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ARTICLE

Observed hydrolysis of fluorine substituted bis(β -diketonato)-dichlorotitanium(IV) complexes

ite this: DOI: 10.1039/x0xx00000x

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Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Novel fluorine substituted mononuclear $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes have been synthesised and shown to be involved in a partial hydrolysis reaction in solution, in which the hydrolyzed dinuclear $\{\text{Ti}(\beta\text{-diketonato})_2\text{Cl}\}_2(\mu\text{-O})$ is in equilibrium with the monomer. This is in contrast to the solution behaviour of the more electron rich $\text{Ti}(\text{CH}_3\text{COCHCOCH}_3)_2\text{Cl}_2$, $\text{Ti}(\text{PhCOCHCOCH}_3)_2\text{Cl}_2$ and $\text{Ti}(\text{PhCOCHCOPh})_2\text{Cl}_2$ complexes, under the same conditions. Variable temperature (^1H and ^{19}F) NMR spectra and X-ray structure analyses reveal that the partially hydrolyzed dinuclear complex exists both in solution and in solid state, bridging through a single μ -oxo bridge and having one labile chloro-ligand per titanium center. Inclusion of electron-withdrawing CF_3 groups into the already electron-deficient Ti complexes, led to the formation of $\{\text{Ti}(\text{CF}_3\text{COCHCOCF}_3)_2\text{Cl}\}_2(\mu\text{-O})$ (dinuclear) and $[\text{Ti}(\text{CF}_3\text{COCHCOCF}_3)_2(\mu\text{-O})]_4$ (tetranuclear) complexes in CDCl_3 with trace amounts of water. DFT calculated free energies of hydrolysis support the existence of $\text{Ti}(\text{CH}_3\text{COCHCOCH}_3)_2\text{Cl}_2$ as a monomer while the electron-poor $\text{Ti}(\text{CF}_3\text{COCHCOCF}_3)_2\text{Cl}_2$ exists as an equilibrium reaction between the monomer and partially hydrolyzed dinuclear complex in solution.

Introduction

Titanium(IV) complexes have attracted wide attention, due to their application as catalysts in different organic reactions,¹ as well as their encouraging anticancer activity in various cell lines.² Currently, cytotoxic titanium complexes are divided into three classes, *viz.* titanocene dichloride (CpTiCl_2) derivatives,³ bis(β -diketonato)-complexes such as budotitane⁴ and diamino-bis(phenolato) “salan” complexes.⁵ The mechanism of bioactivity and the nature of the active species for cytotoxic titanium complexes are not well understood, and more detailed studies are required in order to establish whether partial hydrolysis of the labile ligands is an activating mechanism, as has been found for cisplatin, or a deactivating mechanism, leading to the formation of non-toxic polynuclear oxo-titanium species.⁶ Recently, a partially hydrolyzed, dinuclear intermediate of a titanium salan complex, was reported to be highly cytotoxic, surpassing its monomeric predecessors.⁶ Hence the nature of hydrolysis and solution behaviour of this case study is of fundamental importance.

The bis(β -diketonato)titanium(IV) complexes are a well documented class of compounds; they have an octahedral structure and can adopt more than one isomeric form; see Figure 1. However, all known dichloro bis(β -diketonato) Ti(IV) complexes exist in solution exclusively as a mixture of the monomeric *cis* geometrical configurations, with Cl in the *cis* position.^{7,8,9,10} This orientation allows for the bidentate β -diketonato ligand to enhance the stability of the electron-

deficient *cis*- $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complex through ligand \rightarrow metal π -electron donation. Each β -diketonato ligand has one π -donor orbital on an O-atom, which interacts with the empty Ti d_{z^2} -type orbital, to form this π -electron bonding.^{11,12} According to the NMR data and Computational chemistry results (force field and density functional theory (DFT) calculations), configurations with the Cl ligands in the *trans* position are unlikely.^{13,14,15} The diiodo complex $\text{Ti}(\text{acac})_2\text{I}_2$, is the only known bis(β -diketonato) titanium(IV) complex which shows evidence of the *trans* configuration, occurring as an equilibrium mixture of rapidly isomerising *cis* and *trans* isomers.⁸ At room temperature, the complexes are fluxional, exchanging axial and equatorial substituents on the diketonato ligands *via* an intramolecular trigonal twist mechanism.^{11,13,16} Identification of the *cis*-isomers and fluxional behavior, have been established by variable temperature NMR.

In this study, we have investigated the effect of introducing electron-withdrawing fluorine substituents onto the β -diketonato ligands of the already electron-deficient (12 electron mononuclear) $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes, thus further decreasing the electron density on the titanium centre. The introduction of fluorine substituents onto the β -diketonato ligands, produced large changes in the properties of the resulting β -diketonates, compared to non-fluorinated analogues.¹⁷ Hence we compare the solution behaviour and partial hydrolysis of fluorinated $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes, as compared to non-fluorinated analogues.

Results and discussion

Synthesis

The series of four novel bis(β -diketonato)dichloro titanium(IV) complexes, all containing β -diketonato ligands with a CF_3 group, $(\text{CF}_3\text{COCHCOR})^-$ where $\text{R} = \text{CF}_3$ (hfaa) [1], CH_3 (tfaa) [2], C_4H_9 (tffa) [3] or $\text{C}_4\text{H}_3\text{O}$ (tffu) [4], were synthesised from the appropriate β -diketonate and TiCl_4 in chloroform, under an inert atmosphere. Selected data for $\text{Ti}(\text{acac})_2\text{Cl}_2$, $\text{Ti}(\text{ba})_2\text{Cl}_2$ and $\text{Ti}(\text{dbm})_2\text{Cl}_2$ ($\text{acac} = (\text{CH}_3\text{COCHCOCH}_3)^-$, $\text{ba} = (\text{CH}_3\text{COCHCO}_2\text{C}_6\text{H}_5)^-$ and $\text{dbm} = (\text{C}_5\text{H}_6\text{COCHCO}_2\text{C}_6\text{H}_5)^-$), originally synthesized by Fay *et al.*,^{9,10} will also be presented for comparative reasons.

