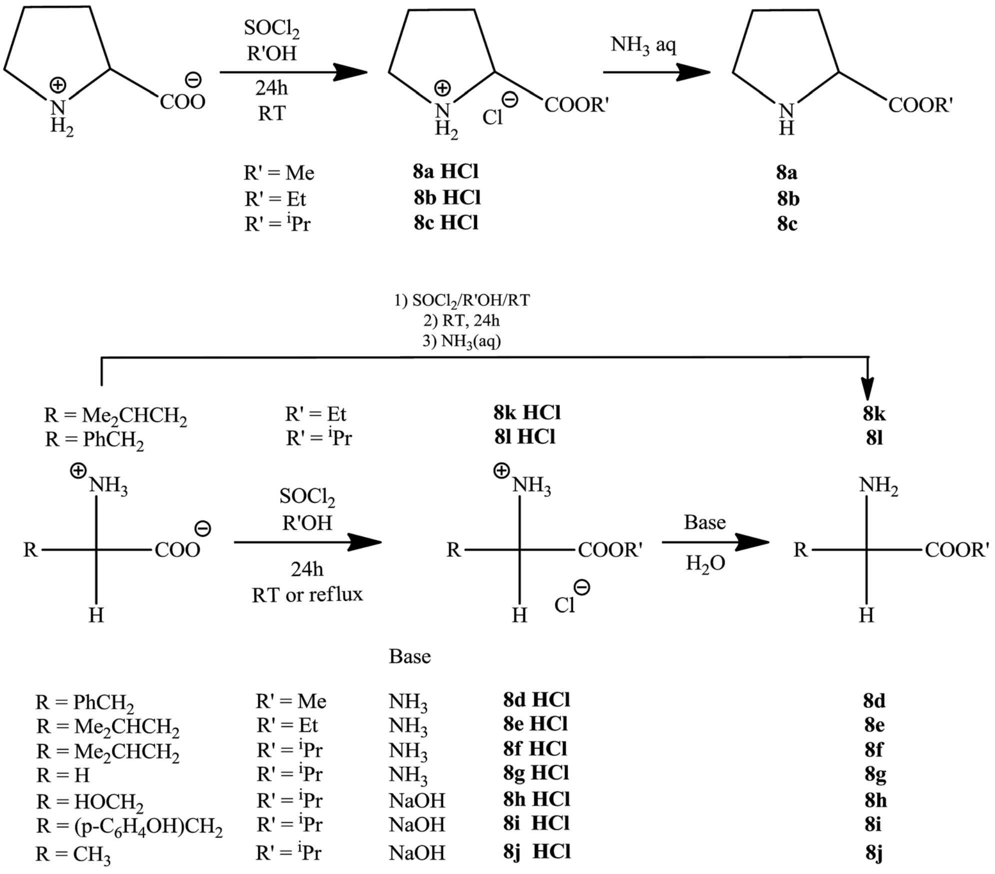
Preparation of α-amino acid ester hydrochlorides and α-amino acid esters. The α-amino acid ester derivatives, **8**, were prepared from the corresponding hydrochlorides, **8·HCl**, which were in general isolated (Scheme 8). Although most of the compounds **8** and **8·HCl** have been already appeared in the literature,[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 α-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.[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[17a]).[13c,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 ^1H 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



Scheme 9 Coordination compounds from the reactions of NbF_5 with L-proline ethylester and L-leucine methylester.



Scheme 8 Synthesis of α-amino acid esters.

gives raise 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.[13c,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 $[NbF_4(Me_2CHCH_2CHNH_2CO_2Me)_2]^+$ cation, comprising two O,N-ligated α-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 $[NbF_4(Me_2CHCH_2CHNH_2CO_2Me)_2][NbF_6]$ salt is slightly more stable compared to its neutral isomer $NbF_5(Me_2CHCH_2CHNH_2CO_2Me)$. The metal centre in this last species should be eight-coordinated, the α-amino acid ester behaving as N,O-donor chelating ligand (Fig. S4†).

It worth noting that the majority of coordination complexes containing α-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 L-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_2Cl_2 in a closed tube, while L-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 α-amino carboxylate ligand. Dinuclear geometries with the α-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 ESI†).

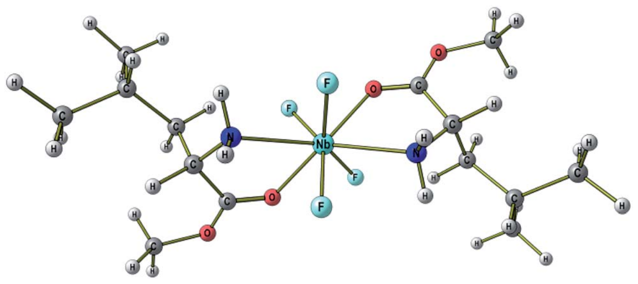


Fig. 5 DFT-optimized geometry of the cation of **9** (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 2.273, 2.273; Nb–N 2.364, 2.364; Nb–F 1.900, 1.900, 1.900, 1.900; C–O(Nb) 1.234, 1.234; C–O(Me) 1.303, 1.303; N–H 1.019, 1.019, 1.019, 1.020. Selected computed angles (°): O–Nb–N 68.3,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

We extended the present study to the interaction of α-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 α-amino acid ester ligands to the same metal centre within a cation. The presence of the $[NbCl_6]^-$ anion in **11a–c** is the consequence of unsymmetrical cleavage of the dinuclear $NbCl_5$ structure,[13c,33,46] and was unambiguously evidenced by a sharp ^{93}Nb NMR resonance occurring in the interval 4–13 ppm.[13c,33]

DFT calculations were carried out on the cation of **11a**, considering either one or two α-amino acid esters in the niobium sphere. The coordination of another equivalent of the α-amino acid ester to $[NbCl_4(Me_2CHCH_2CHNH_2CO_2Me)]^+$ resulted a favourable process, being the associated ΔG variation

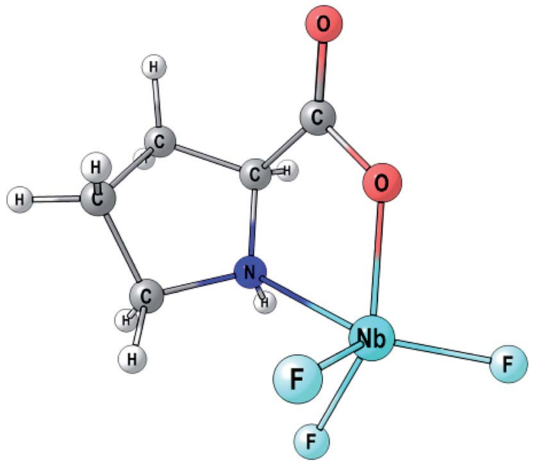
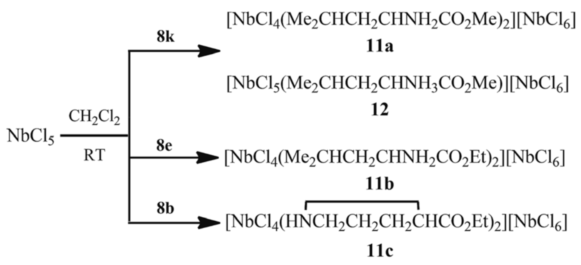


Fig. 6 DFT-optimized geometry of the cation of **10** (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 1.902; Nb–N 2.243; Nb–F 1.833, 1.835, 1.857; C–O 1.365; C═O 1.192; N–H 1.022. Selected computed angles (°): O–Nb–N 73.5; O–Nb–F 97.7, 97.7, 147.3; C–O–Nb 131.0.



Scheme 10 Synthesis of niobium pentachloride derivatives of α-amino acid esters.

around −25 kcal mol^{-1}. The DFT-optimized geometry of $[NbCl_4(Me_2CHCH_2CHNH_2CO_2Me)_2]^+$ 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 $[NbCl_5(CH_3)_2CHCH_2CHNH_3CO_2Me)]^+$ cations and $[NbCl_6]^-$ 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_3-group of the cation and the chlorides of $[NbCl_6]^-$ are present within the crystals (see Table S2B† for details). Compound **12** crystallizes in the chiral space group *P*2$_1$ and the C(2) atom of the α-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 α-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 η^6-bonded L-phenylalaninium methyl ester was reported.[47] More commonly, α-amino acid esters act as ligands in the neutral form $RCHNH_2$-CO_2R', *via* the N-atom or both N and O.[44,45]

We moved to study the reaction of $NbCl_5$ with L-serine isopropylester, **8h**, *i.e.* a α-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 $NbCl_3(OCHCH_2NHCOO^iPr)$, **13**, as a colourless precipitate. The ν(C═O) stretching band in **13** (1732 cm^{-1}) is only slightly shifted respect to **8h** (1728 cm^{-1}), thus indicating that the ester group is not involved in coordination.

