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Chiral, Enantiopure Aluminum(III) and Titanium(IV) Azatranes

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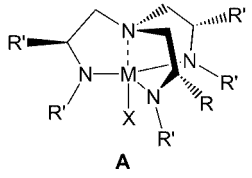
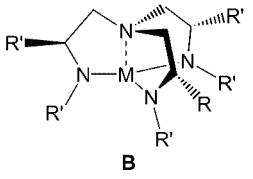
Al^{III} and Ti^{IV} complexes of C_3-symmetric tetradentate trisamidoamine ligands with trigonal bipyramidal coordination geometry, containing chlorine or dialkylamido groups, or with a free coordination site in the apical position, have been synthesised by salt metathesis and amine elimination. Products with threefold symmetry were generally obtained for tetravalent titanium, whereas for the aluminium complexes either asymmetric structures with two of the three podand arms taking part in coordination to the metal or symmetric arrangements possessing the full threefold symmetry were formed depending on the steric properties of the ligands.

Introduction

The preparation of chiral ligands capable of efficient chirality transfer is crucial for successful asymmetric metal catalysis.[1,2] Several factors need to be considered in the design of new ligands, including steric and electronic effects, kinetic properties, hapticity and bite angles.[3,4] Another factor that occasionally plays an important role is symmetry. C_2-Symmetric ligands have, in many situations, proven to offer advantageous properties over those lacking symmetry, and such ligands have been extensively employed in asymmetric catalysis and various processes involving chiral recognition.[5] C_3-Symmetric ligands, however, have been considerably less investigated,[6] although extensive studies have been performed on achiral ligands possessing threefold rotational axes. Particularly detailed studies have been performed by the groups of Verkade[7,8] and Schrock[9] on complexes with derivatives of tris(2-aminoethyl)amine (TREN) most of them bearing bulky substituents such as trialkylsilyl or pentafluorophenyl groups on nitrogen. Metal complexes with TREN or its derivatives have also been used in several applications. Some recent examples include nitrogen activation by Mo^{IV} complexes with *N*,*N*′*N*′′-aryl-substituted TREN ligands,[10] alkene epoxidation by Mn^{III} and Fe^{III} complexes,[11] phosphoester hydrolysis[12] and CO_2 fixation[13] by Zn^{II} complexes, and thiosulfate oxidation by Cu^{II} complexes.[14] Furthermore, a Cu^{II} complex has been shown to react reversibly with oxygen,[15] and Cu^{II} and Ni^{II} complexes to bind nucleobases.[16]





Triamidoamines usually serve as tetradentate ligands, forming rigid trigonal bipyramidal (**A**) or, in the absence of an apical ligand, trigonal monopyramidal (**B**) complexes with a variety of transition metals and main-group elements.[7,9,17] The M–N_{ap} distances vary significantly, occasionally resulting in complexes lacking a transannular bond, thus leading to tridentate coordination.[7–17] Other coordination modes are possible, however, as shown by the recently determined structures of $[Ni(tren)(abpt)](NO_3)_2$ [abpt = 4-amino-3,5-bis(pyrid-2-yl)-1,2,4-triazole],[18] $[Ni(tren)Sb_2S_4]$,[19] $[Co(tren)(amino\ acidato\text{-}N,O)]X_2$,[20] and $[Co(tren)(N_3)_2]Br$,[21] which exhibit octahedral coordination.

Several methods have been employed for metal complex formation of TREN derivatives. Usually the ligand is treated with a base such as butyllithium prior to reaction with a transition metal salt,[22] although ligands with acidic protons on nitrogen may react directly with the metal com-

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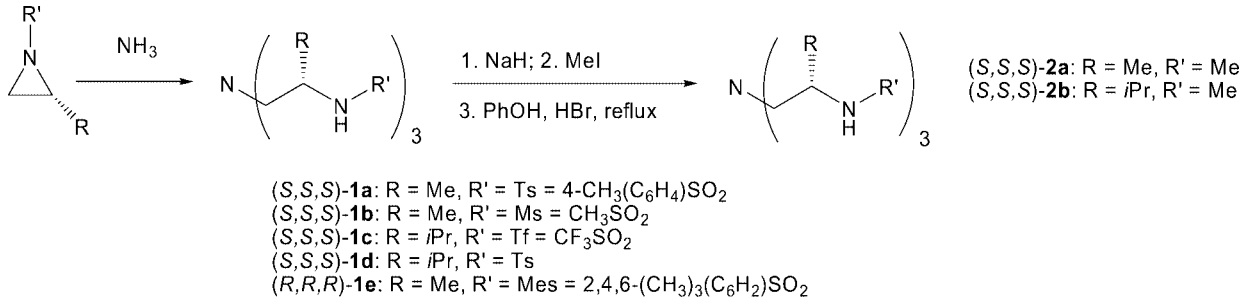


Scheme 1. Synthesis of the C_3-chiral TREN ligands **1a**–**1e** and **2a**,**b**.

pound.[23] Metal halides and metal amide complexes are the most commonly used metal sources.

A few chiral tetradentate TREN analogues with the chirality residing in the ligand backbone[24–27] or in substituents on the equatorial nitrogen atoms,[28] as well as tridentate ligands lacking an apical nitrogen,[29] have been prepared. Upon metal complex formation, a chiral pocket with a C_3-symmetric environment is created in the apical position, a favourable situation for asymmetric catalysis.[30] Some of the chiral ligands, notably those by Gade, have indeed been assessed in asymmetric reactions and were found to induce moderate to high enantioselectivity in stoichiometric[30a] and catalytic[30c] alkylations of aryl aldehydes. Proazaphosphatranes have been shown to serve as excellent catalysts in a vast number of base-mediated[31] and metal-catalysed[32] processes, but their chiral analogues[26,28,33] have not yet been applied in catalysis. Titanatranes have been employed in asymmetric ring-opening of *meso* epoxides and enantioselective oxidation of sulfides,[34] but no reports on the use of azatitanatranes, first described in 1991,[35] have appeared.

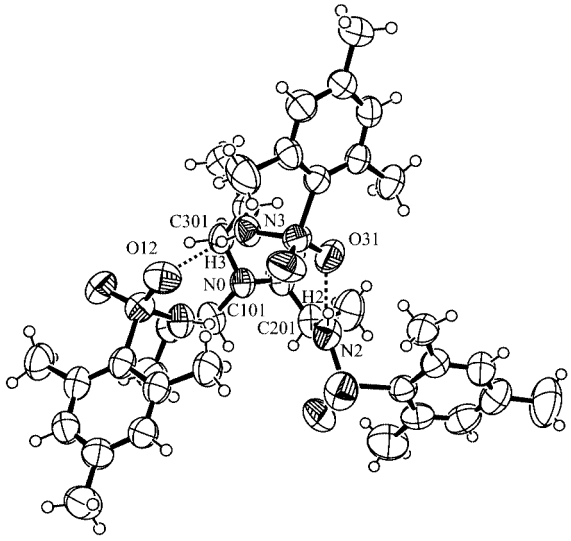
Since we have access to a versatile method for the preparation of chiral TREN derivatives,[24] we initiated a study of the formation of amido metal complexes[36,37] for potential use in asymmetric catalysis.