All $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes were stored under an argon atmosphere since they are highly susceptible to hydrolysis. The fluorinated $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes are considerably less stable with respect to hydrolysis than the non fluorinated $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ when tested under the same conditions as Keppler and Heim on $\text{Ti}(\text{ba})_2\text{Cl}_2$ (determined by the time till development of turbidity of the complex when dissolved in 0.01% water/ CH_3CN , as a result of the precipitation on TiO_2).^{18,19,20} The non fluorinated $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ were stable to atmospheric moisture while the fluorinated monomeric $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes when exposed to moisture, decompose rapidly to titanium dioxide (TiO_2).

While the proton spectra of $\text{Ti}(\text{acac})_2\text{Cl}_2$, $\text{Ti}(\text{ba})_2\text{Cl}_2$ and $\text{Ti}(\text{dbm})_2\text{Cl}_2$ reveal the expected single methine (ring H) resonance (and corresponding peaks for the R groups) at room temperature,^{9,10,19} all the CF_3 - β -diketonato analogues presented here, show two resonances in the methine region (and two sets of corresponding peaks for the R groups) indicating that two NMR distinguishable complexes (we will refer to them as **A** and **B**) are present. The new fluorinated $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes of this study, appear to behave in a strikingly different manner under the same conditions.

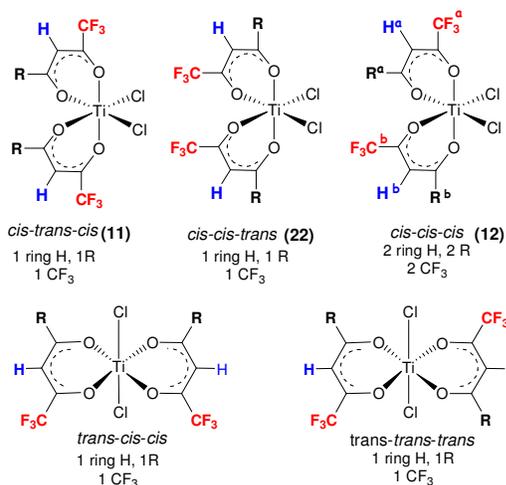


Figure 1. The five possible geometric-isomers of octahedral $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes due to the unsymmetrical β -diketonates (with one CF_3 group) and expected number of ^1H and ^{19}F NMR signals are shown. For symmetrical β -diketonates, when $\text{R} = \text{CF}_3$, only one *cis* (1 ring H and 2 CF_3 NMR signals) and one *trans* (1 ring H and 1 CF_3 NMR signals) isomers are possible.²¹

The ^1H NMR measurement for the four fluorinated bis(β -diketonato)dichloro titanium(IV) complexes [1] - [4] show downfield shifts of *ca.* 0.4 and 0.25 ppm for **A** and **B**, respectively, for the methine proton of the metal chelate ring, relative to the uncoordinated β -diketonate. The downfield shifts of ~ 0.4 ppm for resonance **A** is comparable to those found in $\text{Ti}(\text{acac})_2\text{Cl}_2$, $\text{Ti}(\text{ba})_2\text{Cl}_2$ and $\text{Ti}(\text{dbm})_2\text{Cl}_2$ relative to the uncoordinated β -diketonate, see **Table S1** in the Supplementary Information. Since it has been shown that the complexes, $\text{Ti}(\beta)_2\text{Cl}_2$ with $\beta = \text{acac}$, ba and dbm , are in the *cis*-conformation,^{8,13,14} peak **A** is assigned to the signal for the *cis*-geometric isomers. To obtain insight into the structure of **B**, the NMR tubes were sealed under Ar atmosphere in order for the complex to slowly crystallize.

Crystal structures

Single crystals were obtained from a solution of $\text{Ti}(\text{hfaa})_2\text{Cl}_2/\text{CDCl}_3$ in sealed NMR tubes. Due to trace amounts of water in the deuterated chloroform, partially hydrolyzed dinuclear and tetranuclear titanium(IV) β -diketonate complexes were obtained from separate NMR tubes. Molecular diagrams indicating atom labelling of dinuclear, $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ and tetranuclear, $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ are shown in Figure 2 and Figure 3 respectively and the crystal and structure refinement data are given in Table S3 of the Supplementary Information.

$\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ crystallized in the tetragonal $I4_1/a$ ($Z = 8$) space group with molecules situated on inversion centres at the bridging O atoms. The metal coordination environment is distorted due to chelation of the β -diketonato ligands (averaged O-Ti-O angles is $82.92(16)^\circ$). The larger Cl ligand forces all Cl-Ti-O larger than 90° as expected. The Ti-O bond distances are unequal, primarily to the electronically different *trans* donor atoms. The largest Ti-O distances are found for the bonds *trans* to the bridging O, as well as those *trans* to the Cl atom (averaged at $2.0737(15)$ Å), whereas the *trans* O-Ti-O averaged at $1.9656(14)$ Å. The β -diketonato ligands are slightly bend out of their respective coordination planes (ranging from $6.91(9)^\circ$ and $9.91(9)^\circ$ for hfaa with donor atoms O1/O2 and O3/O4 respectively). Packing in the crystal is primarily instigated by weak $\text{C-H}\cdots\text{Cl}$ and $\text{F}\cdots\text{F}$ contacts, listed in Table S4.