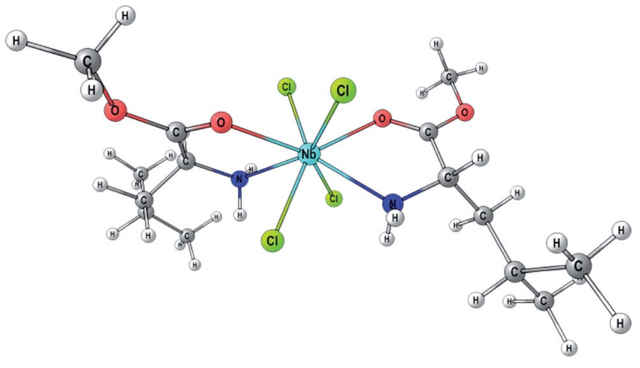


Fig. 7 DFT-optimized geometry of the cation of **11a** (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 2.261, 2.266; Nb–N 2.377, 2.381; Nb–Cl 2.380, 2.382, 2.413, 2.414; C–O(Nb) 1.236, 1.237; C–O(Me) 1.294, 1.294; N–H 1.020, 1.021, 1.020, 1.021. Selected computed angles (°): O–Nb–N 68.4, 68.4; O–Nb–O 136.2; N–Nb–N 132.9; C–O–Nb 123.7, 123.8.

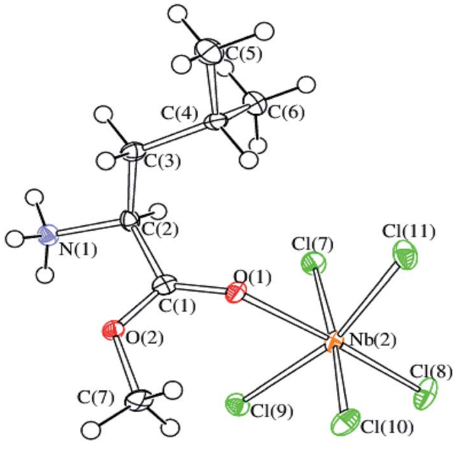


Fig. 8 ORTEP drawing of the $[NbCl_5(CH_3)_2CHCH_2CHNH_3CO_2Me)]^+$ cation in **12**. The $[NbCl_6]^-$ anion is reported in Fig. S6.† Displacement ellipsoids are at the 50% probability level.

Table 3 Selected bond distances (Å) and angles (°) for the $[NbCl_5(CH_3)_2CHCH_2CHNH_3CO_2Me)]^+$ cation in **12**. The data relative to the $[NbCl_6]^-$ anion are reported in Tables S2A and S2B

Nb(2)–Cl(7)	2.3555(9)	Nb(2)–Cl(8)	2.2641(10)
Nb(2)–Cl(9)	2.3318(10)	Nb(2)–Cl(10)	2.3250(10)
Nb(2)–Cl(11)	2.2918(9)	Nb(2)–O(1)	2.209(2)
C(1)–O(1)	1.231(4)	C(1)–O(2)	1.291(4)
C(7)–O(2)	1.473(3)	C(1)–C(2)	1.499(4)
C(2)–N(1)	1.506(4)	C(2)–C(3)	1.534(4)
Cl(7)–Nb(2)–Cl(10)	174.26(3)	Cl(9)–Nb(2)–Cl(11)	163.09(3)
Cl(8)–Nb(2)–O(1)	177.18(6)	Nb(2)–O(1)–C(1)	145.2(2)
O(1)–C(1)–O(2)	125.5(3)	O(1)–C(1)–C(2)	121.0(3)
O(2)–C(1)–C(2)	113.5(3)	C(1)–C(2)–C(3)	112.3(3)
C(1)–C(2)–N(1)	109.4(2)	N(1)–C(2)–C(3)	108.4(3)

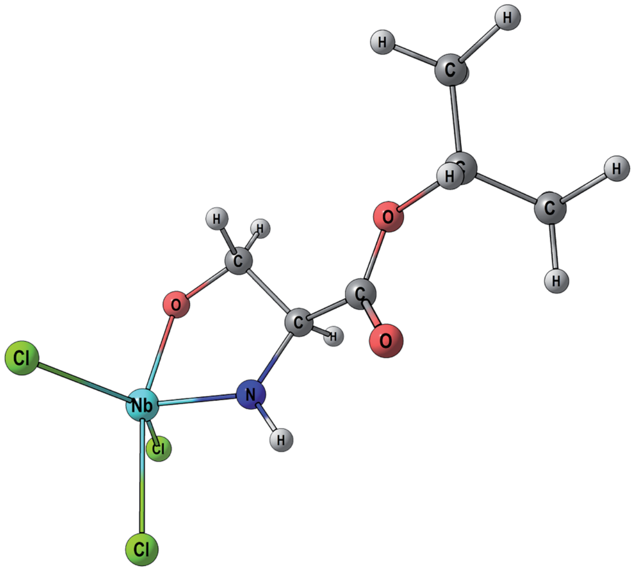


Fig. 9 DFT-optimized geometry of **13** (C-PCM/M06 calculations). Selected computed bond lengths (Å): Nb–O 1.873; Nb–N 1.943; Nb–Cl 2.359, 2.368, 2.389; N–H 1.019. Selected computed angles (°): O–Nb–N 76.0; O–Nb–Cl 93.3, 96.7, 157.8; N–Nb–Cl 82.0, 109.3, 110.0.

Compound **13** showed a single set of signals in ^{1}H and ^{13}C NMR spectra (in CD_3CN); ^{1}H resonances are shifted to higher ppm values with respect to **8h** [most notably δ(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.*, δ(CO) from 175 ppm in **8h** to 167 ppm in **13**].

At variance to the other α-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/α-amino acid ester (M = Nb, Ta). However, NMR investigations outlined the release of ethyl bromide from L-proline ethylester, in the presence of MBr_5 (see Experimental for details).

Conclusions

The reactions of $TiCl_4$ with a series of α-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 α-amino acidic frame. On the other hand, the interaction of L-proline with $NbCl_5$/$NHEt_2$ has provided the first example of C–C bond forming self-condensation of a α-amino acid, although in modest yield. The overall transformation may be regarded as a Lewis acid induced intramolecular redox reaction, in which the carboxylate group is reduced and the pyrrolidine ring is oxidized. The combination of $NbCl_5$ or WCl_6 with the chlorinating power of PCl_5 has been exploited to develop a simple synthetic method affording isolable salts of otherwise unstable α-ammonium acylchloride cations. α-Amino acid esters usually behave as bidentate O,N-ligands towards niobium and tantalum pentahalides, however activation of the ester function with release of alkyl halides has been observed in some cases.

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 °C prior to use, evacuated (10^{-2} mmHg) and then filled with argon. $TiCl_4$, NbX_5 (X = F, Cl), PCl_5 and WCl_6 were purchased from Strem (>98% purity) and stored in sealed tubes under argon atmosphere. $NbBr_5$ and $TaBr_5$ were prepared according to literature procedures and stored under argon atmosphere.[48] 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 measurement was carried out using an Eutech Con 700 instrument (cell constant = 1.0 cm^{-1}).[49] 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.[50] Carbon, hydrogen and nitrogen analyses were performed on a Carlo Erba mod. 1106 instrument. The chloride/bromide content was determined by the Mohr method[51] 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_2O_5 (M = Nb, Ta), obtained by hydrolysis of the samples followed by calcination in a platinum crucible.

Reactions of $TiCl_4$ with α-amino acids: synthesis of $TiCl_4$(aa) (aa = L-proline, 1a; L-phenylalanine, 1b; sarcosine, 1c; *N*,*N*-dimethylglycine, 1d)

General procedure. A suspension of the appropriate α-amino acid (1.50 mmol) in CH_2Cl_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*.

*$TiCl_4$(L-proline), **1a**.* Yellow solid, yield 321 mg (70%). Anal. calcd for $C_5H_9Cl_4NO_2Ti$: 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): ν = 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_3CN): δ = 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_3CN): δ = 176.1 (OCO); 61.6 (CH); 47.6, 28.6, 23.7 (CH_2) ppm.