Results and Discussion

Ligand Preparation

Ligands (*S*,*S*,*S*)-**1a**–**c**[24] and -**1d**[38] were prepared as described previously, starting from the appropriate enantiopure aziridine and ammonia. Ligand (*R*,*R*,*R*)-**1e** was prepared analogously in 60% overall yield. Compounds (*S*,*S*,*S*)-**2a** and (*S*,*S*,*S*)-**2b** were obtained from (*S*,*S*,*S*)-**1a** and (*S*,*S*,*S*)-**1d**, respectively, by N-methylation followed by deprotection of the tosyl groups with HBr[24b] (Scheme 1).

Upon crystallisation by vapour-diffusion from chloroform/hexane, ligand (*R*,*R*,*R*)-**1e** afforded suitable crystals for X-ray analysis (Figure 1). Interestingly, the molecular structure of (*R*,*R*,*R*)-**1e** deviates only slightly from threefold symmetry. Two hydrogen bonds between NH functions and sulfonylic oxygen atoms (Figure 1, dashed lines) hold the ligand structure in a bent conformation which is similar to that observed upon coordination to metal ions (azametallatranes **A** and **B**). The TREN structure is approximately C_3-symmetric, with the angles centred around the bridgehead nitrogen atom being almost identical (Figure 1). The TREN arm labelled as **III** in Figure 1 participates in two hydrogen bonds involving carboxamide proton H3, which interacts with the sulfonyl oxygen atom in arm **I** (O12), whereas its sulfonyl unit forms a hydrogen bond with H2(N2). Both hydrogen bonds have similar metric parameters (N–H···O = 0.86 Å, N–H–O = 170°–175°).



Selected bond lengths (Å) and angles (deg) for crystal structure of **1e**

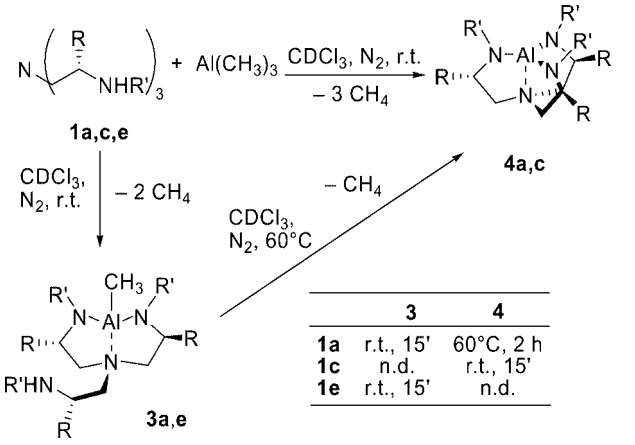
H Bonds, Å			N–H···O Angles (deg)	N0-Centered Angles (deg)	
	N-H	***H···O***		C201-N0-C301	110
N2-H2···O31	0.86	2.11	175	C201-N0-C101	111
N3-H3···O12	0.86	2.19	170	C301-N0-C101	114

Figure 1. ORTEP view of the molecular structure of (*R*,*R*,*R*)-**1e** (30% thermal ellipsoids). Dashed lines indicate hydrogen bonds. The hydrogen atoms were included at calculated positions with fixed thermal parameters.

The ligands **1a**–**e** bearing electron-withdrawing substituents on the nitrogen atoms possess relatively acidic NH protons and were found to react directly with metal amides in a transamination reaction. On the other hand, coordination of the *N*-alkylated TREN derivatives (*S*,*S*,*S*)-**2a** and (*S*,*S*,*S*)-**2b** required initial metallation with *n*BuLi and subsequent reaction with $M^{(n)}Cl_n{\cdot}(THF)_m$ in a salt metathesis step.

Metal Complex Formation: Aluminum(III) Complexes

Complex formation between ligands (*S*,*S*,*S*)-**1a**,**c** and (*R*,*R*,*R*)-**1e** and suitable Al^{III} precursors was initially studied whilst monitoring the course of the reactions by ^1H NMR spectroscopy. Addition of one equivalent of $Al(OiPr)_3$ did not afford any new Al^{III} complex, even upon prolonged heating at 100 °C. However, the addition of one equivalent of $AlMe_3$ to (*S*,*S*,*S*)-**1a** (Scheme 2) was accompanied by instantaneous gas evolution.



Scheme 2. Synthesis of Al^{III} complexes of ligands **1a**, **1c** and **1e**.

The ^1H NMR spectrum recorded after 15 minutes at room temperature is consistent with the quantitative formation of a new metal complex containing three diastereotopic ligand arms and thus being devoid of threefold symmetry (Figure 2, spectrum b). The presence of one N*H* (doublet at δ = 4.70 ppm) and one Al–CH_3 signal (singlet at δ = –0.39 ppm) suggested the new species to be **3a** (R = Me, R′ = Ts), with a structure similar to a complex obtained from a dipodal analogue of **1** and trimethylaluminium.[39] This assumption was corroborated by the modifications observed upon heating at 60 °C. Further evolution of gas was detected, followed by the slow formation (2 h) of the symmetrical species **4a** (Scheme 2). The disappearance of the N*H* signal and the accompanying downfield shift of almost all the signals in the spectrum of **4a** with respect to those of the uncomplexed ligand (Figure 2, spectrum c) provided evidence that the coordination of (*S*,*S*,*S*)-**1a** to aluminium had occurred. A particularly evident deshielding effect ($\Delta\delta \approx 0.5$ ppm) was observed for one of the diastereotopic CH_2 resonances (doublet of doublets, from δ = 2.13 ppm in **1a** to δ = 2.60 ppm in **4a**).

The same experiment was repeated with (*R*,*R*,*R*)-**1e**. With this sterically more demanding ligand no symmetrical complex was obtained, and only the formation of **3e** (R = Me, R′ = Mes) was observed even after heating at 60 °C for 48 h (Scheme 1). In contrast, reaction of trimethylaluminium with the more reactive triflate derivative (*S*,*S*,*S*)-**1c** afforded **4c** (R = *i*Pr, R′ = Tf) directly without detection of any intermediate complex of type **3** (Scheme 2). The monomeric nature of **4a** and **4e** is supported by the single set of resonances in their NMR spectra (^1H, ^{13}C and ^{19}F in the case of complex **4e**), which reflect the C_3 symmetry of the complex. Verkade and co-workers provided analogous symmetry considerations derived from the NMR spectral pattern to demonstrate the monomeric nature of their *N*-trimethylsilylazaalumatrane.[40]

