(4-Acyl-5-pyrazolonato)titanium Derivatives: Oligomerization, Hydrolysis, Voltammetry, and DFT Study

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Twenty 4-acyl-5-pyrazolonato (Q) titanium derivatives of varied nuclearity have been synthesized from $Ti(OR)_4$ or $TiCl_4$ and characterized with spectroscopic methods (IR, NMR, ESI-MS). While Ti–(β-diketonato) cleavage is not seen in isolated solids, Ti–O(alkoxy) (or Ti–Cl) bonds cleave upon hydrolysis, leading to several structural forms, including oligomers. Ionic Q species with no Ti, i.e., obtained after Ti–Q cleavage, are seen for some Ti–Q derivatives by ESI-MS, which also indicates a varied nuclearity for a given species, e.g., the isolated polynuclear $[Q_2Ti\text{-}\mu\text{-}O]_n$ has several "*n*" values. Mononuclear Ti complexes are obtained under rigorous anhydrous conditions. The *cis* structures of the mononuclear species $(Q^T)_2Ti(OCH_3)_2$, Q^T = 3-methyl-4-(neopentylcarbonyl)-1-phenylpyrazol-5-onato have been analyzed with DFT methods. A *trans* influence is a major driving force that accounts for several sets of Ti–O bonds. One of the *cis* stereoisomers is 56 kcal/mol higher in energy than the other two. In contrast, all $(Q^T)_2TiCl_2$ *cis* isomers show similar energies. Voltammetry of the mononuclear species $(Q^T)_2Ti(OnPr)_2$ and the antitumor tetranuclear compound $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$, ($Q^B$ = 4-benzoyl-3-methyl-1-phenylpyrazol-5-onato) indicate that the Ti^{IV} is less prone to reduction to Ti^{III} in the latter (Ep_c for the Ti^{IV}/Ti^{III} couple is –1.71 V and –1.46 V versus Fc^+/Fc, respectively). Potential antitumor compounds having a Ti/Q ratio of 1:1 do not disproportionate, unlike the equivalent acetylacetonato derivatives, and are water-soluble.

Introduction

Titanium tetraalkoxides react with β-diketones to give products formulated as (β-diketonato)$Ti(OR)_3$ and (β-diketonato)$_2Ti(OR)_2$.[1,2] For $(bzac)_2Ti(OEt)_2$, bzac = benzoylacetonato, an equilibrium mixture of the three possible octahedral *cis* stereoisomers is seen in CH_3CN/H_2O solution.[3] Qualitatively, the *cis* configurations are more strained but are preferred due to electronic effects caused by $p_\pi - d_\pi$ (t_{2g}) bonding of the β-diketonato ligand.[4,5] $[(acac)_2TiO]_2$, acac = acetylacetonato, consists of a cyclic dimer with titanium centers linked by oxygen atoms.[5]

Other stable polynuclear oxo-bridged species have been isolated as Ti is a hard acid that forms strong metal–oxygen bonds. For example, hydrolysis of $(\eta^5\text{-}C_5H_5)_2TiCl_2$ and $(\eta^5\text{-}C_5H_5)TiCl_3$ yields the two related oxo-bridged titanium dimers $[(\eta^5\text{-}C_5H_5)_2TiCl]_2O$ and $[(\eta^5\text{-}C_5H_5)TiCl_2]_2O$, respectively.[6–8]

The success of cisplatin,[11,12] *cis*-$(NH_3)_2PtCl_2$, has prompted studies of metal-based antitumor compounds[9,10] with other metal derivatives.[13–15] The (β-diketonato)titanium species mentioned above, $(bzac)_2Ti(OEt)_2$ (Figure 1), known as budotitane,[16] was the first non-Pt metal compound to reach clinical trials.[17] It undergoes stereoisomer interconversion[3] and a theoretical[18] study shows a calcu-

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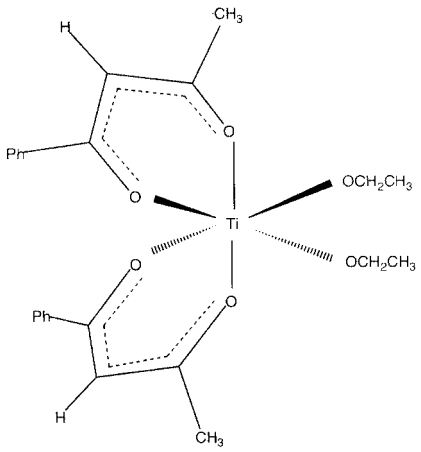

Figure 1. Isomer of budotitane, $(bzac)_2Ti(OCH_2CH_3)_2$; bzac = benzoylacetonato

lated isomer distribution that agrees with ^1H NMR spectroscopic data.

Budotitane was selected for development on the basis of structure-activity studies in which metal atom, β-diketonato substituents, and leaving groups (ethoxy in budotitane) were modified.[3] The ethoxy derivative gave the best pharmacological formulation (a limiting feature in budotitane) because hydrolysis is reduced when ethanol is added to it. These studies showed that asymmetric β-diketonates induce higher activity.[3] This structural feature is fulfilled by 4-acyl-5-pyrazolones, a sub-class of asymmetric β-diketones having a fused pyrazole ring and three useful positions for substitution (Figure 2).

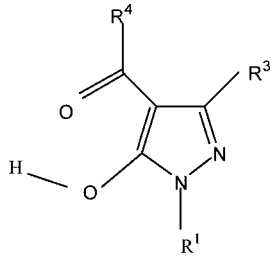

Figure 2. 4-Acyl-5-pyrazolones (keto-enol form), HQ

Recently, one such derivative, *cyclo*-tetrakis[bis(4-benzoyl-3-methyl-1-phenylpyrazolon-5-ato)(μ-oxo)titanium(IV)], $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$, has demonstrated potent and selective antitumor activity in vitro and in vivo, with an increased life span (T/C ≈ 300%), in the TA-3 mouse mammary adenocarcinoma[19] (Figure 3).