*$TiCl_4$(L-phenylalanine), **1b**.* Light orange solid, yield 388 mg (73%). Anal. calcd for $C_9H_{11}Cl_4NO_2Ti$: 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): ν = 3030 m-br, 1600 m, 1558 vs, 1445 vs-br, 1336 m, 1047 w, 744 m, 698 ms cm^{-1}. ^{1}H NMR (CD_3CN): δ = 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_3CN): δ = 170.0 (OCO); 134.1 (*ipso*-Ph); 129.8, 129.2, 127.9 (C_6H_5); 61.8 (CH); 35.3 (CH_2) ppm.

*$TiCl_4$(sarcosine), **1c**.* Yellow solid, yield 448 mg (78%). Anal. calcd for $C_3H_7Cl_4NO_2Ti$: C, 12.93; H, 2.53; N, 5.02; Cl, 50.87; Ti, 17.17. Found: C, 13.02; H, 2.43; N, 4.98; Cl, 36.23; Ti, 12.80. IR (solid state): ν = 3185 m, 2930 vw, 2810 vw, 1575 ms, 1561 vs,

1454 s, 1429 w, 1409 ms, 937 w, 792 s, 689 m-w cm^{-1}. ^{1}H NMR (CD_3CN): $\delta = 7.26$, 7.00 (br, 2H, NH_2); 4.03 (br, 2H, CH_2); 2.81 (br, 3H, CH_3) ppm.

$TiCl_4$(N,N-dimethylglycine), ***1d***. Yellow solid, yield 312 mg (71%). Anal. calcd for $C_4H_9Cl_4NO_2Ti$: C, 16.41; H, 3.10; N, 4.78; Cl, 48.43; Ti, 16.35. Found: C, 16.29; H, 3.17; N, 4.91; Cl, 48.26; Ti, 16.57. IR (solid state): $\nu = 3091$ m-w, 2983 w, 1573 vs, 1438 s, 1401 m, 1364 s, 1324 m, 1142 m-w, 932 m-w, 857 m, 716 m cm^{-1}. ^{1}H NMR (CD_3CN): $\delta = 7.7$ (br, 1H, NH); 4.09 (br, 2H, CH_2); 3.01 (br, 6H, CH_3) ppm.

Reactions of $TiCl_4$ with α-amino acid/NEt_3: synthesis of [$NHEt_3$][$TiCl_4$(aa)] (aa = l-phenylalanine, 2a; *N*,*N*-dimethylphenylalanine, 2b)

General procedure. A suspension of the appropriate α-amino acid (1.00 mmol) in CH_2Cl_2 (*ca.* 10 mL) was treated with a solution (100 mg mL^{-1}) of $TiCl_4$ (1.00 mmol) in heptane. The mixture was stirred at room temperature overnight, then hexane (*ca.* 30 mL) was added. The liquors were eliminated with a syringe, then CH_2Cl_2 (20 mL) and NEt_3 (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*.

[$NHEt_3$][$TiCl_4$(l-phenylalanine)], ***2a***. Light brown solid, yield 297 mg (65%). Anal. calcd for $C_{15}H_{26}Cl_4N_2O_2Ti$: 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): $\nu = 3306$ w, 3240 w-br, 2984 w-br, 2675 w-br, 2488 w-br, 1691 vs, 1652 vs, 1568 s, 1454 s, 1228 m, 1099 m-s, 1070 m-s, 749 vs, 702 s cm^{-1}. ^{1}H NMR (CD_2Cl_2): $\delta = 9.09$ (s, 1H, NH); 7.39–7.30 (5H, Ph); 4.38 (m, 1H, CH); 4.13, 3.62 (br, 2H, NH_2); 3.26 (m, 6H, NCH_2); 3.40, 3.17 (dd, 2H, C*H*$_2$Ph); 1.40 (t, $^{3}J_{HH} = 7.34$ Hz, 9H, NCH_2CH_3) ppm. ^{13}C NMR (CD_2Cl_2): $\delta = 179.5$ (OCO); 135.9 (*ipso*-Ph); 129.4, 129.2, 127.5 (Ph); 61.7 (CH); 47.1 (NCH_2); 38.6 (*C*H$_2$Ph); 9.0 (NCH_2CH_3) ppm.

[$NHEt_3$][$TiCl_4$(l-N,N-dimethylphenylalanine)], ***2b***. Yellow solid, yield 290 mg (60%). Anal. calcd for $C_{17}H_{30}Cl_4N_2O_2Ti$: C, 42.18; H, 6.25; N, 5.79; Cl, 29.29; Ti, 9.89. Found: C, 42.36; H, 6.08; N, 5.65; Cl, 29.41; Ti, 9.72. IR (solid state): $\nu = 3260$ w-br, 2963 w-br, 2679 w-br, 1702 s, 1660 vs, 1581 vs, 1454 vs, 1260 m, 1012 s, 741 s, 699 s cm^{-1}. ^{1}H NMR (CD_2Cl_2): $\delta = 8.0$ (br, 1H, NH); 7.36–7.26 (5H, Ph); 4.47 (m, 1H, CH); 3.32 (m, 6H, NCH_2); 3.19, 3.07 (m, 2H, C*H*$_2$Ph); 2.95, 2.73 (s, 6H, NMe_2); 1.42 (t, $^{3}J_{HH} = 7.34$ Hz, 9H, NCH_2CH_3) ppm. ^{13}C NMR (CD_2Cl_2): $\delta = 178.8$ (OCO); 138.9 (*ipso*-Ph); 129.9, 129.2, 128.6, 126.6 (Ph); 75.6 (CH); 50.9, 47.6 (NMe_2); 47.5 (NCH_2); 30.8 (*C*H$_2$Ph); 8.9 (NCH_2CH_3) ppm.

Reaction of $NbCl_5$ with l-proline/NH^iPr_2: synthesis and isolation of $Nb_2Cl_8\{\mu\text{-}\kappa^2O,\kappa^2N\text{-}[\overline{CH_2CH_2CH_2C(N})C(O)]\}_2$, 3, and [$NH_2{}^iPr_2$][$NbCl_6$], 4

$NbCl_5$ (0.385 g, 1.42 mmol) and l-proline (0.163 g, 1.42 mmol) were allowed to react in CH_2Cl_2 (20 mL). The solution was repetitiously purged with nitrogen gas in order to remove released HCl. After six hours, the yellowish mixture was treated with NH^iPr_2 (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. calcd for $C_{10}H_{12}Cl_8N_2Nb_2O_2$: C, 18.15; H, 1.83; N, 4.23; Cl, 42.86. Found: C, 18.43; H, 1.63; N, 4.51; Cl, 43.12. IR (solid state): $\nu = 1580$ m-s ($\nu_{C=N}$), 1183 m-s ($\nu_{C\text{–}O}$) cm^{-1}.

The mother liquors were dried *in vacuo*, hence the residue was dissolved into $CHCl_3$ (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. calcd for $C_7H_{16}Cl_6NNb$: C, 20.03; H, 3.84; N, 3.34; Cl, 50.67. Found: C, 19.84; H, 3.75; N, 3.20; Cl, 49.95. IR (solid state): $\nu =$ 3130 s-br, 3080 s-br, 2987 w-m, 1606 m, 1565 m, 1424 m cm^{-1}. ^{1}H NMR (CD_3CN): $\delta = 6.30$ (br, 1H, NH); 3.48 (m, 2H, CH); 1.31 (m, 12H, Me) ppm. ^{13}C NMR (CD_3CN): $\delta = 47.7$ (CH); 18.2 (Me) ppm. ^{93}Nb NMR (CD_3CN): $\delta = -0.2$ ($\Delta\nu_{\frac{1}{2}} = 95$ Hz) ppm.

Reactions of α-amino acids with PCl_5/$NbCl_5$: synthesis of [(R)(Me)NHCH(R′)C(O)Cl][$NbCl_6$] (R = Me, R′ = CH_2Ph, 5a; R = R′ = H, 5b)

General procedure. A suspension of PCl_5 (169 mg, 0.81 mmol) and $NbCl_5$ (220 mg, 0.81 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 2–3 h. Then the appropriate α-amino 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 [$PhCH_2 = NMe_2$][$NbCl_6$] and $NbCl_5(O{=}PCl_3)$, **6**, were obtained from PCl_5/$NbCl_5$/l-*N*,*N*-dimethylphenylalanine and PCl_5/$NbCl_5$/sarcosine, respectively.