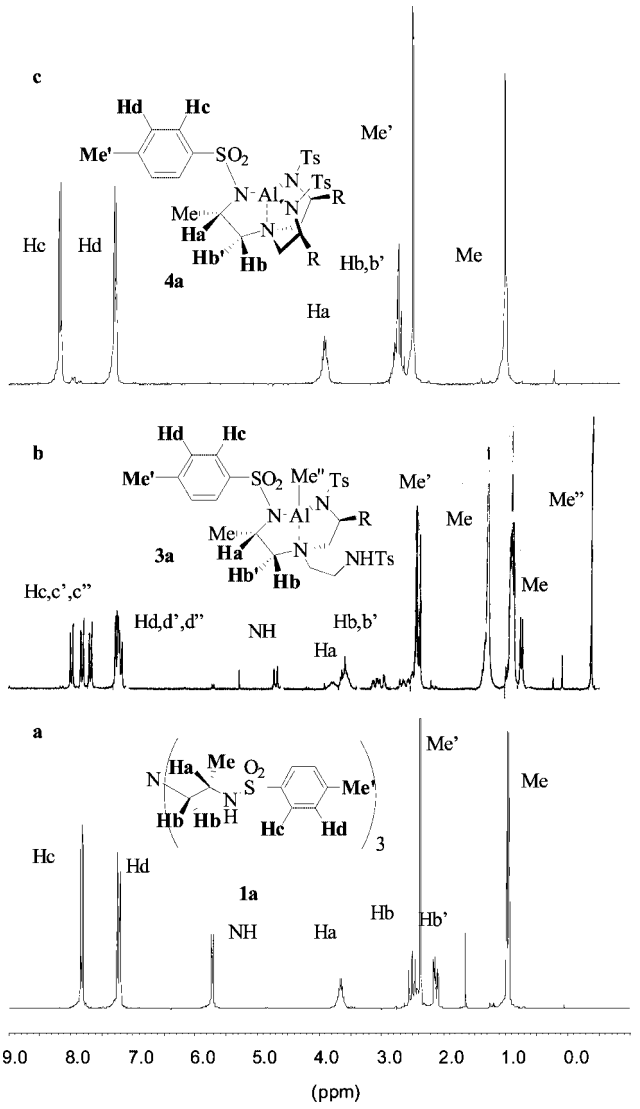


Figure 2. Reaction of $AlMe_3$ (0.020 M) with (*S*,*S*,*S*)-**1a** (0.020 M) in $CDCl_3$ under nitrogen monitored by ^1H NMR spectroscopy (250 MHz): a) (*S*,*S*,*S*)-**1a**; b) addition of $AlMe_3$ (1 equiv.), room temp., 15 min; c) after heating at 60 °C, 2 h: **4a**.

A synthetic procedure that allowed the preparation of **4a** on a one-gram scale was achieved by carrying out the reaction of Scheme 1 under slightly modified conditions. Complex **4a** was obtained in 99% yield by adding trimethylaluminium to a saturated solution of (*S*,*S*,*S*)-**1a** in dry THF and refluxing the reaction mixture under nitrogen until a white precipitate separated from the colourless solution. Isolation of pure **4a** was possible by washing with dry pentane and centrifugation. Despite its tendency to afford dendritic precipitates, layering of a concentrated solution of **4a** in dichloromethane with a 1:1 mixture of dichloromethane/diethyl ether and with pure diethyl ether allowed the growth

of colourless single crystals suitable for X-ray diffraction analysis.

The crystal structure of **4a** is depicted in Figure 3 along with the principal bond lengths and angles.

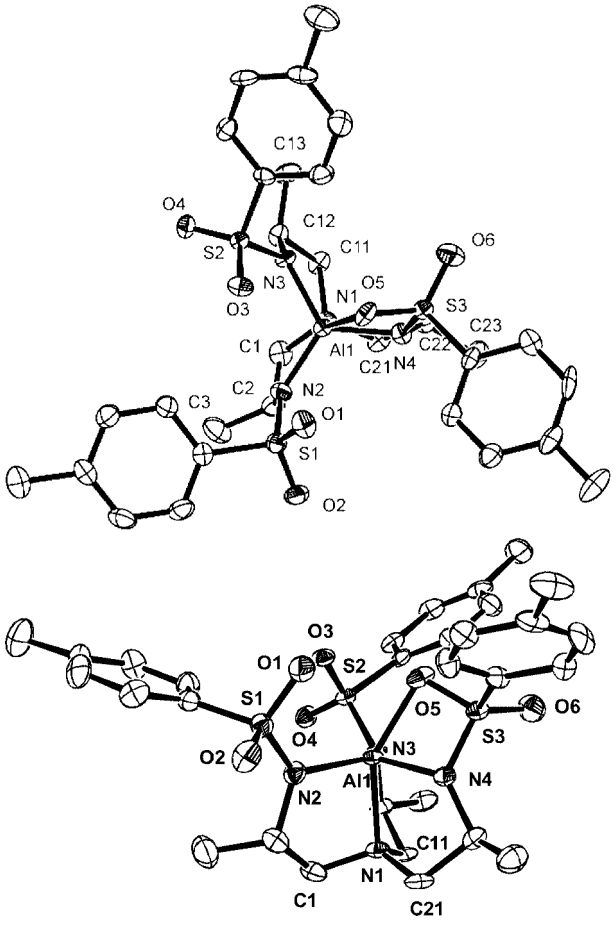


Figure 3. ORTEP views of (*S*,*S*,*S*)-**4a** (50% probability level thermal ellipsoids). Principal bond lengths [Å] and angles [°]: Al–N(1) 2.042(4), Al–N(2) 1.861(5), Al–N(3) 1.872(4), Al–N(4) 1.897(4), Al–O(5) 2.054(4), S(1)–O(1) 1.445(4), S(1)–O(2) 1.433(4), S(2)–O(4) 1.442(3), S(2)–O(3) 1.450(4), S(3)–O(5) 1.495(4), S(3)–O(6) 1.423(4); N(2)–Al–N(3) 117.5(2), N(2)–Al–N(4) 116.8(2), N(3)–Al–N(4) 122.2(2), C(1)–N(1)–C(11) 112.0(4), C(1)–N(1)–C(21) 113.3(4), C(11)–N(1)–C(21) 110.1(4), N(2)–Al–N(1) 86.4(2), N(3)–Al–N(1) 84.8(2), N(4)–Al–N(1) 80.4(2), N(1)–Al–O(5) 120.7(2), Al–O(5)–S(3) 93.9(2). All hydrogen atoms have been omitted for clarity.

Azaalumatrane **4a** crystallises in the space group $P2_12_12_1$ with a dichloromethane molecule present in the unit cell. The complex is monomeric and approximately C_3-symmetric, as is evident from the observed N_{eq}–Al–N_{eq} angles (116.8–122.2°), which is in accordance with the structural features derived from the NMR spectroscopic data recorded in solution. The five-coordinate aluminium complex possesses a highly distorted trigonal-bipyramidal coordination geometry, the metal centre being slightly displaced above the equatorial plane [N(1)–Al–N_{eq} = 80.4–86.4°]. The equatorial N–Al bond lengths (1.861–1.897 Å) are comparable to those reported for analogous azaalumatranes[17,41,42] and to nitrogen–aluminium distances in five-coordinate Al^{III}/amido complexes (1.897–1.976 Å).[43] The transannular interaction in **4a** [N(1)–Al = 2.042(4) Å] is stronger than in the *N*-methyl-substituted azaalumatrane **4f** [R = H and R′ = Me; 2.124(6) Å], which is a dimer bearing a trigonal-bipyramidal geometry around the five-coordinate aluminium.[43] On the other hand a considerably stronger transannular bond [1.983(6) Å] is found in the *N*-trimethylsilyl-substituted analogue **4g** (R = H and R′ = $SiMe_3$), in which the bulky $SiMe_3$ groups prevent dimerisation and leave a coordinatively unsaturated aluminium.[42] Interestingly, the transannular interaction observed in **4a** lies within the range found in the analogous Al^{III}/trialkanolamine complexes.[44] Distortion of the bipyramidal geometry is due to the coordination of one of the sulfonyl oxygen atoms belonging to a tosyl group to aluminium, the angle along the axial direction deviating considerably from 180° [N(1)–Al–O(5) = 120.7°]. This Al–O(5) interaction results in a bond length [2.054(4) Å] which is comparable to that of the transannular bond [2.042(4) Å]. As a consequence, both the sulfur–oxygen covalent bond [S(3)–O(5) = 1.495(4) Å, compared to an average S–O distance of 1.439 Å] and the N_{eq}–Al bond [N(4)–Al = 1.897(4) Å compared 1.861–1.872 Å for the remaining two Al–N bonds] are elongated.