Ti−O(ethoxy) bonds in budotitane tend to hydrolyze, yielding Ti−OH derivatives. Subsequently, condensation of two Ti−OH units from different molecules produce a Ti−O−Ti linkage while releasing a molecule of water.[3] Ti−(β-diketonato) bond hydrolysis also occurs in budotitane and the system evolves towards polynuclear compounds that ultimately yield harmless titanium dioxide. While letting $TiCl_4$ react to obtain $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$ a similar hydrolytic process for the Ti−Cl bonds is seen, but without hydrolysis of the Ti−(β-diketonato) bonds.[19] This is important for the antitumor activity of Ti derivatives. In fact, budotitane and titanocene dichloride,[20] Cp_2TiCl_2 (an antitumor compound currently in clinical phase II trials),[21] are characterized by rapid hydrolysis of ethoxy and Cl^-, respectively, in comparison with a much slower hydrolysis of bzac and Cp. This slow hydrolysis was recently suggested to be a key property for biological activity in antitumor Ti compounds.[22,23] Following our interest in antitumor inorganic compounds[19,22−24] we report here the synthesis of novel Ti−(4-acyl-5-pyrazolonato) compounds with several degrees of polymerization (Table 1). Since recent results[25] show that, in addition to Ti^{IV} complexes, Ti^{III} species may also display antitumor activity (a property also shown by Pt^{II} and Pt^{IV} species),[26] we also describe the redox behavior of one mononuclear and one tetranuclear Ti−(β-diketonato) compound. Structural features are analyzed with Density Functional Theory (DFT) methods. Electrospray ionization mass spectrometry (ESI-MS) is a powerful tool with which to study charged species in the gas phase[27,28] and has been successfully applied to address

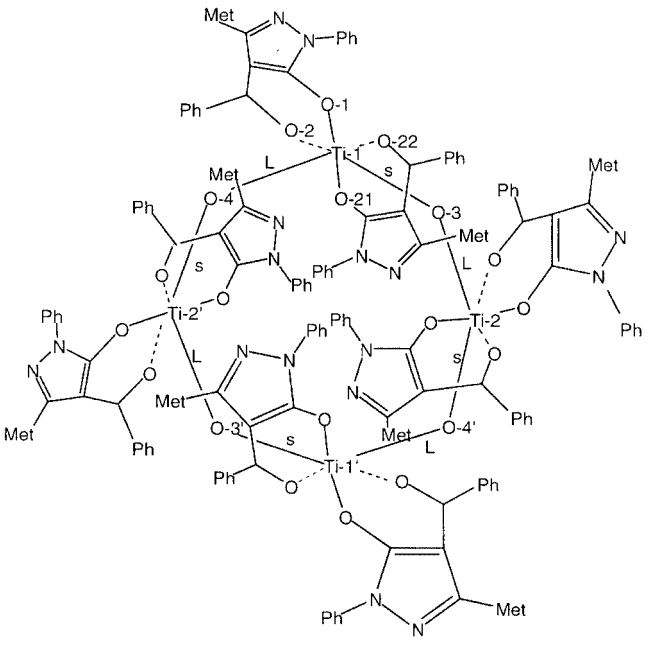

Figure 3. Tetranuclear (4-acyl-5-pyrazolonato)−Ti antitumor species, *cyclo*-tetrakis[bis(4-benzoyl-3-methyl-1-phenylpyrazolon-5-ato)(μ-oxo)titanium(IV)], $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$ (**1**) ($R^1 = R^4 = Ph$, $R^3 = CH_3$), dashed bonds indicate weak Ti−O bonds; L (s) indicate long (short) bonds in the eight-membered ring

Table 1. 4-Acyl-5-pyrazolones used

4-Acyl-5-pyrazolone	R^1	R^3	R^4
HQ^B	Ph	Me	Ph
HQ^T	Ph	Me	CH_2tBu
HQ^A	Ph	Me	C_6H_4-4-OMe
HQ^N	Ph	Me	C_6H_4-4-NO_2
HQ^C	Ph	Me	Cy
HQ^L	Ph	Me	CH_2Ph
HQ^E	Ph	Me	$[CH_2]_5Me$
HQ^P	Ph	Ph	Ph

biochemical questions[29] and the speciation of inorganic complexes of various metals, including Ti.[30,31] We also describe here an ESI-MS study.

Results and Discussion

Synthesis and Spectroscopic Characterization

Polynuclear (oxo)titanium β-diketonates **1**−**8** (Table 2) have been obtained by treating TiX_4 (X = Cl or OR; R = Me, Et, *n*Bu, or *n*Pr) with 4-acyl-5-pyrazolones (HQ) in alcoholic solvent in the presence of KOH [see Equation (1) for tetranuclear species **1**]. KCl is removed after centrifugation of the suspension containing a soluble Ti-Q derivative. Insoluble Ti-Q products are separated from KCl after dissolution in CH_2Cl_2. Alternatively, **1**−**8** can be obtained in refluxing benzene (without addition of base) with an excess of Q ligands.