[$Me_2NHCH(CH_2Ph)C(O)Cl$][$NbCl_6$], ***5a***. Orange solid, yield 214 mg (47%) from PCl_5/$NbCl_5$/l-*N*,*N*-dimethylphenylalanine. Anal. calcd for $C_{11}H_{15}Cl_7NNbO$: C, 25.49; H, 2.92; N, 2.70; Cl, 47.88; Nb, 17.92. Found: C, 25.23; H, 2.80; N, 2.67; Cl, 47.60; Nb, 18.10. IR (solid state): $\nu = 3087$ w-m, 3029 w, 2939 w, 1767 vs ($\nu_{C=O}$), 1460 s, 1440 m, 1411 w, 1374 w, 1340 w, 1287 w, 1198 w, 1172 w, 1138 w, 1078 w, 1033 m, 1016 w, 991 w-m, 936 m, 917 w, 896 vs, 839 m, 820 w, 745 m, 726 vs, 693 vs cm^{-1}. ^{1}H NMR (CD_2Cl_2): $\delta = 7.68$ (br, 1H, NH); 7.47–7.35 (m, 5H, Ph); 4.83 (s, 1H, CH); 3.62 (m, 2H, CH_2); 3.34, 3.22 (s, 6H, NMe_2) ppm. ^{13}C NMR (CD_2Cl_2): $\delta = 170.6$ (C=O); 130.7, 130.0, 129.2 (Ph); 127.7 (*ipso*-Ph); 76.5 (CH); 44.4, 43.4 (NMe_2); 34.6 (CH_2) ppm. ^{93}Nb NMR (CD_2Cl_2): $\delta = 8.1$ ($\Delta\nu_{\frac{1}{2}} = 3\cdot10^2$ Hz) ppm.

[$MeNH_2CH_2C(O)Cl$][$NbCl_6$], ***5b***. Yellow solid, yield 144 mg (43%) from PCl_5/$NbCl_5$/sarcosine. Anal. calcd for $C_3H_7Cl_7NNbO$: C, 8.70; H, 1.70; N, 3.38; Cl, 59.92; Nb, 22.43. Found: C, 8.80; H, 1.59; N, 3.31; Cl, 59.60; Nb, 22.55. IR (solid state): $\nu =$ 3138 m-s ($\nu_{N\text{–}H}$), 2983 w, 2943 w, 1766 vs ($\nu_{C=O}$), 1546 w-m, 1454 m, 1430 m, 1414 m, 1397 vs, 1341 m, 1160 m, 1129 w, 1036 m, 999 vs, 926 vs, 789 vs, 767 vs cm^{-1}. ^{1}H NMR (CD_3CN): $\delta = 7.42$ (br, 2H, NH_2); 4.67 (t, 2H, $^{4}J_{HH} = 5.38$ Hz, CH_2); 3.21 (q, 3H, $^{4}J_{HH}$ = 5.38 Hz, Me) ppm. ^{13}C NMR (CD_3CN): $\delta = 169.0$ (C=O); 58.2 (CH_2); 35.9 (Me) ppm. ^{93}Nb NMR (CD_3CN): $\delta = 0.1$ ($\Delta\nu_{\frac{1}{2}} = 31$ Hz) ppm.

Reactions of α-amino acids with PCl_5/WCl_6: synthesis of $[NH_2(CH_2)_3CHC(O)Cl][WCl_6]$, 7a, $[Me_2NHCH(CH_2Ph)C(O)Cl][WCl_6]$, 7b, and $[(R)NH_2CH(R')C(O)Cl]^+$ (R = Me, R′ = H; R = H, R′ = CH_2CH_2SMe)

General procedure. A suspension of PCl_5 (163 mg, 0.78 mmol) and WCl_6 (310 mg, 0.78 mmol) in CD_2Cl_2 (4 mL) was stirred at room temperature overnight. Then the appropriate α-amino acid (0.78 mmol) was added. The resulting mixture was stirred at room temperature for 3 h. Thus ^{31}P NMR analyses revealed the presence of $POCl_3$ as unique phosphorous species. In addition, ^1H and ^{13}C NMR analyses on PCl_5/WCl_6/L-*N*,*N*-dimethylphenylalanine and PCl_5/WCl_6/sarcosine solutions pointed out the clean formation of **7a** and $[MeNH_2CH_2C(O)Cl]^+$. 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 $[MeNH_2CH_2C(O)Cl]^+$ salts. In the cases of PCl_5/WCl_6/L-methionine and PCl_5/WCl_6/L-proline, dark solid materials precipitated, which were isolated from the respective yellow solutions and dried *in vacuo*.

In a different experiment, a 1 : 1 PCl_5/WCl_6 mixture obtained in CD_2Cl_2 (3 mL) was analyzed. Λ_M (CD_2Cl_2) = 0.3 S cm^2 mol^{-1}. ^{31}P NMR (CD_2Cl_2): $\delta = -81.1$ (PCl_5) ppm. Cl analysis was carried out on the solid residue obtained by removal of the volatiles *in vacuo*. Anal. calcd for $Cl_{11}PW$: Cl, 64.48. Found: Cl, 63.91. Magnetic measurement: diamagnetic.

*$[NH_2(CH_2)_3CHC(O)Cl][WCl_6]$, **7a***. Green solid, yield 302 mg (73%) from PCl_5/WCl_6/L-proline. Anal. calcd for $C_5H_9Cl_7NOW$: C, 11.31; H, 1.71; N, 2.64; Cl, 46.72. Found: C, 11.20; H, 1.78; N, 2.50; Cl, 46.33. IR (solid state): ν = 3133 m (ν_{N-H}), 3073 m, 2955 w, 1768 vs ($\nu_{C=O}$), 1563 m, 1455 w, 1375 w-m, 1343 w-m, 1079 w, 1043 m, 996 vs, 942 m, 906 w, 864 m cm^{-1}. ^1H NMR (CD_3CN): δ = 7.36 (t, 2H, $^3J_{HH}$ = 50 Hz, NH_2); 4.80 (m, 1H, CH); 3.45 (m, 2H, NCH_2); 2.60, 2.36 (m, 2H, CH_2); 2.14–2.06 ppm (m, 2H, CH_2) ppm. ^{13}C NMR (CD_3CN): δ = 171.7 (C=O); 68.3 (CH); 48.4 (NCH_2); 29.1, 23.7 ppm (CH_2) ppm. Magnetic measurement: $\chi_M^{corr} = 3.60 \times 10^{-4}$ cgsu, μ_{eff} = 0.93 BM.

*$[Me_2NHCH(CH_2Ph)C(O)Cl][WCl_6]$, **7b***. Dark yellow – brown solid, yield 285 mg (60%) from PCl_5/WCl_6/L-*N*,*N*-dimethylphenylalanine. Anal. calcd for $C_{11}H_{15}Cl_7NOW$: C, 21.69; H, 2.48; N, 2.30; Cl, 40.73. Found: C, 21.78; H, 2.35; N, 2.20; Cl, 40.32. IR (solid state): ν = 3122 m-br, 3073 m, 2987 w-m, 2946 w, 2789 w, 1783 vs ($\nu_{C=O}$), 1564 w, 1455 m, 1433 w-m, 1400 m, 1347 w, 1260 w, 1164 w-m, 1041 w, 1001 s, 952 m, 930 m, 857 s, 802 s, 774 s cm^{-1}. ^1H NMR (CD_2Cl_2): δ = 7.74 (br, 1H, NH); 7.49–7.39 (m, 5H, Ph); 4.66 (br, 1H, CH); 3.62 (m-br, 2H, CH_2); 3.31, 3.19 (s, 6H, NMe_2) ppm. ^{13}C NMR (CD_2Cl_2): δ = 170.8 (C=O); 131.3, 130.0, 129.9, 129.2 (Ph); 78.3 (CH); 50.2, 48.1 (NMe_2); 36.7 (CH_2) ppm. Magnetic measurement: $\chi_M^{corr} = 4.02 \times 10^{-4}$ cgsu, μ_{eff} = 0.98 BM.