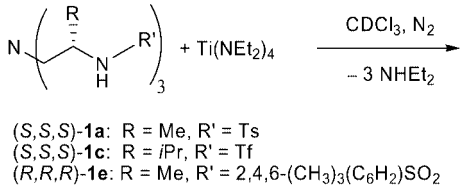
As mentioned above, achiral azaalumatranes have been prepared and studied previously by Verkade.[41–43] For the monomeric complexes an interconversion between the λ and δ chelate ring conformations was observed, which was rapid on the NMR timescale down to –95 °C.[42] On the other hand, interconversion between the spiral diastereomers of **4a** was not observed at room temperature, which implies that the presence of the ring-methyl substituents of ligand **1a** increases the interconversion barrier and prevents such a conformational twist. Moreover, it is evident from the molecular structure of **4a** (Figure 3, horizontal view) that these methyl substituents play a crucial structural role and appear to determine the orientation of the N–SO_2–Ar moieties. This implies that the chirality of the C_3 cavity around the metal centre (the "chiral pocket") is determined by the orientation of the methyl groups and thus by the absolute configuration of the ligand.

The use of azaalumatranes as precursors for the synthesis of a variety of transition metal or main group element azatranes by transmetallation has been reported.[43] However, the potential of this type of complex to serve as a Lewis acid, and thus to increase the coordination number by apical coordination, is as yet essentially unexplored, although Al complexes of dipodal analogues have been employed as chiral Lewis acid catalysts.[45] We note that achiral Al complexes have in fact been used as Lewis acid catalysts in the ring-opening polymerisation of heterocycles,[39] and chiral analogues may be of interest for controlling the tacticity of the polymers.

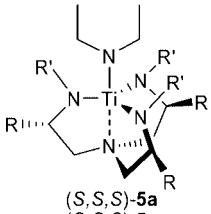
Metal Complex Formation: Titanium(IV) Complexes

The reaction of ligand **1a** with [Ti(NEt_2)$_4$] in a 1:1 stoichiometry was initially performed in $CDCl_3$ in an NMR

tube and monitored by ^{1}H NMR spectroscopy (Scheme 3). Whereas a poorly resolved spectrum was recorded after 15 min, which indicated the presence of fluxional species of low symmetry in solution, the spectral patterns simplified and sharpened up over a period of three days at ambient temperature. The highly resolved spectrum recorded at that stage is consistent with the formation of a monomeric complex with threefold symmetry (**5a**) possessing one residual diethylamido group. Complex formation was further supported by the liberation of diethylamine and the observation that the methylene proton resonances of the Et_2N ligand give an AB system (δ = 4.36 and 4.51 ppm respectively). The reaction was accompanied by a change of colour from yellow to reddish-brown. An analogous complex was formed from ligand **1e** and [Ti(NEt$_2$)$_4$] within six days at room temperature or within six hours upon heating at 60 °C; **1c** exhibits higher reactivity, undergoing instantaneous complex formation (Scheme 3).



(*S*,*S*,*S*)-**1a**: R = Me, R' = Ts
(*S*,*S*,*S*)-**1c**: R = *i*Pr, R' = Tf
(*R*,*R*,*R*)-**1e**: R = Me, R' = 2,4,6-(CH$_3$)$_3$(C$_6$H$_2$)SO$_2$



5	
1a	r.t., 72 h
1c	r.t., 15 min
1e	60°C, 6 h

(*S*,*S*,*S*)-**5a**
(*S*,*S*,*S*)-**5c**
(*R*,*R*,*R*)-**5e**

Scheme 3. Synthesis of Ti^{VI} complexes of ligands **1a**, **1c** and **1e**.

The ^{1}H NMR spectra of azatitanatranes **5a**, **5c** and **5e** are all consistent with the formation of highly symmetric monomeric species. In all cases the resonances of the triamidoamine ligands have undergone significant shifts with respect to the uncomplexed ligand (see Table 1).

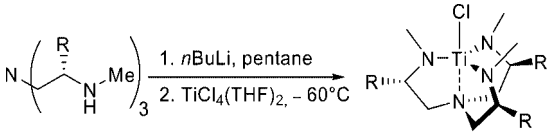
Table 1. Selected ^{1}H NMR spectroscopic data [ppm] for ligands **1a**, **1c** and **1e** and complexes **5a**, **5c** and **5e**.

	NC*H*$_2$CHR–N		Ti–N(C*H*$_2$Me)$_2$	
Ti(NEt$_2$)$_4$	–	–	3.46	3.46
(*S*,*S*,*S*)-**1a**	2.13	2.50	–	–
(*S*,*S*,*S*)-**5a**	2.52	3.05	4.36	4.50
(*S*,*S*,*S*)-**1c**	2.24	2.90	–	–
(*S*,*S*,*S*)-**5c**	2.62	3.30	4.24	4.80
(*R*,*R*,*R*)-**1e**	2.17	2.83	–	–
(*R*,*R*,*R*)-**5e**	3.47	4.63	3.48	3.92

A different behaviour is observed for complex **5e** and complexes **5a** and **5c**. Thus, in complex **5e** a remarkable deshielding (ca. 1 ppm) of the signals of the methylene protons of the TREN moiety is observed (from δ = 2.52 and 3.05 ppm in **5a** and δ = 2.63 and 3.30 ppm in **5c** to δ = 3.50 and 4.63 ppm in **5e**) due to a shielding of the protons of the apical diethylamido group (δ = 3.48 and 3.92 ppm vs. δ = 4.36 and 4.50 ppm for **5a** and δ = 4.24 and 4.80 ppm for **5c**). The observed difference in δ values very likely originates from a more open structure of complex **6e** compared to the other two, which is caused by the more hindered nature of the mesitylene groups. The bulkier substituents on the external part of the ligand remove the sulfonyl moieties from the inner part of the cavity, thus moving the aromatic rings closer to the methylene groups of the TREN backbone. This fact diminishes the magnetic anisotropy effect of the S=O groups on the apical ligand and increases the effect of the peripheral aromatic ring on the protons of the TREN backbone. ^{1}H NOESY experiments on complexes **5a** and **5c** were in agreement with such hypothesis. In fact, a significant difference in the distances between the aromatic *meta* protons and the hydrogen atoms in the methyl group of the ligand backbone was found (3.00 and 2.25 Å for **5a** and **5e**, respectively).