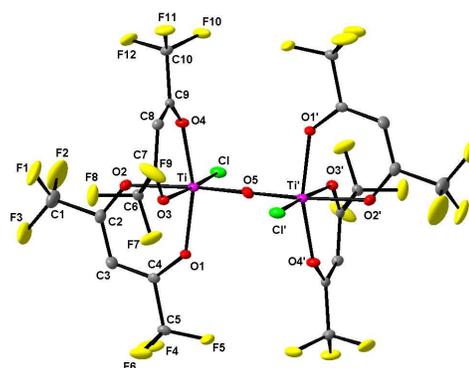


Figure 2. Molecular diagram of $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ with thermal ellipsoids drawn at a 30% probability level. Accented lettering indicate atoms generated by symmetry ($1-x, -y, -z$)

Molecules of $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ crystallized in the monoclinic $P 2_1/c$ ($Z = 4$) space group on general positions with each of the Ti metal centres showing distortion from the ideal octahedral environment, see Figure 3. These distortions can be ascribed to the strain caused by the chelation of the hfaa ligands as well as the bridging sp^3 O atoms to form the tetranuclear complex. The distortion of the Ti coordination environments can be quantified from the O–Ti–O angles for the chelating hfaa ligands varying from $81.82(6)^\circ$ to $83.25(6)^\circ$, and the O–Ti–O for the bridged O atoms forming the tetranuclear complex varying from $99.82(7)^\circ$ to $102.35(7)^\circ$. The square formed by the Ti and O atoms also severely distorted/twisted (See Figure 4 of backbone) with opposing Ti–O–Ti angles for O1 and O3 averaging $172.71(10)^\circ$ whereas O2 and O4 are substantially smaller at $157.88(9)^\circ$. The β -diketonato ligands are also not planar to their respective coordination planes (ranging from $1.41(10)^\circ$ up to $26.46(7)^\circ$). In addition to the above distortion in angles, there are also large deviations observed for the Ti–O bond distances. These deviations, which are probably due to the *trans* effect from electronically differ O-donor atoms, can be organised as follow: a) bridging O–Ti–O distances average at 1.7970 (15) Å, b) Ti–O bond *trans* to the bridging O atoms average at 2.1016 (14) Å, and c) axial Ti–O distances average at 1.9828 (15) Å. Despite the numerous aromatic β -diketonato backbones in the structure the only possible π - π stacking in the crystal packing arrangement have slippage values of >3 Å. Packing in the crystal primarily governed by $\text{H}\cdots\text{F}$ interactions listed in Table S4.

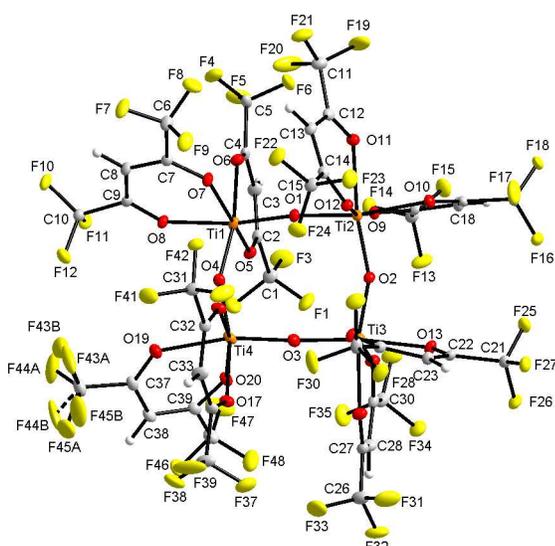


Figure 3. Molecular diagram of $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ with thermal ellipsoids drawn at a 30% probability level.

Both $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ and $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ were stable to atmospheric moisture and poorly soluble in CHCl_3 . It was possible to dissolve crystals of $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ in heated CDCl_3 . Once dissolved in CDCl_3 , the ^1H NMR spectra (Figure 5 (b)), revealed two main peaks which matched the peaks of **A** and **B** in the spectra of $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ (Figure 5 (c)). This observation is most easily interpreted in terms of the hydrolysis and equilibrium reactions given in Figure 6, in which mononuclear $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ and dinuclear $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ are involved in an equilibrium hydrolysis reaction. Due to trace amounts of acid and water in the CDCl_3 , this reaction is possible. The reaction between **A** and **B** would imply the

breaking and forming of Ti–O and Ti–Cl bonds. This is conceivable, since the strength of the Ti–O and Ti–Cl bonds are very similar, i.e., 478 and 494 kJ mol^{-1} , respectively.^{22,23} The ^1H NMR spectra of the tetranuclear $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ showed only one methine peak (Figure 5 (a)). The latter peak was not observed on the NMR of $\text{Ti}(\text{hfaa})_2\text{Cl}_2$, or $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$.

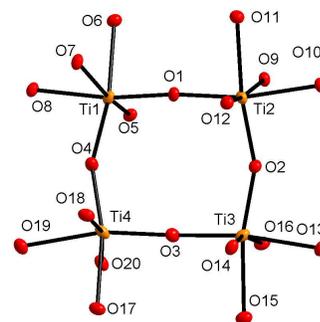


Figure 4. Molecular diagram of $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ showing the deformed Ti octahedral coordination environments.