Table 2. Synthesized compounds

1	$[(Q^B)_2Ti(\mu\text{-}O)]_4$	**11**	$(Q^T)_2Ti(O\textit{n}Pr)_2$
2	$[(Q^T)_2Ti(O)(H_2O)]_n$	**12**	$(Q^T)_2Ti(O\textit{n}Bu)_2(H_2O)$
3	$[(Q^A)_2Ti(O)(H_2O)]_n$	**13**	$[(Q^A)Ti(OH)_3(H_2O)]_n$
4	$[(Q^N)_2Ti(O)(H_2O)]_n$	**14**	$[(Q^C)Ti(OH)_3]_n$
5	$[(Q^C)_2Ti(O)(H_2O)_2]_n$	**15**	$[(Q^B)Ti(OH)_2(O\textit{n}Pr)](H_2O)$
6	$[(Q^L)_2Ti(O)(H_2O)_2]_n$	**16**	$[(Q^B)Ti(OH)_2(O\textit{n}Bu)](H_2O)$
7	$[(Q^E)_2Ti(O)(H_2O)]_n$	**17**	$[(Q^L)Ti(O)(OH)]_n$
8	$[(Q^P)_2Ti(O)(H_2O)]_n$	**18**	$[(Q^E)Ti(O)(OH)]_n$
9	$(Q^B)_2Ti(O\textit{n}Pr)_2$	**19**	$(Q^B)_2TiCl_2$
10	$(Q^T)_2Ti(OMe)_2$	**20**	$(Q^T)_2TiCl_2$

X-ray data for **1** show a tetranuclear structure,[19] which agrees with the measured molecular weight of 2200 (the expected value for the tetranuclear arrangement is 2473.9). This technique suggests a mixture of di- and other polynuclear species for **4**, that is $[(Q^N)_2Ti(O)(OH_2)]_n$ (n = 2.8). In a related study of budotitane, after dissolution in CH_3CN/H_2O the species $[(bzac)_2Ti(O)]_n$ with n = 2.4 is formed.[3]

Compounds **1**−**8** are generally soluble in chlorohydrocarbons, acetonitrile, and DMSO, insoluble in ethers and alcohols, and are very stable in the air at room temperature. Compound **3**, however, is insoluble in CH_2Cl_2 and $CHCl_3$ due, probably, to the formation of bridges between different metal centers via hypervalent oxygen atoms of the OMe group.

$$8\ HQ + 16\ KOH + 4\ TiCl_4 \rightarrow [Q_2Ti(\mu\text{-}O)]_4 + 16\ KCl + 12\ H_2O \quad (1)$$

Complexes $Q_2Ti(OR)_2$ **9**−**12** have been prepared in excellent yields by treating stoichiometric amounts of the β-diketone and the titanium alkoxide in refluxing benzene according to Equation (2). These complexes are soluble in DMSO, CH_2Cl_2, and $CHCl_3$, acetonitrile and nitrobenzene, slightly soluble in benzene and acetone, and nearly insoluble in diethyl ether, water, and saturated hydrocarbons. In $CHCl_3$ they seem to hydrolyze to a large extent as several signals were found for each group of protons. Molecular weight measurements in solution further confirmed this hypothesis; the ratio between experimental and calculated molecular weights for compounds **9** and **11** being 0.62 and 0.53, respectively. Ionic species are excluded on the basis of conductivity data.

$$Ti(OR)_4 + 2\ HQ \rightarrow Q_2Ti(OR)_2 + 2\ ROH \quad (2)$$

The reaction between $Ti(OR)_4$ and HQ in a 1:1 ratio, in the presence of KOH, gave the hydroxy derivatives **13**−**16**. In addition, TiO_2 was obtained as a sub-product, probably from $Ti(OR)_4$. Compounds **13**−**16** are generally very soluble in water and behave as sol-gel precursors, a property observed in other Ti−(β-diketones) used as "modifiers" in sol-gel processing.[32] The literature is somewhat ambiguous about the structures and behavior of such species present in solution. The partially hydrolyzed hydroxy(oxo) complexes **17** and **18** are also water-soluble.

As already mentioned, compound **1** is a potent and selective cytotoxic agent that is water-insoluble and, therefore, is formulated as a liposome for pharmacological use.[19] Compounds **13**−**18** (Ti/Q = 1:1), however, are water-soluble and are thus interesting candidates for simpler formulation. They do not disproportionate, in contrast to acac-related derivatives,[33] and they resemble related Ti−Cp antitumor compounds.

$TiCl_4{\cdot}2THF$ reacts with HQ^B and HQ^T in methanol, in the presence of an equimolar amount of NaOMe, to give the mononuclear Q_2TiCl_2 complexes **19**−**20** in good yields [Equation (3)], under rigorous anhydrous conditions.

$$TiCl_4{\cdot}2THF + 2\ HQ + 2\ NaOMe \rightarrow Q_2TiCl_2 + 2\ NaCl + 2\ MeOH + 2\ THF \quad (3)$$

Therefore, reaction in basic (KOH) alcohol solution yields polynuclear products **1**−**2** whereas replacing KOH with NaOMe, under anhydrous conditions, furnishes the corresponding mononuclear compounds **19**−**20**. However, mononuclear species are more simply obtained in benzene, where hydrolysis is hindered.

Conductance data in the ionizing solvents acetone, DMSO or nitrobenzene show that complexes **1**−**20** are non-electrolytes.

Compounds **1**−**8** can be also obtained by hydrolysis of bis(4-acyl-5-pyrazolonato)dialkoxytitanium(IV) or bis(4-acyl-5-pyrazolonato)dichlorotitanium(IV). With excess β-diketone some titanium alkoxides are converted into (oxo)titanium β-diketonates. Compounds **9**−**11** also appear to hydrolyze, in solution, more rapidly than **19**−**20**.