A synthetic protocol allowing the preparation of Ti^{IV} complex **5a** on a gram scale was worked out as well. Azatitanatrane **5a** was prepared in 95% yield and high NMR purity by carrying out the reaction in a 3:1 pentane/THF mixture at room temperature from a concentrated solution of the reactants (0.2 M); it was isolated as a yellowish solid by filtration.

Finally, the Ti complexes of **2a** and **2b** (**6a** and **6b**) were prepared as previously reported for the achiral analogue [{(MeNCH$_2$CH$_2$)$_3$N}TiCl][46] by salt metathesis of the lithium salt of the triamidoamine ligands and [TiCl$_4$(THF)$_2$] as metal source (Scheme 4). The ^{1}H and ^{13}C NMR spectra are consistent with the assumed threefold symmetry of the complexes. Unfortunately, attempts to obtain single crystals for X-ray structure determination failed.



(*S*,*S*,*S*)-**2a**: R = Me
(*S*,*S*,*S*)-**2b**: R = *i*Pr

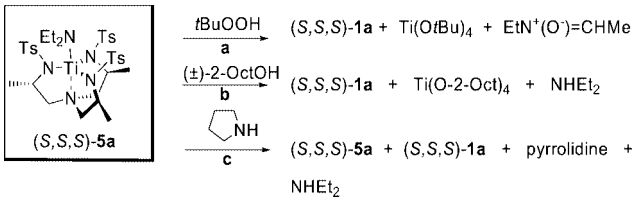
(*S*,*S*,*S*)-**6a**: R = Me
(*S*,*S*,*S*)-**6b**: R = *i*Pr

Scheme 4. Synthesis of Ti^{VI} complexes of ligands **2a** and **2b**.

All attempts to displace the apical amido ligand in the N-sulfonated azatitanatranes **5a**–**c** with both O- and N-based nucleophiles only yielded mixtures or led to complex degradation, as was established upon monitoring the reactions by ^{1}H NMR spectroscopy.

Several examples of reactivity studies performed with the tris-tosyl azatitanatrane **5a** are summarised in Scheme 5. Upon addition of *tert*-butyl hydroperoxide (from 1 to 10 equiv.) no formation of peroxoazatitanatrane complexes was observed (Scheme 5, path a); a complete decomposition of the starting complex occurred with concurrent slow oxidation of the free diethylamine.[47] This behaviour is in contrast to the previously established oxygenation behaviour of titanatrane complexes.[48] In the same way, treatment with racemic 2-octanol resulted, again, in complete decomposi-

tion of the complex with formation of ligand **1a** and titanium alkoxides (Scheme 5, path b). The oxophilic nature of titanium(IV) compounds is well documented[49] and this argument can be invoked to explain the high reactivity towards oxygen-containing species observed for **5a**. Verkade has reported that attempts to displace an apical NMe_2 group from an achiral azatitanatrane (R′ = Me, L = NMe_2) with *tert*-butyl alcohol give only a mixture of starting material, titanium alkoxide and alcoholysis products, with no detectable evidence for the displacement product.[50] Similar results were obtained in the attempted exchange of the apical diethylamido ligand for N-based nucleophiles. Addition of up to 10 equivalents of pyrrolidine to **5a** in $CDCl_3$ only returned the unreacted starting materials, and additional heating resulted in partial decomposition of the complex (Scheme 5, path c).[51]



Scheme 5. Reactivity of complex **5a** with O- and N-based nucleophiles.

From these preliminary results it seems clear that the apical diethylamido ligand in complex **5a**, in analogy with the previously reported azatitanatranes,[35] is not easily displaced and this limits its use as a catalyst by the activation of apical substituents. Since apical chloro ligands can be replaced by alkylation to yield the corresponding alkyltitanium compounds[22a,52] or, alternatively, may be abstracted by treatment with silver salts to generate, for example, triflate derivatives,[49] or replaced by a siloxyl (R_3SiO) group by reaction with sodium siloxide,[53] such azatrane derivatives may be more suitable for use as Lewis acid catalysts. Such work is currently in progress.

Conclusion

Enantiopure C_3-symmetric Al^{III} and Ti^{IV} complexes have been obtained from chiral trisamidoamine derivatives with threefold symmetry. Further studies are needed in order to ascertain whether the complexes have the key properties required for catalysis, such as a sufficiently large cavity for substrate binding, fast exchange of coordinated substrate, and efficient transfer of chirality from the chiral complex to the substrate undergoing reaction.

Experimental Section

General Remarks: All metal-containing compounds were prepared under dry nitrogen on a high vacuum line using standard Schlenk techniques or in a glove box. All reaction flasks were heated prior to use and solvents and solutions were transferred by needle/septum techniques. Separation of solids from suspensions was performed by centrifugation with a Rotina 48 centrifuge (Hettich Zentrifugen, Tuttlingen, Germany) equipped with a specially designed Schlenk tube rotor.[54] Solvents were dried according to standard procedures and used under nitrogen: diethyl ether, THF, toluene and pentane were distilled from sodium/benzophenone and stored over a potassium mirror, except for diethyl ether, which was stored over activated 4-Å molecular sieves. Dichloromethane was distilled from calcium hydride and stored over activated 4-Å molecular sieves. The deuterated solvents used for NMR experiments were dried with activated 4-Å molecular sieves. Deuterated chloroform was additionally treated with a small amount of dry potassium carbonate. Pellets and powdered 4-Å molecular sieves were purchased from Aldrich and activated before use. The ^1H and ^{13}C NMR spectra were recorded with Bruker AC 200 SY (^1H: 200.13 MHz; ^{13}C: 50.32 MHz), AC 250 (^1H: 250.18 MHz; ^{13}C: 62.90 MHz), DRX 300 (^1H: 300.13 MHz; ^{13}C: 75.46 MHz) and Bruker Avance 400 (^1H: 400.00 MHz; ^{13}C: 100.58 MHz) instruments and referenced to the residual signals from $CDCl_3$ (^1H: δ = 7.26 ppm; ^{13}C: δ = 77.2 ppm) and C_6D_6 (^1H: δ = 7.20 ppm) ppm. ^{19}F NMR spectra were recorded with the Bruker DRX 300 spectrometer using $CFCl_3$ as internal reference (^{19}F: 282.35 MHz; $CFCl_3$ δ = 0 ppm). Melting points are uncorrected and were determined withy a Reichert Austria apparatus. Optical rotations were measured with a Perkin–Elmer 241 polarimeter (λ = 589 nm, sodium D-line) at 25 °C using a quartz cell (10 cm). Chromatographic separations were performed with Macherey–Nagel silica gel (70–230 mesh). Flash chromatography was performed as described in the literature[55] using Macherey–Nagel 60 silica gel (0.040–0.063 mm, 230–400 mesh). TLC analyses were run using Macherey–Nagel POLYGRAM®SIL G/UV_{254} silica pre-coated plastic sheets (40 × 80 mm, 0.2 mm thickness). $Al(CH_3)_3$ (2.0 M solution in heptane) was purchased from Aldrich. The ligands used for the preparation of metal complexes were dried under vacuum and stored over P_2O_5 or under nitrogen. All other chemicals were obtained commercially and used without further purification.