$[MeNH_2CH_2C(O)Cl]^+$. Green solid, from PCl_5/WCl_6/sarcosine. IR (solid state): ν = 3104 m-br (ν_{N-H}), 2980 w, 2938 w, 2796 w, 1765 vs ($\nu_{C=O}$), 1562 w-m, 1455 m, 1431 m, 1406 m, 1345 w-m, 1165 w-m, 1136 w, 1037 w, 1009 s, 991 vs, 951 m, 929 vs, 854 s, 806 vs, 773 vs, 728 s cm^{-1}. ^1H NMR (CD_3CN): δ = 7.29 (br, 2H, NH_2); 4.58 (s, 2H, CH_2); 3.21 (s, 3H, Me) ppm. ^{13}C NMR (CD_3CN): δ = 169.0 (C=O); 63.2 (CH_2); 40.4 (Me) ppm. Magnetic measurement: $\chi_M^{corr} = 1.13 \times 10^{-3}$ cgsu.

$[NH_3CH(CH_2CH_2SMe)C(O)Cl]^+$. Brown solid, from PCl_5/WCl_6/L-methionine. IR (solid state): ν = 3350 w-m (ν_{N-H}), 3008 w, 2921 w, 1779 s ($\nu_{C=O}$), 1569 w, 1480 w, 1449 w-m, 1415 m, 1367 w-m, 1309 w, 1263 w, 1176 w, 1144 w, 1094 w, 1025 m, 964 vs, 897 s, 759 s, 733 m, 699 w, 661 w cm^{-1}. Magnetic measurement: $\chi_M^{corr} = 7.08 \times 10^{-4}$ cgsu.

Synthesis of α-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)/α-amino acid (*ca.* 35 mmol) combination. $SOCl_2$ (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 Et_2O (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).** $SOCl_2$ (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 α-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 Et_2O (50 mL) for 2 h. The suspension was filtered and the resulting solid was dried *in vacuo* at 40 °C.

*L-Proline methylester hydrochloride, **8a·HCl**.*[40a,b] Colourless solid, yield 97%. IR (liquid film): ν = 3115 w (ν_{N-H}), 3021 w (ν_{N-H}), 2805 m, 1755 vs ($\nu_{C=O}$), 1634 m, 1442 m, 1391 m-s, 1089 m, 1015 m cm^{-1}. ^1H NMR ($CDCl_3$): δ = 10.68, 9.04 (br, 2H, NH_2); 4.51 (m, 1H, CH); 3.86 (s, 3H, OMe); 3.54 (m, 2H, NCH_2); 2.48, 2.20, 2.10 (m, 4H, CH_2) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 169.3 (C=O); 59.2 (CH); 53.6 (OMe); 46.0 (NCH_2); 28.7, 23.6 (CH_2) ppm.

*L-Proline ethylester hydrochloride, **8b·HCl**.*[40a] Colourless solid, yield 79%. ^1H NMR ($CDCl_3$): δ = 10.57, 8.92 (br, 2H, NH_2); 4.42 (m, 1H, CH); 4.24 (q, $^3J_{HH}$ = 5.87 Hz, 2H, OCH_2); 3.50 (m, 2H, NCH_2); 2.40, 2.10 (m, 4H, CH_2); 1.27 (t, $^3J_{HH}$ = 5.87 Hz, 3H, OCH_2CH_3) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 168.7 (C=O); 62.9 (OCH_2); 59.2 (CH); 45.9 (NCH_2); 28.7, 23.6 (CH_2); 14.0 (OCH_2CH_3) ppm.

*L-Proline isopropylester hydrochloride, **8c·HCl**.*[40a] Colourless solid, yield 97%. ^1H NMR ($CDCl_3$): δ = 10.70, 8.81 (br, 2H, NH_2); 5.11 (sept, $^3J_{HH}$ = 6.2 Hz, 1H, OCH); 4.44 (m, 1H, CH); 3.57 (m, 2H, NCH_2); 2.43, 2.12, 2.03 (m, 4H, CH_2); 1.29 (pseudo-t, $^3J_{HH}$ = 6.2 Hz, 6H, $OCHMe_2$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 168.3 (C=O); 71.2 (OCH); 59.3 (CH); 46.1 (NCH_2); 29.0, 23.6 (CH_2); 21.6 ($OCHMe_2$) ppm.

*L-Phenylalanine methylester hydrochloride, **8d·HCl**.*[40b] Colourless crystalline solid, yield 83%. IR (solid state): ν = 3091 m-br (ν_{N-H}), 2944 w-sh, 2906 w-sh, 2838 w, 2625 w, 1743 vs ($\nu_{C=O}$), 1583 w-m, 1495 m, 1447 w-m, 1436 w-m, 1400 m, 1358 w, 1327 w, 1291 w-m, 1238 vs, 1214 vs, 1146 m, 1119 m, 1084 s, 1061 m, 1033 w, 990 m, 934 m, 865 w, 760 n, 741 vs, 701 vs cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.7 (br, 3H, NH_3); 7.31, 7.28 (m, 5H, Ph); 4.38

(br, 1H, CH); 3.72 (s, 3H, OMe); 3.42 (m-br, 2H, CH_2) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 169.2$ (C=O); 133.9 (*ipso*-Ph); 129.6, 129.0, 127.7 (Ph); 54.4 (CH); 53.0 (OMe); 36.3 (CH_2) ppm.

*L-Leucine ethylester hydrochloride, **8e·HCl**.*[40d] Colourless solid, yield 80%. ^1H NMR ($CDCl_3$): $\delta = 8.5$ (br, 3H, NH_3); 4.26 (m, 2H, OCH_2); 4.07 (m, 1H, CH); 1.92 (m, 1H, $CHMe_2$); 1.83 (m, 2H, CH_2); 1.31 (m, 6H, $CH\mathit{Me_2}$); 1.23 (t, $^3J_{HH} = 6.85$ Hz, 3H, OCH_2CH_3) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 169.9$ (C=O); 62.6 (OCH_2); 51.9 (CH); 39.5 (CH_2); 24.5 ($CHMe_2$); 22.2, 22.1 ($CH\mathit{Me_2}$); 14.0 (OCH_2CH_3) ppm.

*L-Leucine isopropylester hydrochloride, **8f·HCl**.*[40e] Colourless solid, yield 81%. ^1H NMR ($CDCl_3$): $\delta = 8.21$, 6.64 (br, 3H, NH_3); 5.11 (m, 1H, OCH); 4.01 (m, 1H, CH); 1.89 (m, 1H, $CHMe_2$); 1.81 (m, 2H, CH_2); 1.28 (m, 6H, $CH\mathit{Me_2}$); 0.98 (m, 6H, $OCH\mathit{Me_2}$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 169.3$ (C=O); 70.8 (OCH); 52.0 (CH); 39.5 (CH_2); 24.8 ($CHMe_2$); 22.2 ($CH\mathit{Me_2}$); 21.6 ($OCH\mathit{Me_2}$) ppm.

*Glycine isopropylester hydrochloride, **8g·HCl**.*[40f] Colourless solid, 97% yield. ^1H NMR ($CDCl_3$): $\delta = 8.50$ (br, 3H, NH_3); 5.10 (sept, $^3J_{HH} = 6.1$ Hz, 1H, OCH); 3.96 (q, $^3J_{HH} = 4.2$ Hz, 2H, CH_2); 1.26 (d, $^3J_{HH} = 6.1$ Hz, 6H, $CH\mathit{Me_2}$) ppm.

*L-Serine isopropylester hydrochloride, **8h·HCl**.*[40g] Colourless solid, 98% yield. ^1H NMR (DMSO-d_6): $\delta = 8.51$ (br, 3H, NH_3); 5.71–5.52 (m, 1H, OH); 5.05–4.94 (m, 1H, $CHMe_2$); 4.04–3.98 (m, 1H, CHH'); 3.83–3.78 (s, 2H, CHH' + CHN); 1.26–1.21 (m, 6H, $CH\mathit{Me_2}$) ppm. $^{13}C\{^1H\}$ NMR (DMSO-d_6): $\delta = 167.6$ (CO); 69.6 ($CHMe_2$); 59.5 (CH_2); 54.4 (CHN); 21.5 and 21.4 ($CH\mathit{Me_2}$) ppm.

*L-Tyrosine isopropylester hydrochloride, **8i·HCl**.*[40h] Colourless solid, 71% yield. ^1H NMR (DMSO-d_6): $\delta = 9.49$ (s, 1H, OH); 8.49 (br, 3H, NH_3); 7.01 (d, $^3J_{HH} = 8.2$ Hz, 2H, Ar); 6.71 (d, $^3J_{HH} = 8.2$ Hz, 2H, Ar); 4.88 (sept, $^3J_{HH} = 5.9$ Hz, 1H, OCH); 4.07 (t, $^3J_{HH} = 6.6$ Hz, 1H, NCH); 3.17–2.83 (m, 2H, CH_2); 1.16 (d, $^3J_{HH} = 6.2$ Hz, 3H) and 1.06 (d, $^3J_{HH} = 6.2$ Hz, 3H, $CH\mathit{Me_2}$) ppm.