Nujol mull IR spectra of the oxo complexes contain bands in the chelating carbonyl stretching region 1600−1300 cm^{-1}; similar frequencies are observed for other metal 4-acyl-5-pyrazolonato derivatives.[34−41] No bands were observed in the 1600−1750 cm^{-1} region, where ketonic carbonyl modes are expected for the pyrazolonato keto form. Therefore, both carbonyl groups are coordinated

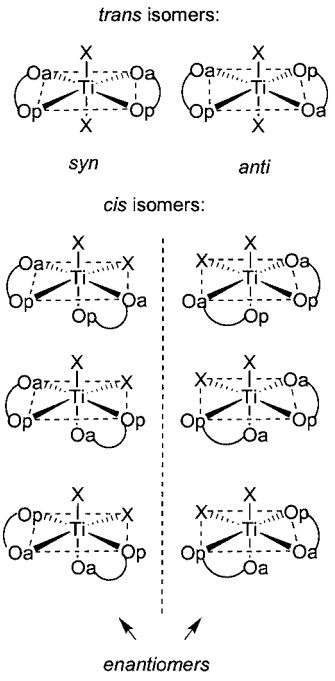

Figure 4. Possible Q_2TiX_2 stereoisomers; Oa = O(acyl), Op = O(pyrazolonato), X = Cl, OEt, O*n*Pr, O*i*Pr, or O*n*Bu; the three pairs of *cis* stereoisomers are ordered as CIS3, CIS2, and CIS1 as defined in the text

to the Ti atom. Broad bands in the 500−400 cm^{-1} region and some strong absorption in the 400−300 cm^{-1} region are associated with Ti−O bonds.[5,33−43]

Six-coordinate titanium derivatives can theoretically exist in solution as a mixture of several *cis* and *trans* isomers (Figure 4). However, for related dialkoxy- and dihalobis(acetylacetonato)titanium(IV) derivatives, steric interactions influence the relative stabilities of the isomers and *cis* forms are strongly preferred.[18,42] In particular, the low-temperature ^1H NMR spectrum of budotitane exhibits four signals for the different methyl groups due to the three *cis* isomers. Our own ^1H NMR variable-temperature experiment on compounds **9** and **11** revealed only one signal (also at 273 K) for each equivalent proton of the propoxy groups and two signals having the same integrals for the methyl group of Q^B and Q^T. This can be assigned to the equatorial and axial methyl groups of the CIS2 isomer (Figure 4) − that is only one *cis* conformer is detected under such experimental conditions. It is worth noting that 20 min after dissolution of **9** and **11** in $CHCl_3$, *n*PrOH formation was observed, i.e., hydrolysis of the Ti−O*n*Pr bond occurred. Hydrolysis is fast at high temperatures and complete 48 h after dissolution. It is also reversible as the addition of *i*PrOH or *n*PrOH to the NMR solutions showed signals due to (TiO*i*Pr)- and (TiO*n*Pr)-containing species. In contrast, derivative **10** was immediately hydrolyzed in solution, as indicated by ten signals, due to OMe groups at room temperature, seen 10 min after dissolution.

The spectrum of the monomer species $(Q^B)_2TiCl_2$ **19** carried out in non-anhydrous deuterated benzene (98%) and recorded at least 1 h after dissolution of the sample, showed some multiplets at 283 and 353 K, analogous to those in the spectrum of **1**, i.e., the mononuclear $(Q^B)_2TiCl_2$ hydrolyzed and became a polynuclear species. The same spectrum was obtained after adding H_2O (0.01 mL) to a deuterated anhydrous benzene (99.9%) solution of **19**. This shows faster hydrolysis since the spectrum was taken after 15 min.

Hydrolysis is avoided by not adding water and working under N_2 to avoid air humidity in deuterated anhydrous benzene (99.9%). This additional variable-temperature ^1H NMR of **19** shows a single sharp resonance for the methyl protons at 353 K. At 313 K line broadening is observed and the methyl resonance begins to split into two peaks. At 303 K further splitting of these peaks gives a total of four signals. The same multiplicity was found at 283 K. This sequence of increasing peaks as the temperature decreases is assigned to the four non-equivalent methyl groups of the three diastereoisomers.[18] The line broadening could be due to a rapid isomerization process. Broadening of the multiplets obscures the fine structure due to spin coupling of *ortho*, *meta*, and *para* protons.

The same experiment in $CDCl_3$ shows hydrolysis, as indicated by more than 15 lines at 218 K for the methyl groups of Q^B. Addition of MeOH to the NMR solution of **19** generates a signal at $\delta = 4.70$ ppm due to an OMe group coordinated to Ti after formation of a Ti(OMe)-containing species.

The extraordinarily high number of signals detected for each equivalent group of protons in the ^1H spectra of derivatives **1**−**3** suggests the formation of several different nuclearities (like mono-, di-, trititanium species, etc.), in solution, and perhaps even dissociation of the pyrazolonato ligands. The latter is, probably, a reversible dynamic feature, as elemental analyses of the isolated products **1**−**3** show a Ti/Q ratio of 1:2, indicating no Ti−Q cleavage in the solid. We further describe these features below.

Electrospray

Positive electrospray mass spectra of complexes **1**−**2**, **5**−**7**, **15**−**16**, **18**−**20** (the most relevant data are reported in the Exp. Sect.) indicate that, in solution, these derivatives undergo loss of the anionic pyrazolonato ligands which immediately interact with proton, sodium and/or potassium ions, yielding 1−6 polynuclear monocharged species such as $[NaH(Q)]^+$, $[NaK(Q)]^+$, $[Na_3(Q)_2]^+$, $[Na_2K(Q)_2]^+$, $[NaK_2(Q)_2]^+$, $[Na_3H(Q)_3]^+$, $[Na_2KH(Q)_3]^+$, $[NaK_2H(Q)_3]^+$, $[Na_4H(Q)_4]^+$, $[Na_3KH(Q)_4]^+$, $[Na_2K_2H(Q)_4]^+$, $[Na_4KH_2(Q)_6]^+$, $[Na_3K_2H_2(Q)_6]^+$. In general, protonated species are more abundant than Na, K, or mixed Na/K compounds. The population of polynuclear species increases as trinuclear > hexanuclear > higher isomers whereas acetonitrile derivatives containing H, Na, and K are far less abundant. Na and K adducts are common in ESI-MS spectra[44] because the O-donors immediately interact and aggregate with the small quantities of Na and K that are always present in H_2O solvent.