Ligand (*R*,*R*,*R*)-1e: (*R*,*R*,*R*)-**1e** was obtained in 60% yield (0.99 g) following the procedure previously described for **3a**.[24] M.p. 177–178 °C, $[\alpha]_D^{20}$ = –82.6 (*c* = 1.2, $CHCl_3$). ^1H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = 0.91 (d, *J* = 6.2 Hz, 9 H), 2.17 (dd, *J* = 12.7 and 4.5 Hz, 3 H), 2.27 (s, 9 H), 2.67 (s, 18 H), 2.83 (dd, *J* = 12.6 and 11.1 Hz, 3 H), 3.68–3.91 (m, 3 H), 5.88 (d, *J* = 7.2 Hz, 3 H), 6.91 (s, 6 H) ppm. ^{13}C NMR (62.90 MHz, $CDCl_3$, 25 °C): δ = 19.6 [CH_3, 3 C, –CH(*C*H_3)], 20.8 (CH_3, 3 C, *p*-*C*H_3), 23.0 (CH_3, 6 C, *o*,*o*′-*C*H_3), 45.9 (CH, 3 C, CH_2*C*HMeN), 57.3 (CH_2, 3 C, N*C*H_2CHMe-), 131.7 (CH, 6 C, *C*H arom.), 135.8 (C_q, 3 C, CH*C*MeCH arom.) 138.8 (C_q, 6 C, -SO_2*C*CMeCH- arom.), 141.6 (C_q, 3 C, SO_2*C* arom.) ppm. $C_{36}H_{54}N_4O_6S_3$ (735): calcd. C 58.83, H 7.40, N 7.62; found C 58.95, H 7.42, N 7.60.

Synthesis of Al^{III} Complexes of Ligands (*S*,*S*,*S*)-1a and (*S*,*S*,*S*)-1c in situ: Ligand **1** (0.020 mmol) was added to a 1-mL volumetric flask and dissolved in $CDCl_3$. Trimethylaluminium (2.0 M in heptane, 0.010 mL, 0.020 mmol) was then added and the solution (0.500 mL) was transferred into a screw-cap NMR tube, which was sealed under nitrogen and kept at room temperature. The reaction was followed by ^1H NMR spectroscopy. Once the complete formation of the complex was observed, the sample was kept at 0 °C in the refrigerator.

Complex (*S*,*S*,*S*)-3a: Upon addition of ligand (*S*,*S*,*S*)-**1a** (13.02 mg) to $AlMe_3$, formation of **3a** (colourless solution) was quantitative after 15 min. ^1H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = –0.39 (s, 3 H), 0.72 (d, *J* = 6.6 Hz, 3 H), 0.86 (d, *J* = 5.3 Hz, 3 H), 0.87 (d, *J* = 5.3 Hz, 3 H), 2.35 (s, 3 H), 2.40 (s, 3 H), 2.42 (s, 3 H), 2.47 (dd, *J* = 13.6 and 12.3 Hz, 1 H), 2.62 (dd, *J* = 16.7 and 10.1 Hz, 1

H), 2.98 (dd, J = 15.4 and 2.2 Hz, 1 H), 3.08 (dd, J = 13.6 and 4.4 Hz, 1 H), 3.69–3.42 (m, 1 H), 3.91–3.69 (m, 1 H), 4.72 (d, J = 10.5 Hz, 1 H), 7.20 (d, J = 8.3 Hz, 2 H), 7.27 (d, J = 8.3 Hz, 4 H), 7.69 (d, J = 8.3 Hz, 2 H), 7.83 (d, J = 8.3 Hz, 2 H), 7.99 (d, J = 8.3 Hz, 2 H) ppm.

Complex (*R*,*R*,*R*)-3e: This complex was prepared from $AlMe_3$ and ligand (*R*,*R*,*R*)-**1e** (14.70 mg). Quantitative formation occurred in 15 min; colourless solution. ^{1}H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = –0.41 (s, 3 H), 0.56 (d, J = 5.9 Hz, 3 H), 0.73 (d, J = 5.6 Hz, 3 H), 0.90 (d, J = 6.6 Hz, 3 H), 2.25 (s, 3 H), 2.29 (s, 3 H), 2.31 (s, 3 H), 2.36 (dd, J = 14.4 and 2.9 Hz, 1 H), 2.50–2.71 (m, 2 H), 2.62 (s, 6 H), 2.67 (s, 6 H), 2.74 (s, 6 H), 3.04 (dd, J = 7.9 and 4.3 Hz, 1 H), 3.20 (dd, J = 14.3 and 2.9 Hz, 1 H), 3.38–3.53 (m, 1 H), 3.54–3.69 (m, 2 H), 3.70–3.91 (m, 1 H), 4.53 (d, J = 10.3 Hz, 1 H), 6.87 (s, 2 H), 6.94 (s, 2 H), 6.98 (s, 2 H) ppm.

Complex (*S*,*S*,*S*)-4a: This complex was prepared from $AlMe_3$ and ligand (*S*,*S*,*S*)-**1a** (13.02 mg). The solution was heated at 60 °C for 15 d, resulting in 100% conversion to (*S*,*S*,*S*)-**4a**. The solution was colourless. ^{1}H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = 0.87 (d, J = 6.0 Hz, 9 H), 2.37 (s, 9 H), 2.43–2.76 (m, 6 H), 3.73–3.90 (m, 3 H), 7.25 (d, J = 8.3 Hz, 6 H), 8.15 (d, J = 8.3 Hz, 6 H) ppm. ^{13}C NMR (62.90 MHz, $CDCl_3$, 25 °C): δ = 19.1 [CH_3, 3 C, –CH(*C*H_3)–N–], 21.5 (CH_3, 3 C, *C*H_3 arom.), 46.4 (CH, 3 C, CH_2C*H*MeN), 55.8 (CH_2, 3 C, NC*H*$_2$CHMe), 128.1 (CH, 6 C, CH arom.), 129.2 (CH, 6 C, CH arom.), 139.3 (C_q, 3 C, CH arom.), 142.6 (C_q, 3 C, CH arom.) ppm.

Complex (*S*,*S*,*S*)-4c: This complex was prepared from $AlMe_3$ and ligand (*S*,*S*,*S*)-**1c** (13.37 mg). Full conversion to colourless **4c** was observed after 2 h at 60 °C. ^{1}H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = 0.96 (d, J = 7.0 Hz, 9 H), 1.00 (d, J = 7.0 Hz, 9 H), 2.02–2.90 (m, 3 H), 2.23 (dd, J = 13.2 and 4.8 Hz, 3 H), 2.88 (dd, J = 13.2 and 10.8 Hz, 3 H), 3.65–3.79 (m, 3 H) ppm. ^{13}C NMR (62.90 MHz, $CDCl_3$, 25 °C): δ = 17.1 (CH_3, 9 C, CH*C*H_3), 17.9 (CH_3, 9 C, CH*C*H_3), 31.0 [CH, 3 C, –*C*H(CH_3)$_2$], 53.1 (CH, 3 C, –CH_2*C*H*i*Pr), 56.9 (CH, 3 C, –*C*H_2CH*i*Pr), 119.2 (C_q, $J_{C,F}$ = 320.9 Hz, 3 C, CF_3) ppm. ^{19}F NMR (282.35 MHz, C_6D_6, 28 °C): δ = –77.95 ppm.