Synthesis of α-amino acid esters. Three different procedures were adopted. Compounds **8a–g** were prepared by treating the appropriate α-amino acid ester hydrochloride with $NH_{3(aq)}$ as described in detail for **8a**. Compounds **8h–j** were prepared by treating the appropriate α-amino acid ester hydrochloride with $NaOH_{(aq)}$ as described in detail for **8h**. Compounds **8k–l** were obtained directly from the appropriate alcohol/α-amino acid (*ca.* 50 mmol) combination, followed by treatment with $NH_{3(aq)}$; attempts to isolate **(8k–l)·HCl** led to mixtures of products.

L-Proline methylester, 8a.[40a,c] Compound **8a·HCl** (10.2 g, 60.4 mmol) was dissolved into CH_2Cl_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_2Cl_2 (2 × 50 mL). The organic phase was filtered through an alumina pad and solvent was removed by distillation at 40 °C and $p = 700$ mbar. The product was obtained as a pale orange liquid, which was stored under argon. Yield 4.71 g (60%). ^1H NMR ($CDCl_3$): $\delta = 3.54$ (s, 3H, CH_3); 2.92 (m, 1H, CH); 2.48 (m, 2H, CH_2N); 1.99, 1.64 (m, 4H, CH_2) ppm.

L-Proline ethylester, 8b.[40a] Pale yellow liquid, yield 65%. IR (liquid film): $\nu = 1730$ vs ($\nu_{C=O}$) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 4.12$ (q, $^3J_{HH} = 6.85$ Hz, 2H, OCH_2); 3.73 (m, 1H, CH); 3.03, 2.90 (m, 2H, NCH_2); 2.07, 1.81, 1.73 (m, 4H, CH_2); 1.22 (t, $^3J_{HH} = 6.85$ Hz, 3H, OCH_2CH_3) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 173.9$ (C=O); 61.0 (OCH_2); 59.7 (CH); 46.9 (NCH_2); 30.2, 25.4 (CH_2); 14.2 (OCH_2CH_3) ppm.

L-Proline isopropylester, 8c.[40i] Pale orange liquid, yield 60%. ^1H NMR ($CDCl_3$): $\delta = 5.03$ (sept, $^3J_{HH} = 6.3$ Hz, 1H, OCH); 3.71 (dd, $^3J_{HH} = 8.3$, 5.6 Hz, 1H, CH); 3.12–3.04 (m, 1H, $NCHH'$); 2.94–2.85 (m, 1H, $NCHH'$); 2.28 (br, 2H, NH_2); 2.18–2.06 (m, 1H) and 1.86–1.67 (m, 3H, CH_2CH_2); 1.25 (d, $^3J_{HH} = 3.5$ Hz, 3H, $CHMeMe'$); 1.23 (d, $^3J_{HH} = 3.6$ Hz, 3H, $CHMeMe'$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 174.6$ (C=O); 68.0 (OCH); 59.6 (CH); 46.8 (NCH_2); 30.1, 25.2 (CH_2); 21.5 ($OCH\mathit{Me_2}$) ppm.

L-Phenylalanine methylester, 8d.[40c] Pale orange liquid, yield 63%. IR (liquid film): $\nu = 3381$ w (ν_{N-H}), 3062 w, 3028 w, 2951 w, 1732 vs ($\nu_{C=O}$), 1603 w-m, 1496 m, 1454 m, 1436 m, 1266 m, 1195 s, 1172 s, 1111 m, 1076 m, 1009 m, 826 m, 812 m, 744 m-s, 699 vs cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 7.24$–7.12 (5H, Ph); 3.66 (m, 1H, CH); 3.63 (s, 3H, OMe); 3.01, 2.80 (m, 2H, CH_2) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 175.3$ (C=O); 137.3 (*ipso*-Ph); 129.3, 128.5, 126.7 (Ph); 55.8 (OMe); 51.8 (CH); 41.0 (CH_2) ppm.

L-Leucine ethylester, 8e.[40d] Pale yellow liquid, yield 74%. ^1H NMR ($CDCl_3$): $\delta = 4.16$ (m, 2H, OCH_2); 3.44 (m, 1H, CH); 1.77 (m, 1H, $CHMe_2$); 1.65 (s, 2H, NH_2); 1.55, 1.43 (m, 2H, CH_2); 1.27 (t, $^3J_{HH} = 6.85$ Hz, 3H, OCH_2CH_3); 0.93 (m, 6H, $CH\mathit{Me_2}$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 176.5$ (C=O); 60.7 (OCH_2); 52.9 (CH); 44.0 (CH_2); 24.7 ($CHMe_2$); 22.9, 21.8 ($CH\mathit{Me_2}$); 14.2 (OCH_2CH_3) ppm.

L-Leucine isopropylester, 8f.[40e] Pale yellow liquid, yield 55%. ^1H NMR ($CDCl_3$): $\delta = 5.05$ (sept, 1H, OCH); 3.49 (m, 1H, CH); 2.90 (s, 2H, NH_2); 1.80 (m, 1H, $CHMe_2$); 1.57, 1.50 (m, 2H, CH_2); 1.26 (m, 6H, $OCH\mathit{Me_2}$); 0.94 (m, 6H, $CH\mathit{Me_2}$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 175.1$ (C=O); 68.5 (OCH); 52.8 (CH); 43.5 (CH_2); 24.7 ($CHMe_2$); 22.9, 21.9 ($CH\mathit{Me_2}$); 21.7 ($OCH\mathit{Me_2}$) ppm.

Glycine isopropylester, 8g.[40f] Pale yellow viscous liquid, yield 60%. ^1H NMR ($CDCl_3$): $\delta = 5.05$ (sept, $^3J_{HH} = 6.3$ Hz, 1H, OCH); 3.40 (s, 2H, CH_2); 1.89 (br, 2H, NH_2); 1.24 (d, $^3J_{HH} = 6.2$ Hz, 6H, $CH\mathit{Me_2}$) ppm.

L-Serine isopropylester, 8h.[40f] Compound **8h·HCl** (1.61 g, 8.75 mmol) was dissolved in NaOH 1.0 M (8.75 mL, 8.75 mmol) in a 25 mL round bottom flask. The solution was stirred at room temperature for 10 minutes then extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was dried with Na_2SO_4, filtered and the solvent was removed by distillation at 40 °C and $p = 700$ mbar. The product was obtained as a colourless viscous liquid, 1.11 g, yield 87%. IR(liquid film): $\nu = 3500$–3100 br, 3362 w, 3308 w, 2981 w, 2938 w, 2879 w, 1728 s ($\nu_{C=O}$), 1595 w, 1468 w, 1455 w, 1384 w-sh, 1375 m, 1326 w, 1209 m, 1179 m, 1145 m, 1105 s, 1039 m, 933 m, 903 w, 849 w, 822 m cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 5.07$ (sept, $^3J_{HH} = 6.2$ Hz, 1H, OCH); 3.85 (dd, $^2J_{HH} = 10.2$ Hz, $^3J_{HH} = 2.5$ Hz, 1H, CHH'); 3.71 (dd, $^2J_{HH} = 10.7$ Hz, $^3J_{HH} = 5.8$ Hz, 1H, CHH'); 3.66–3.60 (m, 1H, CHN); 2.59 (br, 3H, NH_2 + OH); 1.29–1.25 (m, 6H, $CH\mathit{Me_2}$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 173.3$ (CO); 68.8 (OCH); 63.9 (CH_2); 56.1 (CHN); 21.7 (Me_2) ppm. ^1H NMR (CD_3CN): $\delta = 4.97$ (sept, $^3J_{HH} = 6.3$ Hz, 1H, OCH); 3.62–3.58 (m, 2H, CH_2); 3.38 (t, $^3J_{HH} = 4.8$ Hz, 1H, CHN); 2.19 (br, 3H, NH_2 + OH); 1.23–1.20 (m, 6H, Me_2) ppm. $^{13}C\{^1H\}$ NMR (CD_3CN): $\delta = 174.6$ (CO); 68.9 (OCH); 65.1 (CH_2); 57.3 (CHN); 22.0 and 21.9 (Me_2) ppm. The compound was dissolved in $CDCl_3$ and stored in a graduated Schlenk tube under nitrogen. The concentration of the solution was determined by ^{1}H NMR, using CH_2Br_2 as internal standard.