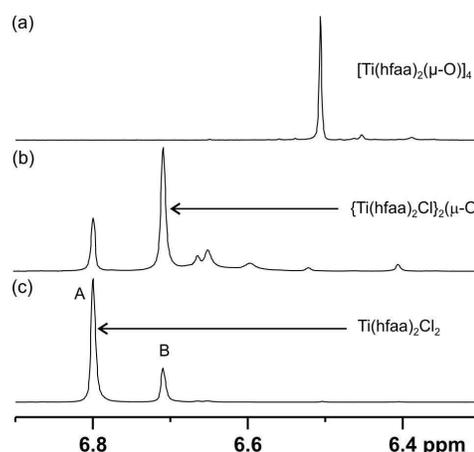


Figure 5. ^1H NMR spectra in CDCl_3 of (a) tetranuclear $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ at 50°C , (b) dinuclear $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ at 50°C and (c) $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ (reaction of Figure 6) at RT. In (b) the equilibrium hydrolysis reaction shown in Figure 6 is re-instated in solution.

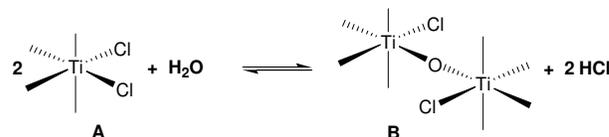


Figure 6. Proposed reaction between mononuclear $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ (**A**) and dinuclear $\{\text{Ti}(\beta\text{-diketonato})_2\text{Cl}\}_2(\mu\text{-O})$ (**B**) in CDCl_3 containing trace amounts of water and acid. The β -diketonato ligands have been omitted for clarity.

NMR temperature study

To exclude the possibility that **B**, observed on NMR, is the *trans*-isomer of $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ (Figure 1), variable temperature NMR was employed. The room temperature spectra are time averaged spectra and do not reveal the stereochemistry and true nature of complexes **A** and **B**.

^1H and ^{19}F NMR spectra of $\text{Ti}(\text{hfaa})_2\text{Cl}_2$, in the temperature range of RT to $-50\text{ }^\circ\text{C}$, are shown in Figure 7, where the two observed complexes are marked **A** and **B**. Since the complex contains a symmetric β -diketonato ligand, only one *cis*-monomer, one *trans*-monomer and one hydrolyzed $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ structure are possible. For the ^1H spectra, two methine peaks (**A** and **B**) are observed at room temperature. As the temperature is lowered to $-50\text{ }^\circ\text{C}$, resonance **A**, remains a singlet but resonance **B** splits into two peaks. The initially large broad peak observed in the ^{19}F spectra, splits with temperature lowering; the CF_3 peaks for **A** splits into two equally intense lines while for **B**, it splits into four peaks. This low-temperature one-line methine (ring H) and two-line CF_3 spectra of structure **A** is consistent with complex **A** having the *cis* conformation in solution. For complex **B**, the low-temperature two-line methine (ring H) and four-line CF_3 spectra does not support complex **B** being the *trans*-monomer, because one expects the methine- and the CF_3 -resonances, to remain single peaks due to the high symmetry of the *trans*-isomer. However it is evidence for complex **B** having an O-bridged dinuclear structure, $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$, as indicated in Figure 7, also supported by the solid state crystal structure presented in this study, see Figure 2.

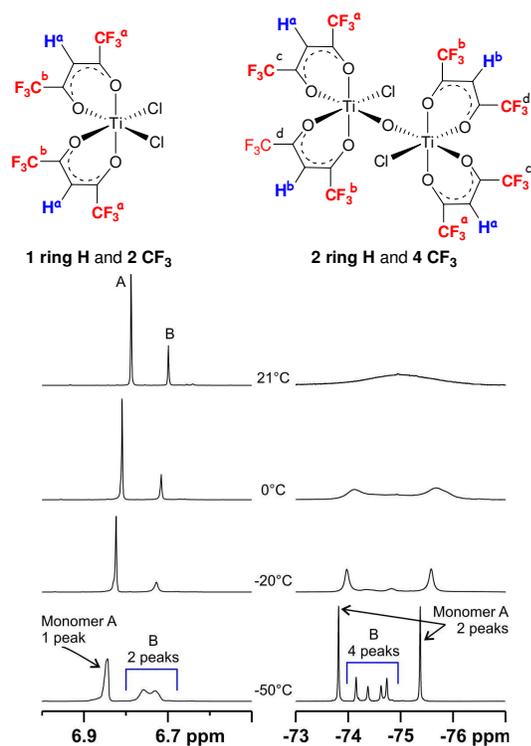


Figure 7. Variable temperature NMR spectra (CDCl_3) of $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ in the methine (ring H) region for ^1H NMR spectra and the CF_3 region for ^{19}F NMR spectra. Temperature range: $21\text{ }^\circ\text{C}$ to $-50\text{ }^\circ\text{C}$. At the top the structures of monomeric *cis*- $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ and partially hydrolyzed dinuclear $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ are shown with expected ^1H and ^{19}F NMR signals.

The remaining complexes, [2], [3] and [4], all have asymmetric β -diketonato ligands which leads to more complicated NMR spectra since the possible number of isomers increase for both the monomer **A** (three *cis*-isomers, with 4 ring H and 4 CF_3 NMR signals, or two *trans*-isomers, with 2 ring H and 2 CF_3

NMR signals see Figure 1) and hydrolyzed dinuclear **B** (ten isomers, with 36 ring H and 36 CF_3 NMR signals).