The aggregation behavior is strongly dependent on the ligands. For some systems, aggregation of Ti and Q is seen significantly in acetonitrile even at 10^{-3} M, and aggregates

containing Na^+, K^+, or H^+ dominate significantly over larger adducts. Relevant peaks present in the spectra of **1** are due to the interaction of tetranuclear species with Na^+, K^+, or H^+. The most abundant Ti-containing species are the trinuclear ions $[H(Q^B)_6Ti_3O_3]^+$, $[NaTi_3(Q^B)_6O_3]^+$, and $[KTi_3(Q^B)_6O_3]^+$. For derivative **2** additional signals due to the dinuclear species $[H(Q^T)_4Ti_2O_2]^+$, $[Na(Q^T)_4Ti_2O_2]^+$, and $[K(Q^T)_4Ti_2O_2]^+$ are present. The isotopic distribution of these species agrees with the calculated composition.

The absence of ions containing MeCN indicates that there is no binding between the solvent and Ti.

The ESI-MS spectrum of **6**, recorded in the negative detection mode, is dramatically improved and simpler. It shows four main peaks, assigned to the tri- $\{[Na_3(Q)_4]^-\}$, di- $\{[Na_2(Q)_3]^-\}$, and mono-Na anions $\{[Na(Q)_2]^-\}$, and the free anionic ligand $[Q]^-$.

Since only charged species are transferred from solution to the gas phase, quantitative ESI-MS results do not represent the real relative distribution of species in solution. The strong association of Na and K cations and protons to the Q ligands concurs with an X-ray structure of an Rh^I derivative that has 4-acyl-5-pyrazolonato as a counteranion.[45]

The ESI-MS spectra clearly indicate different nuclearities within polymeric species, in agreement with the high number of NMR signals for the methyl group in **1**−**3**.

As shown in the Exp. Sect., Ti-Q compounds are isolated as mono-, tetra-, and polynuclear species, whereas the synthesis of budotitane derivatives yields only mononuclear species. However, in a biological environment for antitumor therapy, budotitane undergoes extensive hydrolysis, first on the Ti−O(ethoxy) bonds and later on the Ti−bzac moiety, to eventually yield titanium dioxide.[3] In other words, for mononuclear $(bzac)_2Ti(OEt)_2$ all of the Ti substituents, ethoxy and benzoylacetonato, are cleaved, whereas in (4-acyl-5-pyrazolonato)titanium synthesis it is the alkoxy (or Cl) bonds that cleave. Although the ESI-MS spectra suggest that the Ti−Q bonds are labile, the different environments in each case may explain such differences, as shown in the literature.[46−48]

Structural Features Obtained with DFT

As we could not obtain crystals suitable for X-ray diffraction studies, we calculated the minimum energy geometry using DFT (Density Functional Theory) theoretical methods. As shown in Figure 4 a mononuclear species can have three *cis* stereoisomer conformers, we name them CIS1, CIS2, and CIS3. For $(Q^T)_2Ti(OMe)_2$, CIS3 has the lowest energy and selected geometrical parameters are shown in Table 3. This CIS3 conformer shows both O(methoxy) groups opposite to O(pyrazolonato) atoms. A *trans* influence is seen for the two pairs of opposite bonds (Ti−O3 = 1.801 Å, Ti−O1 = 2.084 Å, and Ti−O4 = 1.816 Å, Ti−O51 = 2.046 Å) where the shorter Ti−O(methoxy) bond is opposite the longer Ti−O(pyrazolonato) bond. Completing the coordination sphere are two opposing

Table 3. Selected structural parameters of bis(4-acyl-5-pyrazolonato)titanium conformers, Q_2TiY_2, obtained with DFT methods, and related polynuclear Ti−(β-diketonato) compounds, obtained with diffraction methods

Conformer	Ti−Y3[a]	Ti−Y4[a]	Ti−O1[b]	Ti−O2	Ti−O51	Ti−O52	Y−Ti−Y	Ti ligands
			1st chelate		2nd chelate			
CIS1[c]	2.235	2.233	1.952	2.038	1.966	2.027	102.6	Q^T
	Y = Cl	Y = Cl					Y = Cl	Cl
CIS2[c]	2.233	2.236	2.021	1.968	1.955	2.048	102.3l	Q^T
	Y = Cl	Y = Cl					Y = Cl	Cl
CIS3[c]	2.234	2.237	2.041	1.950	2.047	1.957	98.8	Q^T
	Y = Cl	Y = Cl					Y = Cl	Cl
CIS3[d]	1.797	1.801	2.085	2.012	2.042	2.010	95.0	Q^B
	Y = O	Y = O					Y = O	CH_3O
CIS3[e]	1.801	1.816	2.084	1.994	2.046	1.992	95.1	Q^T
	Y = O	Y = O					Y = O	CH_3O
Polynuclear compounds	Ti−O3	Ti−O4	Ti−O1 1st chelate	Ti−O2	Ti−O51 2nd chelate	Ti−O52	O−Ti−O[f]	Ti−O−Ti[g]
$[(Q^B)_2Ti(\mu\text{-}O)]_4$[h]	1.767	1.868	1.979	2.146	1.980	2.056	99.2	150.5, 153.8
2nd Ti unit	1.758	1.859	1.983	2.163	1.978	2.076	100.2	150.5, 153.8
$[L_2Ti(\mu\text{-}O)]_4$[i]	1.804	1.818	1.969	2.116	1.969	2.117	100.5	170.3, 169.3
2nd Ti unit	1.810	1.810	1.968	2.120	1.968	2.120	100.3	170.3, 169.3
3rd unit	1.793	1.793	1.969	2.132	1.969	2.132	99.4	170.3, 169.3
$[(L')_2Ti(\mu\text{-}O)]_2$[j]	1.831	1.824	1.968	2.059	1.974	2.059	83.4	97.1, 97.1