Complex (*S*,*S*,*S*)-4a: Ligand (*S*,*S*,*S*)-**3a** (1.042 g, 1.60 mmol) was placed in a 100-mL Schlenk-tube. Dry THF (10 mL) was added followed by trimethylaluminium (2.0 M in heptane, 0.800 mL, 1.60 mmol) while stirring under nitrogen. After gently heating up to reflux, gas evolution was observed from the colourless solution. The reaction mixture was heated at 60 °C for 2 h and formation of a white precipitate was observed. Complex (*S*,*S*,*S*)-**5a** (1.069 g, 1.59 mmol, 99% yield) was isolated as a white solid after centrifugation and washing with dry THF (2 × 10 mL) and pentane (2 × 10 mL). ^{1}H and ^{13}C NMR as reported above. $C_{30}H_{39}AlN_4O_6S_3$ (675): calcd. C 53.39, H 5.82, N 8.30; found C 53.52, H 5.89, N 8.47.

Synthesis and Characterisation of Ti^{IV} Complexes of Ligands (*S*,*S*,*S*)-1a, (*S*,*S*,*S*)-1c and (*R*,*R*,*R*)-1e in situ: Ligand **1** (0.027 mmol) was added to a 1-mL volumetric flask and dissolved in $CDCl_3$. Tetrakis(diethylamino)titanium (0.010 mL, 0.028 mmol) was then added and the solution (0.500 mL) was transferred into a screw-cap NMR tube, which was sealed and kept at room temperature. The reaction was followed by ^{1}H NMR spectroscopy. Once the complex was observed, the volatile diethylamine was removed under vacuum and the sample was kept in solution at 0 °C in the refrigerator.

Complex (*S*,*S*,*S*)-5a: Ligand (*S*,*S*,*S*)-**5a** (17.6 mg) gave the complex quantitatively after 3 d, during which time the solution turned reddish-brown. ^{1}H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = 1.03 (d, J = 6.5 Hz, 9 H), 1.21 (t, J = 7.4 Hz, 6 H), 2.38 (s, 9 H), 2.52 (dd, J = 12.1 and 5.0 Hz, 3 H), 3.05 (dd, J = 12.1 and 11.6 Hz, 3 H), 4.12–4.36 (m, 3 H), 4.36 (dq, J = 11.1 and 7.4 Hz, 2 H), 4.50 (dq, J = 11.1 and 7.4 Hz, 2 H), 7.23 (d, J = 8.3 Hz, 6 H), 8.00 (d, J = 8.3 Hz, 6 H) ppm. ^{13}C NMR (62.90 MHz, $CDCl_3$, 25 °C): δ = 13.0 [CH_3, 3 C, NCH_2(*C*H_3)], 19.5 [CH_3, 3 C, –CH(*C*H_3)–N–], 21.5 (CH_3, 3 C, *C*H_3 arom.), 49.8 (CH_2, 6 C, N*C*H_2Me), 53.1 [CH, 3 C, NCH_2*C*H(CH_3)–], 60.7 [CH_2, 3 C, N*C*H_2CH(CH_3)], 127.7 (CH, 3 C, CH arom.), 129.1 (CH, 3 C, CH arom.), 141.1 (C_q, 3 C, CH arom.), 142.2 (C_q, 3 C, CH arom.) ppm.

Complex (*S*,*S*,*S*)-5c: Ligand (*S*,*S*,*S*)-**1c** (18.1 mg) gave the complex immediately with a 100% conversion; the solution turned dark brown. ^{1}H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = 0.93 (d, J = 7.2 Hz, 9 H), 1.03 (d, J = 7.2 Hz, 9 H), 1.14 (t, J = 7.2 Hz, 6 H), 2.22–2.42 (m, 3 H), 2.62 (dd, J = 13.2 and 6.1 Hz, 3 H), 3.30 (dd, J = 13.2 and 12.1 Hz, 3 H), 4.05–4.22 (m, 3 H), 4.24 (dq, J = 14.8 and 7.2 Hz, 2 H), 4.80 (dq, J = 14.8 and 7.2 Hz, 2 H) ppm. ^{13}C NMR (62.90 MHz, $CDCl_3$, 25 °C): δ = 14.1 [CH_3, 3 C, NCH_2(*C*H_3)], 16.6 (CH_3, 9 C, CH*C*H_3), 20.2 (CH_3, 9 C, CH*C*H_3), 31.2 [CH, 3 C, –*C*H(CH_3)$_2$], 52.8 (CH_2, 6 C, N*C*H_2Me), 55.7 (CH, 3 C, –CH_2*C*H*i*Pr), 64.5 (CH, 3 C, –*C*H_2CH*i*Pr), 120.1 (C_q, J = 326.2 Hz, 3 C, *C*F_3) ppm. ^{19}F NMR (282.35 MHz, C_6D_6, 28 °C): δ = –72.53 ppm.

Complex (*R*,*R*,*R*)-5e: Ligand (*R*,*R*,*R*)-**1e** (19.9 mg) was used. After 6 d at room temperature followed by 6 h of heating at 60 °C, a dark-yellow solution was obtained, which according to ^{1}H NMR contained 90% of complex **5e**. ^{1}H NMR (250.18 MHz, $CDCl_3$, 25 °C): δ = 0.97 (d, J = 7.1 Hz, 9 H), 1.35 (t, J = 7.1 Hz, 6 H), 2.32 (s, 9 H), 2.71 (s, 18 H), 3.47 (dd, J = 12.5 and 10.9 Hz, 3 H), 3.38–3.63 (m, 2 H), 3.78–4.03 (m, 2 H), 4.38–4.55 (m, 3 H), 4.63 (dd, J = 12.8 and 4.8 Hz, 2 H), 7.00 (s, 6 H) ppm. ^{13}C NMR (62.90 MHz, $CDCl_3$, 25 °C): δ = 14.5 [CH_3, 3 C, N–CH_2(*C*H_3)], 18.4 [CH_3, 3 C, –CH(*C*H_3)–N–], 21.1 (CH_3, 3 C, *p*-*C*H_3), 23.9 (CH_3, 6 C, *o*,*o*-*C*H_3), 43.6 (CH_2, 6 C, N*C*H_2Me), 57.5 (CH, 3 C, CH_2*C*HMeN), 61.3 (CH_2, 3 C, N*C*H_2CHMe-), 132.6 (CH, 6 C, *C*H arom.), 132.9 (C_q, 3 C, CH*C*MeCH arom.), 140.9 (C_q, 6 C, -SO_2C*C*MeCH-arom.), 145.3 (C_q, 3 C, SO_2*C* arom.) ppm.