The three fluorinated $\text{Ti}(\beta)_2\text{Cl}_2$ complexes with asymmetric β -diketonato ligands, show the same NMR pattern as indicated for $\text{Ti}(\text{tfaa})_2\text{Cl}_2$ in Figure 8. For the ^1H spectra at room temperature, two methine peaks (**A** and **B**) are observed with corresponding R-group resonances in the correct ratio (not shown in Figure 8). With decreasing temperature, the peaks first broaden and then fine structure appears. The line broadening is due to the slowing down of the rapid isomerisation process which exchanges R groups of the β -diketonato ligand between the non-equivalent environments. Below a certain temperature, known as the coalescence temperature, the exchange process slows down sufficiently so that separate signals for the individual isomers are detected. Upon temperature lowering, the resonance of complex **A** split into the four expected peaks for the three *cis* isomers, while the resonance of complex **B**, transforms into a multitude of peaks. In the ^{19}F spectra, the large broad peak at RT for **A**, splits into four relatively equal intense lines at low temperature, while for **B**, it splits again into multiple CF_3 peaks. This low-temperature four-line methine (ring H) and four-line CF_3 spectra of structure **A** supports the *cis* configuration of **A** in solution. The spectra of **B** with the methine (ring H) and CF_3 peaks of **B** splitting into multiple peaks is consistent with a dinuclear structure of formulation $\{\text{Ti}(\beta\text{-diketonato})_2\text{Cl}\}_2(\mu\text{-O})$ but does not support the *trans*-isomer.

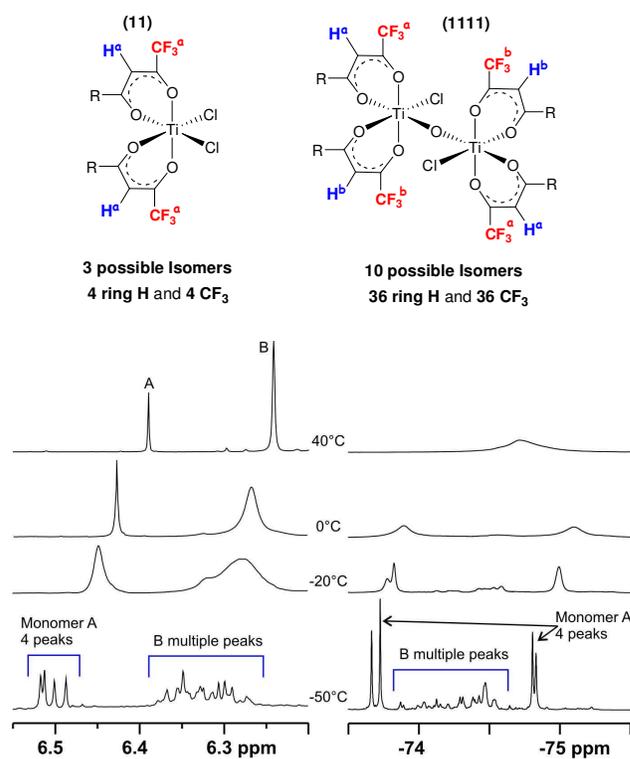


Figure 8. Variable temperature NMR spectra (CDCl_3) of $\text{Ti}(\text{tfaa})_2\text{Cl}_2$ in the methine region for ^1H NMR spectra and the CF_3 region for ^{19}F NMR spectra. Temperature range: $40\text{ }^\circ\text{C}$ to $-50\text{ }^\circ\text{C}$. At the top the structures of monomeric *cis*- $\text{Ti}(\text{tfaa})_2\text{Cl}_2$ and partially hydrolyzed dinuclear $\{\text{Ti}(\text{tfaa})_2\text{Cl}\}_2(\mu\text{-O})$ are shown, with expected ^1H and ^{19}F NMR signals.

The number of isomers, depending on the symmetry of the β -diketonato ligand, was confirmed for **A**, monomeric *cis*-Ti(β -diketonato)₂Cl₂, *i.e.* one *cis*-isomer for symmetric β -diketonato ligands and three *cis*- isomers for asymmetric β -diketonato ligands. However, it was not possible to confirm the number of dinuclear isomers present in solution from the NMR spectra as there were many overlapping peaks and only 16 to 20 peaks could be identified unambiguously. If all 10 isomers were present in solution, a maximum of 36 methine (ring H) and CF₃ peaks respectively, would be expected. The geometries of the possible 10 isomers of {Ti(tfaa)₂Cl}₂(μ -O) were optimized by OLYP/TZP DFT calculations (see Table S5[†]). The isomer distribution for the 10 isomers as calculated with the Boltzmann distribution from the energies of the 10 isomers, showed that 5 of the 10 isomers represent more than 76 % of the population, implying that the observed NMR shifts represents mainly 5 isomers.

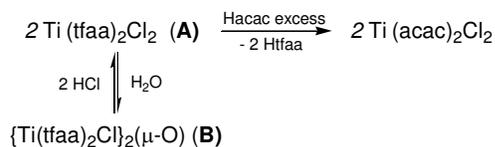
¹H NMR Solution Studies

To more fully characterise the relationship between monomer **A** and partially hydrolyzed dinuclear **B** and determine whether a dynamic equilibrium between **A** and **B** exists (depicted in Figure 6), the following experiments were conducted using ¹H NMR Spectroscopy.