[a] Y3 and Y4 are: O associated to methoxy groups in $(Q^T)_2Ti(OCH_3)_2$ and $(Q^B)_2Ti(OCH_3)_2$; Cl in $(Q^T)_2TiCl_2$; $Q^{[B]}$ = 4-benzoyl-3-methyl-1-phenylpyrazolon-5-ato, Q^T = 3-methyl-4-neopentylcarbonyl-1-phenylpyrazolon-5-ato. In the corresponding columns for the polynuclear compounds Ti−O(oxo) bonds are shown. [b] O1 and O2 belong to the 1st β-diketonato chelate; O51 and O52 belong to the 2nd β-diketonato chelate. [c] Energy: CIS1 has the lowest energy, followed by CIS3 (2 kcal/mol) and CIS2 (2.2 kcal/mol) for $(Q^T)_2TiCl_2$. [d] Energy: CIS1 has the lowest energy, followed by CIS2 (0.3 kcal/mol) and CIS3 (2.8 kcal/mol) for $(Q^B)_2Ti(OCH_3)_2$. [e] Energy: CIS3 has the lowest energy, followed by CIS2 (0.7 kcal/mol) and CIS1 (56 kcal/mol) for $(Q^T)_2Ti(OCH_3)_2$. [f] This parameter is O3−Ti−O4. [g] These parameters are Ti−O3−Ti and Ti−O4−Ti. [h] $[(Q^B)_2Ti(\mu\text{-}O)]_4$ has an inversion center that makes two Ti units equivalent to the other two.[19] Ti conformation is similar to CIS1. [i] $[L_2Ti(\mu\text{-}O)]_4$ has a twofold axis passing on two Ti atoms; L = 2,2,6,6-tetramethylheptane-3,5-dionato.[50] [j] The 2nd Ti unit is crystallographically related by an inversion center; L′ = acetylacetonato.[5]

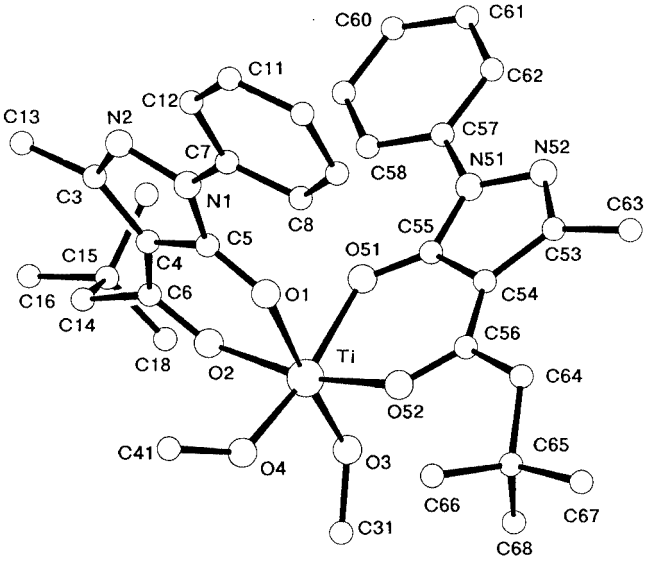

Figure 5. DFT structure of the $(Q^T)_2Ti(OCH_3)_2$ conformer having the lowest energy (CIS3); H atoms are omitted from this and all other DFT pictures