Complex (*S*,*S*,*S*)-5a: Ligand (*S*,*S*,*S*)-**1a** (1.048 g, 1.62 mmol) was placed in a 100-mL Schlenk-tube. Dry toluene (50 mL) was added and the mixture was stirred until the ligand was completely dissolved upon gently heating. Tetrakis(diethylamino)titanium (0.600 mL, 1.60 mmol) was then added while stirring under nitrogen. The reaction mixture turned from colourless to brown and it was refluxed for 4 h. The solvent was then evaporated under vacuum and the resulting brown powder was washed with dry pentane (2 × 20 mL). Pure **5a** (1.221 g, 1.59 mmol, 98% yield) was obtained as a brown powder. ^{1}H and ^{13}C NMR as reported above. $C_{34}H_{49}N_5O_6S_3Ti$ (768): calcd. C 53.18, H 6.43, N 9.12; found C 52.99, H 6.15, N 9.01.

Complex (*S*,*S*,*S*)-6a: Ligand (*S*,*S*,*S*)-**2a** (0.300 g; 1.29 mmol) was added with a syringe to a Schlenk flask followed by pentane (19 mL). The flask was cooled to –50 °C and *n*BuLi (2.5 M in hexanes, 1.51 mL, 3.78 mmol) was added dropwise during 15 min. The temperature was allowed to reach 0 °C during 30 min and the flask was then allowed to stand at room temperature for 2 h. The flask was cooled to –60 °C and [$TiCl_4$(THF)$_2$] (0.429 g, 1.26 mmol) was added under a stream of argon. The flask was slowly allowed to reach room temperature overnight and was then stirred for another 48 h. The flask was centrifuged and the dark-red solution was transferred with a transfer needle to a Schlenk flask. Most of the pentane was removed in vacuo and a crystalline material formed at –30 °C after a few days (0.227 g, 57% yield). ^{1}H NMR

(200.13 MHz, C_6D_6, 25 °C): δ = 0.80 (d, J = 6.0 Hz, 9 H), 2.16 (dd, J = 11.7 and 5.1 Hz, 3 H), 2.62 (dd, J = 11.6 and 11.6 Hz, 3 H), 3.20 (m, 3 H), 3.38 (s, 9 H) ppm. ^{13}C NMR (50.32 MHz, C_6D_6, 25 °C): δ = 19.1 (CH_3, 3 C, CH*C*H$_3$), 43.6 (CH_3, 3 C, NCH_3), 60.6 (CH, 3 C, –CH_2*C*H–Me), 62.4 (CH_2, 3 C, –*C*H$_2$CHMe) ppm. $C_{12}H_{27}ClN_4Ti$ (310): calcd. C 46.39, H 8.76, N 18.03; found C 46.25, H 8.79, N 17.99.

Complex (*S*,*S*,*S*)-6b: The complex with ligand (*S*,*S*,*S*)-**2b** (0.395 g; 1.26 mmol) was prepared in an identical manner in 64% yield (0.318 g). ^{1}H NMR (200.13 MHz, C_6D_6, 25 °C): δ = 0.67 (d, J = 7.0 Hz, 9 H), 0.79 (d, J = 8.5 Hz, 9 H), 1.73 (m, 3 H), 2.13 (dd, J = 11.7 and 5.6 Hz, 3 H), 2.84 (dd, J = 10.5 and 10.5 Hz, 3 H), 3.12 (m, 3 H), 3.28 (s, 9 H) ppm. ^{13}C NMR (50.32 MHz, C_6D_6, 25 °C): δ = 14.2 (CH_3, 3 C, CH*C*H$_3$), 18.3 (CH_3, 3 C, CH*C*H$_3$), 26.6 [CH, 3 C, C*H*(CH_3)$_2$], 43.0 (CH_3, 3 C, NCH_3), 53.6 (CH, 3 C, –CH_2*C*H*i*Pr), 71.7 (CH_2, 3 C, –*C*H$_2$CH*i*Pr) ppm. $C_{18}H_{39}ClN_4Ti$ (395): calcd. C 46.39, H 8.76, N 18.03; found C 46.21, H 8.73, N 17.98.

X-ray Diffraction

(*R*,*R*,*R*)-3e: Crystallized from chloroform/hexane by vapour diffusion. Diffraction data were measured at the Istituto di Chimica Biomolecolare of CNR (Padova), with a Philips PW1100 diffractometer by using graphite-monochromated Cu-K_α radiation (λ = 1.54178 Å) at 293(2) K in the θ–2θ scan mode up to θ = 60°. Formula: $C_{36}H_{54}N_4O_6S_3$. Monoclinic, space group $P2_1$. Unit cell parameters: a = 8.496(2), b = 16.355(3), c = 14.374(3) Å, β = 98.33(4)°. V = 1976.2(3) Å^3. Z = 2. $D_{calcd.}$ = 1.235 g cm^{-3}. μ = 2.095 mm^{-1}. 3176 Collected reflections, 3053 of which were independent (R_{int} = 0.029). The structure was solved by direct methods of the SHELXS 97 program[56] and refined by full-matrix block least-squares on F^2, using all data, with the SHELXL 97 program.[57] A planarity restraint was applied to each of the three phenyl rings. Hydrogen atoms were calculated at idealised positions and refined as riding. Data/restraints/parameters: 3053/10/455. Final R indices: R_1 = 0.038 and wR_2 = 0.097 [$I > 2\sigma(I)$]; R_1 = 0.039 and wR_2 = 0.101 (all data). Goodness of fit (on F^2): 1.063. Max. and min. residual in the final ΔF map: +0.182 and –0.223 e Å^{-3}.

(*S*,*S*,*S*)-5a: Crystals of **5a** were grown by layering a concentrated solution of the pure compound in dichloromethane with diethyl ether, and allowing slow diffusion at room temperature. Diffraction data were collected at the Laboratoire de Chimie Organométallique et de Catalyse (Institut Le Bel, Université Louis Pasteur, Strasbourg) using a Nonius–Kappa CCD diffractometer equipped with a molybdenum source [λ(Mo-K_α) = 0.71073 Å] at 174 K. Formula: $C_{30}H_{39}AlN_4O_6S_3{\cdot}CH_2Cl_2$. Orthorhombic, space group $P2_12_12_1$. Unit cell parameters: a = 7.6495(1), b = 21.4914(3), c = 22.3149(4) Å. V = 3668.5(1) Å^3. Z = 4. $D_{calcd.}$ = 1.380 g cm^{-3}. μ = 0.418 mm^{-1}. 10747 Collected reflections, 6021 of which were independent (R_{int} = 0.06). The Nonius OpenMoleN software package was used for all calculations.[58] The refinement was carried out by least-squares methods against F^2. The hydrogen atoms were included at calculated positions with fixed thermal parameters. Data/restraints/parameters: 3641/0/424. Final R indices: R_1 = 0.051 and wR_2 = 0.071 [$I > 2\sigma(I)$]. Goodness of fit (on F^2): 1.292. Max. and min. residual in the final ΔF map: +0.679 and –0.161 e·Å^{-3}.

CCDC-277426 and -278811 contain the supplementary crystallographic data for (*R*,*R*,*R*)-**3e** and (*S*,*S*,*S*)-**5a**, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): 2D NMR spectra of complex **5a** (NOESY) and **5e** (TOCSY and NOESY).

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