L-Tyrosine isopropylester, 8i.[40j] 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); 3.73–3.63 (m, 1H, NCH); 3.23 (br, 3H, NH_2 + OH); 3.04 (dd, $^2J_{HH} = 13.8$ Hz, $^3J_{HH} = 5.0$ Hz, 1H, CH*H*′); 2.81 (dd, $^2J_{HH} = 13.7$ Hz, $^3J_{HH} = 7.7$ Hz, 1H, C*H*H′); 1.29–1.22 (m, 6H, CH*Me*$_2$) ppm.

L-Alanine ethylester, 8j.[40k] 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, C*H*$_3$CH); 1.13 (t, $^3J_{HH} = 7.1$ Hz, 3H, C*H*$_3$CH$_2$) ppm.

L-Leucine methylester, 8k.[40l] Pale yellow liquid, yield 42%. IR (liquid film): $\nu = 3380$ w-m (ν_{N-H}), 2956 m, 2932 w, 2869 w, 2851 w, 1740 vs ($\nu_{C=O}$), 1610 w, 1468 m, 1436 m, 1384 w, 1368 w, 1316 w, 1270 m, 1198 s, 1145 m, 1010 m, 971 w, 921 w, 869 w, 837 w, 822 w cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 3.64$ (s, 3H, OMe); 3.41 (m, 1H, CH); 1.70 (m, 1H, C*H*Me$_2$); 1.65 (s, 2H, NH_2); 1.4 (m-br, 2H, CH_2); 0.86 (m, 6H, CH*Me*$_2$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 177.1$ (C=O); 53.0 (OMe); 52.0 (CH); 44.2 (CH_2); 24.8 (*C*HMe$_2$); 23.2, 22.0 (CH*Me*$_2$) ppm.

L-Phenylalanine isopropylester, 8l.[40m] Colourless solid, yield 36%. ^{1}H NMR ($CDCl_3$): δ: M7.32–7.22 (5H, Ph); 5.03 (sept, 1H, OCH); 3.71 (m, 1H, CH); 3.08, 2.90 (m, 2H, CH_2); 2.10 (s, 2H, NH_2); 1.24, 1.20 (m, 6H, OCH*Me*$_2$) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): R (174.2 (C=O); 137.2 (*ipso*-Ph); 129.4, 128.5, 126.8 (Ph); 68.6 (OCH); 55.8 (CH); 40.9 (CH_2); 21.7 (OCH*Me*$_2$) ppm.

Reactions of NbF_5 with α-amino acid esters

Synthesis of $[NbF_4(Me_2CHCH_2CHNH_2CO_2Me)_2][NbF_6]$, 9. A suspension of NbF_5 (167 mg, 1.15 mmol) in CH_2Cl_2 (15 mL) was treated with **8k** (167 mg, 1.15 mmol). After 24 h stirring at room temperature, a colourless solution was obtained. By addition of hexane (10 mL), **9** was obtained as a colourless solid, which was recovered by filtration and dried *in vacuo* at room temperature. Yield 185 mg (48%). Anal. calcd for $C_{14}H_{30}F_{10}N_2Nb_2O_4$: C, 25.24; H, 4.54; N, 4.20; Nb, 27.89. Found: C, 25.01; H, 4.1; N, 4.01; Nb, 25.71. IR (solid state): $\nu = 3232$ w (ν_{N-H}), 3064 m, 2966 m, 2877 m, 1648 vs ($\nu_{C=O}$), 1499 m, 1456 m, 1374 w, 1328 w, 1289 w, 1262 w, 1170 w, 1129 w, 1067 w, 834 br-s cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 8.6$, 7.0 (br, 2H, NH_2); 4.66 (s, 3H, OMe); 4.19 (m, 1H, CH); 2.02–1.52 (m, 3H, C*H*Me$_2$ + CH_2); 1.03 (m, 6H, CH*Me*$_2$) ppm. ^{19}F NMR ($CDCl_3$): $\delta = 140$ ($\Delta\nu_{1/2} = 2.5 \times 10^3$ Hz, $NbF_4{}^+$); 103 (decet, $^1J_{NbF} = 345$ Hz, $NbF_6{}^-$) ppm. ^{93}Nb NMR ($CDCl_3$): $\delta = -1553$ (septet, $^1J_{NbF} = 366$ Hz, $NbF_6{}^-$) ppm.

Synthesis of $[NbF_3(\text{H}\overline{\text{NCH}_2\text{CH}_2\text{CH}_2\text{C}}\text{HCO}_2)][NbF_6]$**, 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. calcd for $C_5H_8F_9NNb_2O_2$: 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. IR (solid state): $\nu = 3381$ vw, 2965 w, 1636 vs ($\nu_{C=O}$), 1481 m, 1346 w, 1296 w, 1281 w, 1234 w, 1138 w, 1073 w, 1010 w, 983 m, 925 w, 910 w, 873 m, 765 m, 690 vs cm^{-1}. ^{1}H NMR (CD_3CN): $\delta = 11.77$ (br, 1H, NH); 4.83 (m, 1H, CH); 3.84, 3.70 (m, 2H, NCH_2); 2.60, 2.28, 2.20 (m, 4H, CH_2) ppm. ^{19}F NMR (CD_3CN): $\delta = 100.9$ (decet, $^1J_{NbF} = 343$ Hz, $NbF_6{}^-$) ppm.

The reaction of NbF_5 (0.50 mmol) with **8b** (0.50 mmol) was performed also inside a sealed NMR tube (CD_2Cl_2, 0.70 mL). A complicated mixture of compounds were detected by NMR, including ethyl fluoride [$\delta(^1H) = 4.38$ (m), 1.35 (t) ppm;[52] $\delta(^{13}C) = 77.6$, 13.7 ppm;[52] $\delta(^{19}F) = -209.9$ (br) ppm]. Addition of D_2O (*ca.* 0.1 mL) to a solution of **10** in CD_3CN (0.6 mL)[53] resulted in the formation of an abundant precipitate; a solution was separated whose ^{13}C NMR analysis evidenced the presence of L-proline only.

Reactions of $NbCl_5$ with α-amino acid esters

Synthesis and isolation of $[NbCl_4(Me_2CHCH_2CHNH_2CO_2Me)_2][NbCl_6]$, 11a, and $[NbCl_5(Me_2CHCH_2CHNH_3CO_2Me)][NbCl_6]$, 12. A suspension of $NbCl_5$ (199 mg, 0.736 mmol) in CH_2Cl_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. calcd for $C_{14}H_{30}Cl_{10}N_2Nb_2O_4$: C, 20.24; H, 3.64; N, 3.37; Cl, 42.68; Nb, 22.37. Found: C, 20.05; H, 3.18; N, 3.27; Cl, 42.98; Nb, 23.13. IR (solid state): $\nu = 3292$ w (ν_{N-H}), 3243 w, 2959 w-m, 1633 m ($\nu_{C=O}$), 1569 m, 1467 m, 1387 m, 1327 m, 1290 w-m, 1152 w-m, 1123 m, 1015 w-m, 934 w-m, 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); 1.96 (m, 1H, C*H*Me$_2$); 1.51 (m, 2H, CH_2); 1.10 (m, 6H, CH*Me*$_2$) ppm. ^{93}Nb NMR ($CDCl_3$): $\delta = 7.8$ ($\Delta\nu_{1/2} = 4 \times 10^2$ Hz, $NbCl_6{}^-$) ppm.[42a] Hydrolysis[53] of a CD_3CN solution (0.6 mL) of **11a** resulted in the formation of an abundant precipitate; a solution was separated whose ^{13}C NMR analysis evidenced the presence of **8k** only.

In a different experiment, the reaction solution was set aside at *ca.* −30 °C for two weeks. Thus pale yellow crystals of **12** were collected. Yield 65 mg (25% based on Nb). Anal. calcd for $C_7H_{16}Cl_{11}NNb_2O_2$: C, 11.64; H, 2.23; N, 1.94; Cl, 54.01; Nb, 25.74. Found: C, 11.75; H, 2.16; N, 1.98; Cl, 53.70; Nb, 25.55. IR (solid state): $\nu = 3282$ w-br (ν_{N-H}), 3241 w, 2959 w-m, 1641 m ($\nu_{C=O}$), 1559 m, 1457 m-w, 1377 m, 1327 m, 1281 w-m, 1158 w, 1128 m, 1011 w-m, 922 w-m, 860 vs, 744 m-s cm^{-1}.