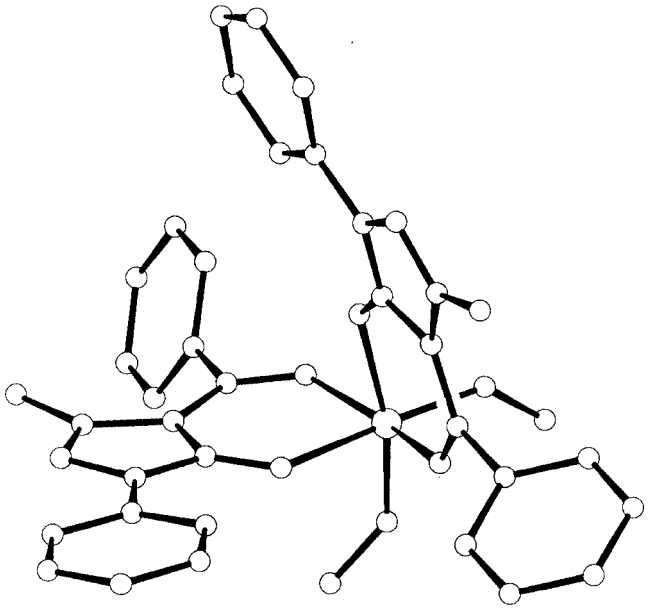

Figure 6. CIS3 DFT structure of $(Q^B)_2Ti(OCH_3)_2$

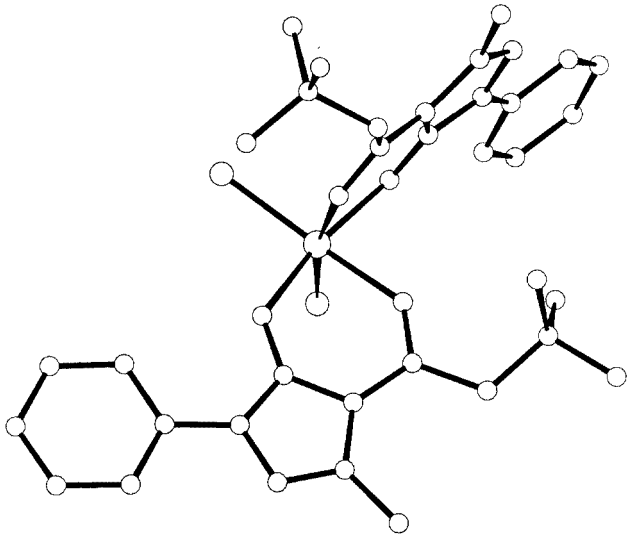

Figure 7. CIS1 DFT structure of $(Q^T)_2TiCl_2$

O(acyl) atoms; here there is no dominant *trans* influence and both Ti−O(acyl) bonds are equal (Ti−O2 = 1.994 Å, Ti−O52 = 1.992 Å).

X-ray structures of Sn-Q derivatives[34−41] show coplanarity between the pyrazole and its attached phenyl due to extended intraligand conjugation. CIS3 agrees with this experimental feature as the torsion angles C5−N1−C7−C8 and C55−N51−C57−C58 are 5.9 and −1.0° (Figure 5). Other DFT conformers studied here also show this feature.

The CIS2 conformer of $(Q^T)_2Ti(OMe)_2$ is 0.7 kcal/mol higher in energy than CIS3, whereas the CIS1 isomer shows markedly higher energy (56 kcal/mol).

We studied $(Q^B)_2Ti(OMe)_2$ and analyzed the role of the R^4 group in these complexes. In contrast with $(Q^T)_2Ti(OMe)_2$ the three *cis* conformers of $(Q^B)_2Ti(OMe)_2$ have similar energies. Thus, the CIS1 conformer shows the lowest energy followed by CIS2 (0.3 kcal/mol) and CIS3 (2.8 kcal/mol). The marked difference between the CIS1 conformers of $(Q^B)_2Ti(OMe)_2$ and $(Q^T)_2Ti(OMe)_2$ may be ascribed to the bulkiness of the neopentyl R^4 group in the latter compared with Ph in the former.

Although the CIS3 conformer of $(Q^B)_2Ti(OCH_3)_2$ (Figure 6) shows the same *trans* influence seen in $(Q^T)_2Ti(OCH_3)_2$ (both shown in Table 3), the former has slightly shorter Ti−O(methoxy) and longer Ti−O(acyl) bonds. This difference is probably related to the lower basicity of the O(acyl) atom attached to an R^4 group that is electron-withdrawing (Ph), in comparison with the more basic neopentyl group in $(Q^T)_2Ti(OCH_3)_2$. Therefore, the shortening of the Ti−O(methoxy) bond in $(Q^B)_2Ti(OCH_3)_2$ seems to arise from the weak O(acyl) basicity.

The role of leaving groups can be analyzed by comparing $(Q^T)_2Ti(OMe)_2$ and $(Q^T)_2TiCl_2$. The three *cis* conformers of the latter have similar energies; the lowest energy being CIS1 (Figure 7) followed by CIS2 (2 kcal/mol, Figure 8) and CIS3 (2.2 kcal/mol, Figure 9). Therefore, the CIS1 conformer of the Cl derivative is not as strained as that of $(Q^T)_2Ti(OCH_3)_2$. This may be associated with a longer Ti−Cl bond compared with Ti−O(methoxy). A lengthening of the Ti−Cl bond is expected due to the longer covalent radius of Cl (0.99 Å) compared to that of O (0.73 Å).[49] However, this difference (0.26 Å) is largely overcome by calculated values of about 0.42 Å (Table 3). The very short Ti−O(methoxy) bonds in $(Q^T)_2Ti(CH_3O)_2$ and $(Q^B)_2Ti(CH_3O)_2$ probably possess partial double bond character that is missing in Ti−Cl bonds. Consequently, stronger Ti−chelate bonds are induced in $(Q^T)_2TiCl_2$; see Ti−O(chelate) bonds for CIS3 isomers of $(Q^T)_2Ti(CH_3O)_2$ and $(Q^B)_2Ti(CH_3O)_2$ in Table 3.

Further agreement between our DFT calculated structures and data from diffraction studies is seen as the O(methoxy) atoms form the shortest Ti−O bonds in CIS1,