When investigating the effect of temperature (between 21°C – 60 °C) on Ti(tfaa)₂Cl₂ in CDCl₃, it was found that the ratio [B]/[A] (determined by the ratio of peak integrals of the non-overlapping corresponding methine signals of the β -diketonato ligand in Ti(tfaa)₂Cl₂ of **A** and **B**), increased with increasing temperature (1.65 at 60°C) and reverted to the initial value at room temperature (1.05 at 21°C). This temperature-dependence supports the **A**-**B** equilibrium as proposed in Figure 6.

When varying the concentration of the solution one expects the [B]/[A] ratio to be affected such that in a concentrated solution, hydrolyzed dinuclear **B** predominates while in a dilute solution monomer **A** predominates (according to Figure 6). However the opposite occurred, *i.e.*, it was found that the higher the concentration, the smaller the [B]/[A] ratio. This observation is interpreted in terms of the limiting effect of the traces amounts of water in the CDCl₃.

In order to shift the equilibrium shown in Figure 6, to the left, (and determine the effect on the amount of **B**), Ti(tfaa)₂Cl₂ of the **A**-**B** equilibrium was removed by adding excess Hacac to Ti(tfaa)₂Cl₂ converting it to Ti(acac)₂Cl₂ *via* β -diketonato exchange reaction. It was found that **B** disappeared.



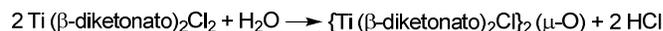
This is consistent with the existence of an equilibrium hydrolysis reaction between **A** and **B**; as monomeric **A**, Ti(tfaa)₂Cl₂, converts to Ti(acac)₂Cl₂, the dinuclear complex **B**, Ti(tfaa)₂Cl(μ -O), converts back to **A** (to re-instate the equilibrium reaction between **A** and **B**) until all **B** is converted

to **A** and all **A** is converted to Ti(acac)₂Cl₂, *via* the exchange reaction. Finally Ti(acac)₂Cl₂ is the final and only Ti product. It should be noted that Ti(acac)₂Cl₂ is not susceptible to hydrolysis in the presence of trace amounts of water. The ¹H NMR spectrum of the final product (excluding the excess Hacac and eliminated Htfaa) compared perfectly to the spectrum of a fresh sample of Ti(acac)₂Cl₂.

The ¹H NMR spectrum of solid state hydrolyzed dinuclear {Ti(hfaa)₂Cl}₂(μ -O) dissolved in fresh CDCl₃ (see Figure 5b) revealed two peaks that correspond to monomeric Ti(hfaa)₂Cl₂ (**A**) and dinuclear (**B**) and unknown decomposition peaks. This evidence supports that **B** is in equilibrium with **A**, since after {Ti(hfaa)₂Cl}₂(μ -O) is dissolved in chloroform (containing trace amounts of acid), the equilibrium between dinuclear {Ti(hfaa)₂Cl}₂(μ -O) and monomer Ti(hfaa)₂Cl₂ is re-instated. This evidence also supports the notion that the **B** in solution is the same as the solid state dinuclear {Ti(hfaa)₂Cl}₂(μ -O), since it explains why complexes **A** and **B** are present in the ¹H NMR spectrum of the dissolved {Ti(hfaa)₂Cl}₂(μ -O) crystals. The accompanied decomposition peaks are expected, since the crystals were crushed in the open atmosphere.

DFT calculated reaction free energy

In order to further evaluate why fluorinated *cis*-Ti(β -diketonato)₂Cl₂ complexes exist in equilibrium with dinuclear {Ti(β -diketonato)₂Cl}₂(μ -O), while complexes where the β -diketonato ligand does not contain a CF₃ group, do not form partially hydrolyzed dinuclear complexes in solution, a DFT computational chemistry study is done. The OLYP/TZP free energy G of the different reactants and products of the proposed partial hydrolyzed dimerization reaction was calculated in chloroform solution.



For β -diketonato = acac = (CH₃COCHCOCH₃)⁻, the reaction free energy, $\Delta G_{\text{reaction}} = G_{\text{products}} - G_{\text{reactants}}$, = 0.56 eV. $\Delta G > 0$ indicates a non-spontaneous reaction and Ti(acac)Cl₂ is not expected to hydrolyze in solution.

For β -diketonato = hfaa = (CF₃COCHCOCF₃)⁻, the reaction free energy, $\Delta G_{\text{reaction}} = G_{\text{products}} - G_{\text{reactants}}$, = -0.06 eV. $\Delta G \approx 0$ indicates an equilibrium reaction, thus both the monomer and the hydrolyzed dinuclear complex are expected in CDCl₃ solution.

To understand why the tetranuclear [Ti(hfaa)₂(μ -O)]₄ is not involved in a monomer-tetranuclear complex reaction in solution, the DFT reaction free energy, $\Delta G_{\text{reaction}}$, is calculated in chloroform solution for the proposed partial hydrolyzed tetranuclear reaction:



For β -diketonato = acac, $\Delta G = 2.10$ eV. $\Delta G > 0$ indicates a non-spontaneous reaction and Ti(acac)Cl₂ is not expected to form a tetranuclear complex in solution.

For β -diketonato = hfaa, $\Delta G = -0.49$ eV. $\Delta G < 0$ indicates a spontaneous reaction, in which the reaction should go to completion. No equilibrium is expected.