Synthesis of $[NbCl_4(Me_2CHCH_2CHNH_2CO_2Et)_2][NbCl_6]$, 11b, $[NbCl_4(\text{H}\overline{\text{NCH}_2\text{CH}_2\text{CH}_2\text{C}}\text{HCO}_2\text{Et})_2][NbCl_6]$**, 11c.** These products were prepared by a procedure analogous to that described for **11a**, from the appropriate niobium pentahalide (*ca.* 0.70 mmol)/α-amino acid ester combination.

***11b*.** Colourless viscous solid, yield 73%. Anal. calcd for $C_{16}H_{34}Cl_{10}N_2Nb_2O_4$: C, 22.38; H, 3.99; N, 3.26; Cl, 41.28; Nb, 21.64. Found: C, 22.25; H, 4.06; N, 3.16; Cl, 41.70; Nb, 21.29. ^{1}H NMR ($CDCl_3$): $\delta = 7.00$ (br, 2H, NH_2); 4.50 (m, 2H, OCH_2); 4.31 (br, 1H, CH); 1.96 (m, 1H, C*H*Me$_2$); 1.47 (m, 2H, CH_2); 1.42 (m, 3H, OCH_2CH_3); 1.07 (m, 6H, CH*Me*$_2$) ppm. ^{13}C NMR ($CDCl_3$): $\delta = 170.2$ (C=O); 65.5 (OCH_2); 54.1 (CH); 39.4 (CH_2); 25.0 (*C*HMe$_2$); 22.3, 21.9 (CH*Me*$_2$); 14.1 (OCH$_2$*C*H$_3$) ppm. ^{93}Nb NMR ($CDCl_3$): $\delta = 13$ ($\Delta\nu_{1/2} = 4 \times 10^2$ Hz, $NbCl_6{}^-$); −540 ($\Delta\nu_{1/2} = 8 \times 10^3$ Hz, $NbCl_4{}^+$) ppm.

***11c*.** Colourless solid, yield 70%. Anal. calcd for $C_{14}H_{26}Cl_{10}N_2Nb_2O_4$: C, 20.34; H, 3.17; N, 3.39; Cl, 42.88; Nb, 22.48. Found:

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

	3	**4**	**5a**	**12**
Formula	$C_{10}H_{12}Cl_8N_2Nb_2O_2$	$C_6H_{16}Cl_6Nb$	$C_{10}H_{12}Cl_8N_2Nb_2O_2$	$C_7H_{16}Cl_{11}NNb_2O_2$
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	$P2_1/c$	$P2_1/c$	$P2_12_12$	$P2_1$
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)	94.036(5)	90	106.428(3)
Cell volume, $Å^3$	1059.6(2)	1515.1(10)	1874.73(18)	1140.2(5)
Z	2	4	4	2
D_c, 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 [$R_{int} = 0.0261$]	3507 [$R_{int} = 0.0656$]	3338 [$R_{int} = 0.0312$]	4492 [$R_{int} = 0.0312$]
Data/restraints/parameters	2315/0/109	3507/2/137	3338/0/195	4492/4/217
Goodness on fit on F^2	1.065	1.073	1.214	1.023
R_1 ($I > 2\sigma(I)$)	0.0406	0.0442	0.0249	0.0217
wR_2 (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

C, 19.98; H, 3.54; N, 3.47; Cl, 42.09; Nb, 21.79. IR (solid state): ν = 2961 w, 2880 w, 1609 vs ($\nu_{C=O}$), 1456 s, 1342 w, 1271 m, 1233 w-m, 1052 w, 974 m, 922 w-m, 869 m, 802 m, 756 m, 656 w-m cm^{-1}. ^1H NMR (CD_3CN): 7.2 (br, 2H, NH_2); 4.73 (m, 1H, CH); 4.31 (m, 2H, OCH_2); 3.79 (br, 2H, NCH_2); 2.58, 2.18 (m, 4H, CH_2); 1.30 (m, 3H, OCH_2CH_3) ppm. ^{93}Nb NMR (CD_3CN): $\delta = 4$ ($\Delta\nu_{1/2} = 3 \times 10^2$ Hz, $NbCl_6^-$); −569 ($\Delta\nu_{1/2} = 2 \times 10^3$ Hz, $NbCl_4^+$) ppm.

Synthesis of $NbCl_3(OCH_2CHNHCO_2{}^iPr)$, 13. A suspension of $NbCl_5$ (258 mg, 0.954 mmol) and **8h** (1.32 mL of a 0.72 M solution in $CDCl_3$, 0.95 mmol) in $CHCl_3$ (8 mL) was refluxed for 31 h. Then, the mixture was allowed to cool to room temperature and the colourless solution was separated from the colourless precipitate. The solid was washed with CH_2Cl_2 (2 × 5 mL) and dried *in vacuo*. Yield 239 mg (66% based on Nb). Anal. calcd for $C_6H_{11}Cl_3NNbO_3$: Cl, 30.9. Found: Cl, 30.8.[54] IR (solid state): ν = 3580–3200 br, 3120 m-br, 2985 m, 2965 m, 2940 m, 1732 s ($\nu_{C=O}$), 1675 w, 1576 m, 1486 m, 1471 m, 1387 m, 1377 m, 1304 w, 1258 s, 1184 w, 1146 m, 1098 s, 1080 s, 1033 s, 937 m, 895 m, 860 w, 800 s, 757 m cm^{-1}. ^1H NMR (CD_3CN): $\delta = 6.98$ (br, 1H, NH); 5.09 (sept, $^3J_{HH} = 6.2$ Hz, 1H, $CHMe_2$); 4.18–4.07 (m,1H, NCH), 4.01–3.92 (m, 2H, CH_2); 1.28 (d, $^3J_{HH} = 6.1$ Hz, 6H, $CHMe_2$) ppm. $^{13}C\{^1H\}$ NMR (CD_3CN): $\delta = 167.3$ (C=O); 72.2 ($CHMe_2$); 63.4 (CH_2); 59.9 (br, NCH); 21.7, 21.6 ($CHMe_2$) ppm. $^{93}Nb\{^1H\}$ NMR (CD_3CN): $\delta = -493.7$ ($\Delta\nu_{1/2} = 2.3 \times 10^3$ Hz) ppm.

A sample of **13** was suspended in D_2O (1 mL) with vigorous stirring for 14 h.[53] NMR analysis of the solution revealed the presence of **8h** only (pH = 1.8).

MBr_5 (M = Nb, Ta) mediated formation of EtBr from L-proline ethylester

The reactions of MBr_5 (*ca.* 0.50 mmol) with **8b** (0.50 mmol) were carried out in CD_2Cl_2 (*ca.* 1 mL). Subsequent NMR analysis pointed out the formation of a complicated mixture of compounds, including ethyl bromide.[52] In a different experiment, the mixture obtained from $NbBr_5$/**8b** was eliminated of the volatile materials; the residue was dissolved into CD_3CN (0.6 mL) and then treated with H_2O (*ca.* 0.2 mL).[53] A yellow solution was separated from an abundant precipitate, and ^{13}C NMR analysis of the solution evidenced the presence of L-proline only.

X-ray crystallographic studies

Crystal data and collection details for **3**, **4**, **5a** and **12** are reported in Table 4. The diffraction experiments were carried out on a Bruker APEX II diffractometer equipped with a CCD detector and using Mo-Kα radiation ($\lambda = 0.71073$ Å). Data were corrected for Lorentz polarization and absorption effects (empirical absorption correction SADABS).[55] Structures were solved by direct methods and refined by full-matrix least-squares based on all data using F^2.[56] 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**) U_{iso} 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,[57] in combination with the 6-31G** basis set (ECP-based LANL2DZ basis set for elements beyond Kr).[58] The "restricted" formalism was applied in all cases. The software used was Spartan 08.[59] Further computational geometry optimizations were carried out without symmetry constrains, using the hyper-GGA functional M06,[60] 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.[61] The C-PCM implicit solvation model ($\varepsilon = 9.08$) was added to M06 calculations.[62] Gaussian '09 was used as software.[63] 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.[64] Vibrational simulation supported the interpretation of experimental IR data. Cartesian coordinates of the optimized geometries are collected in a separated. *xyz* file.

Acknowledgements

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Notes and references

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