From the above free energy calculations it is clear that in the case of $\text{Ti}(\text{acac})_2\text{Cl}_2$ no spontaneous hydrolysis reaction forming dinuclear or tetranuclear complexes in CDCl_3 is expected, in agreement with only the monomer observed on NMR. For fluorinated $\text{Ti}(\text{hfaa})_2\text{Cl}_2$, an equilibrium hydrolysis reaction between monomer and partially hydrolyzed dinuclear $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ is expected in solution, but once the hydrolyzed tetranuclear $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ has formed, no monomer or hydrolyzed dinuclear complex is expected, as observed on NMR. It seems the formation of the dinuclear versus tetranuclear complex is dependent on the amount of water present in solution; in the presence of trace amounts of water (0.01 % in CDCl_3), the partially hydrolyzed dinuclear complex forms (in equilibrium with the monomer) while in solution with increased water content (possibly due to contamination with atmospheric moisture) hydrolysis results in the tetranuclear complex.

Conclusions

Herein we report the synthesis of electron-poor fluorine substituted bis(β -diketonato)dichloro titanium(IV) complexes. NMR, DFT and crystal structure results are in agreement that these CF_3 -substituted complexes exist in CDCl_3 solution as an equilibrium between monomeric *cis*- $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ and a hydrolyzed dinuclear $\{\text{Ti}(\beta\text{-diketonato})_2\text{Cl}\}_2(\mu\text{-O})$ complex. We have shown that incorporation of electron-withdrawing CF_3 groups into the bis(β -diketonato)titanium(IV) system significantly alters the solution behavior. The partial hydrolysis afforded $\mu\text{-oxo}$ bridged dinuclear $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ and tetranuclear $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ complexes in the solid state.

Experimental

Materials and methods

^1H and ^{19}F NMR spectra were recorded on either a Bruker Avance DPX 300 [^1H (300.130 MHz)] or a Bruker Avance II 600 [^1H (600.130 MHz) and ^{19}F (564,686 MHz)] spectrometer in CDCl_3 (Sigma Aldrich, CAS Number 865-49-6, 0.01 % water) dried with activated basic alumina. Chemical shifts are reported as δ values, referenced to SiMe_4 (0.00 ppm) for the ^1H spectra and CFCl_3 (0.00 ppm) for the ^{19}F spectra. Abbreviations used br = broad, Th = $\text{C}_4\text{H}_3\text{S}$ and Fu = $\text{C}_4\text{H}_3\text{O}$. Melting points are uncorrected and were determined with a Reichert Thermopan microscope fitted with a Koffler hot stage (up to 200 °C). Reactants and solvents were obtained from Aldrich.

Synthetic procedures

Since the $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes are readily hydrolyzed, especially in solution, all syntheses, filtrations, crystallizations and storage of the compounds were conducted under anhydrous conditions in a dry Ar atmosphere. All solvents were dried using published methods²⁴ and distilled under N_2 immediately before use. The $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes were synthesized by adaption of published methods.^{9,10} The general procedure used is to add titanium tetrachloride, TiCl_4 , (0.2 ml / 1.0 mmol) in chloroform (0.8 ml) dropwise to a stirred solution of appropriate β -diketone (2.0 mmol) in chloroform (20 ml), resulting in an immediate colour. The reaction mixture was stirred and purged with a slow stream of Ar (to evolve the hydrogen chloride gas) for 20 min. The

solution was refluxed for ½ h (for liquid β -diketones: Hhfaa and Htfaa) and 2 h (for solid β -diketones: Htftth and Htffu). Dry hexane (10 - 20 ml) was added until the reaction mixture turned milky and then the mixture was allowed to precipitate slowly for 12 h at 4 °C. The product was obtained from the filtrate (i) in the case of (hfaa*, tfaa and tftth) and from the precipitate (ii) in the case of tffu.

(i) The solvent was removed from the filtrate by reduced pressure and (ii) the precipitate was filtered off (with a pump) and washed with hexane. Recrystallisation from DCM/*n*-hexane afforded pure product as a mixture of three *cis*-isomers.

*Note: $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ did not precipitate after 12 h but the filtrate was a mixture of products. Only after the crude mixture was allowed to stand for 10 days at 4 °C, was the pure product isolated from the filtrate as above.

In solution in CDCl_3 , a mixture of the monomeric $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complex and a dinuclear $\{\text{Ti}(\beta\text{-diketonato})_2\text{Cl}\}_2(\mu\text{-O})$ complex was observed.

$\text{Ti}(\text{hfaa})_2\text{Cl}_2$ [1] Bis(hexafluoroacetylacetonato-O,O') dichloro titanium(IV): Yield 40 % (0.200 g). M.p. > 200 °C. Colour: yellow. ^1H NMR (600 MHz, δ /ppm, CDCl_3): Monomer: 6.80 (s, 2H, 2x CH). Dimer: 6.70 (s, 2H, 2x CH). ^{19}F NMR (600 MHz, δ /ppm, CDCl_3): Monomer and dimer: -73.51 – -76.60 (br, 6H, 2x CF_3)

$\text{Ti}(\text{tfaa})_2\text{Cl}_2$ [2] Bis(trifluoroacetylacetonato-O,O') dichloro titanium(IV): Yield 60 % (0.250 g). M.p. > 200 °C. Colour: yellow. ^1H NMR (600 MHz, δ /ppm, CDCl_3): Monomer: 2.44 (s, 6H, 2x CH_3), 6.40 (s, 2H, 2x CH). Dimer: 2.36 (s, 6H, 2x CH_3), 6.24 (s, 2H, 2x CH). ^{19}F NMR (600 MHz, δ /ppm, CDCl_3): Monomer and dimer: -72.73 – -76.16 (br, 6H, 2x CF_3)

$\text{Ti}(\text{tftth})_2\text{Cl}_2$ [3] Bis(trifluorothenoylacetonato-O,O') dichloro titanium(IV): Yield 50 % (0.280 g). M.p. > 200 °C. Colour: red. ^1H NMR (300 MHz, δ /ppm, CDCl_3): Monomer: 6.82 (s, 2H, 2x CH), 7.29-7.35 (br, 2H, 2x 1H, ThH), 7.95-8.12 (br, 4H, 2x 2H, ThH). Dimer: 6.63 (s, 2H, 2x CH), 7.13-7.21 (br, 2H, 2x 1H, ThH), 7.75-8.05 (br, 4H, 2x 2H, ThH). ^{19}F NMR (600 MHz, δ /ppm, CDCl_3): Monomer and dimer: -72.78 – -75.72 (br, 6H, 2x CF_3)

$\text{Ti}(\text{tffu})_2\text{Cl}_2$ [4] Bis(trifluorofuroylacetonato-O,O') dichloro titanium(IV): Yield 50 % (0.260 g). M.p. > 200 °C. Colour: red. ^1H NMR (300 MHz, δ /ppm, CDCl_3): Monomer: 6.71-6.82 (br, 2H, FuH), 6.93 (s, 2H, 2x CH), 7.70-7.78 (br, 2H, 2x 1H, FuH), 7.82-7.90 (br, 2H, 2x 1H, FuH). Dimer: 6.61-6.70 (br, 2H, 2x 1H, FuH), 6.75 (s, 2H, 2x CH), 7.59-7.78 (br, 4H, 2x 2H, FuH). ^{19}F NMR (600 MHz, δ /ppm, CDCl_3): Monomer and dimer: -73.54 – -75.50 (br, 6H, 2x CF_3)

Crystallography.

Single crystals of dimer $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ and tetranuclear $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ formed from a sealed CDCl_3 solution of the monomeric $\text{Ti}(\text{hfaa})_2\text{Cl}_2$ complexes at room temperature. The crystals of $\{\text{Ti}(\text{hfaa})_2\text{Cl}\}_2(\mu\text{-O})$ and $[\text{Ti}(\text{hfaa})_2(\mu\text{-O})]_4$ were mounted on glass fibers and used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker X8 Apex II 4K CCD diffractometer area detector system equipped with a graphite monochromator and Mo K_α fine-focus sealed tube ($\lambda = 0.71073 \text{ \AA}$) operated at 1.5 KW power (50 KV, 30 mA). The detector was placed at a distance of 3.75 cm from the crystal. Crystal temperature during the data collection was kept constant at 100(2) K using an Oxford 700 series

cryostream cooler. See Electronic Supplementary Information for more detail.†

Computational methods

Density functional theory (DFT) calculations were carried out using the ADF (Amsterdam Density Functional) 2012 programme²⁵ with the OLYP (Handy-Cohen²⁶ and Lee-Yang-Parr²⁷) GGA (Generalized Gradient Approximation) functional. The TZP (Triple ζ polarized) basis set, with a fine mesh for numerical integration, a spin-restricted formalism and full geometry optimization, applying tight convergence criteria, was used for minimum energy searches.^{28,29} Throughout, all calculations have been performed with no symmetry constraint (C_1). Zero point energy and thermal corrections (vibrational, rotational and translational) were made in the calculation of the thermodynamic parameters. The enthalpy (H) and free energy (G) was calculated from

$$U = E_{\text{TBE}} + E_{\text{IE}}$$

$$H = U + RT \text{ (gas phase) or } H = U \text{ (solution)}$$

$$G = H - TS$$

$$\text{Reaction free energy } (\Delta G_{\text{reaction}}) = G_{\text{products}} - G_{\text{reactants}}$$

where U is the total energy, E_{TBE} is electronic internal energy of the molecule, E_{IE} nuclear internal energy including the zero-point energy correction, R is the gas constant, T is temperature and S is entropy. The entropy (S) was calculated from the temperature dependent partition function in ADF at 298.15 K. Free energy G was calculated by $G = H - TS$. Solvent effects were taken into account for all calculations reported here. The COSMO (Conductor like Screening Model) model of solvation^{30,31,32} was used as implemented in ADF.³³ The COSMO model is a dielectric model in which the solute molecule is embedded in a molecule-shaped cavity surrounded by a dielectric medium with a given dielectric constant (ϵ_0). The type of cavity used is Esurf³⁴ and the solvent used is chloroform ($\epsilon_0 = 4.8$).

Acknowledgements

Financial assistance by the South African National Research Foundation and the Central Research Fund of the University of the Free State is gratefully acknowledged. A grant of computer time from the Norwegian supercomputing program NOTUR (Grant No. NN4654K) is gratefully acknowledged.

Notes and references

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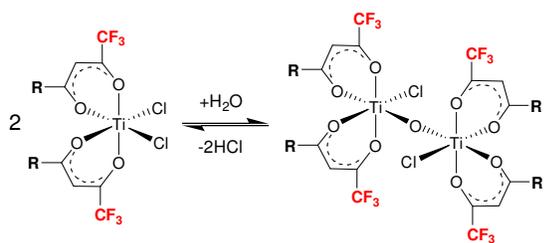
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† Electronic Supplementary Information (ESI) available: Tables containing NMR and crystallographic data, Additional figures and optimized coordinates of DFT calculations. See DOI: 10.1039/b000000x/

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Graphical Contents entry



Hydrolysis reaction of fluorine substituted $\text{Ti}(\beta\text{-diketonato})_2\text{Cl}_2$ complexes.