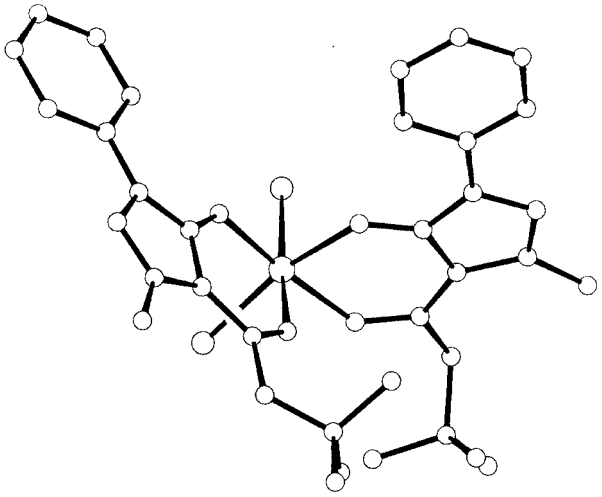

Figure 8. CIS2 DFT structure of $(Q^T)_2TiCl_2$

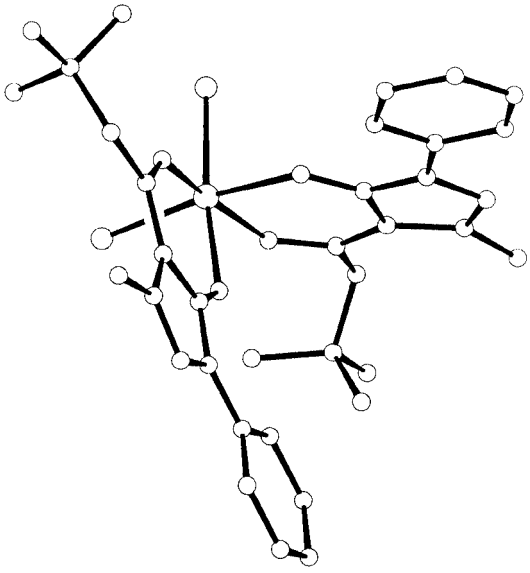

Figure 9. CIS3 DFT structure of $(Q^T)_2TiCl_2$

CIS2, and CIS3, similar to the O(oxo) atoms in the polynuclear Ti−(β-diketonates) $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$,[19] $[L_2Ti\text{-}\mu\text{-}O]_4$ (L = 2,2,6,6-tetramethylheptane-3,5-dionato)[50] and $[(acac)_2Ti\text{-}\mu\text{-}O]_2$,[5] i.e., Ti−O(β-diketonato) bonds are longer.

In conclusion, the *trans* influence determines the structural features in titanium 4-acyl-5-pyrazolonates. O(oxo) in $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$ and O(methoxy) in $Q_2Ti(OCH_3)_2$ are strong donors to Ti, resulting in the shortest Ti−O bonds and weakening their opposite Ti−O bonds in the coordination sphere.

Voltammetry

Because antitumor platinum and gold compounds exist in two metal oxidation states, Pt^{II} [11,12] and Pt^{IV} [26] and Au^{I} and Au^{III},[51−52] respectively, a redox reaction may play a role in the cytotoxic mechanism of metal derivatives. This has been demonstrated for the antitumor drug bleomycin, which forms a bleomycin−Fe^{II}−O_2 species that undergoes $Fe^{II} \rightarrow Fe^{III}$ oxidation before performing DNA cleavage.[53]

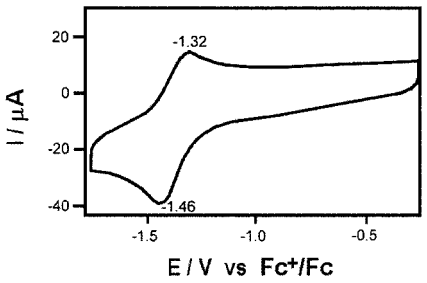

Figure 10. Voltammogram of the antitumor compound $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$(**1**)

Protein Ti-bound transferrin, believed to play a key role in the antitumor mechanism of Ti^{IV} titanocene dichloride, can also be obtained from Ti^{III} citrate.[25]

We have examined the redox behavior of Ti in the tetranuclear antitumor compound $[Q^B)_2Ti\text{-}\mu\text{-}O]_4$ (**1**) and the mononuclear species $(Q^T)_2Ti(O\textit{n}Pr)_2$ (**11**). The results, referred to Fc^+/Fc, for $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$ show a cyclic voltammogram in the cathodic region with a reversible redox couple, assigned to Ti^{IV}/Ti^{III}, with $Ep_c = -1.46$ V (Figure 10), whereas the same process for $(Q^T)_2Ti(O\textit{n}Pr)_2$ has −1.71 V (voltammogram not shown). Therefore, in the tetranuclear species all four Ti atoms undergo the same process and are indistinguishable. In addition, the Ti atom has a greater tendency to be reduced to Ti^{III} in the tetranuclear species than in the mononuclear one. In the related titanium β-diketonato compound $(Cp)_2Ti^{III}(acac)$,[54] the Ti^{IV}/Ti^{III} couple was $Ep_c = -0.85$ V (referred to Fc^+/Fc). Although comparison with the present work is difficult because of markedly different experimental conditions, it seems that the Ep_c value is highly ligand sensitive.

An initial stage in the voltammetric reduction of the mononuclear species $(Q^T)_2Ti(OCH_2CH_2CH_3)_2$ was also studied using DFT methods. Since the CIS3 stereochemistry of $(Q^T)_2Ti(OCH_3)_2$ and $(Q^B)_2Ti(OCH_3)_2$ show low energies, this conformation was expected to be favored for $(Q^T)_2Ti(OCH_2CH_2CH_3)_2$. After convergence, the anionic species $[(Q^T)_2Ti(OCH_2CH_2CH_3)_2]^-$ generally agrees with the structural trends shown by the methoxy derivatives mentioned above. However, the Ti−O*n*Pr bonds (1.840, 1.868 Å) are longer than the equivalent Ti−O(methoxy) bonds in $(Q^T)_2Ti(OCH_3)_2$ (1.801, 1.816 Å) and $(Q^B)_2Ti(OCH_3)_2$ (1.797, 1.801 Å); this seems reasonable as a leaving O*n*Pr group would induce a neutral, more stable $(Q^T)_2Ti^{III}(OCH_2CH_2CH_3)$ species.

Although Ti^{III} tends to oxidize to Ti^{IV}, the voltammetry experiment indicates a lower tendency for Ti^{IV} in the tetranuclear species $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$ and suggests a redox stability for polymeric forms stemming from $[(Q^B)_2Ti^{III}X_2]^-$ units. Such anionic forms can be water-soluble and thus improve their pharmacological formulation by avoiding the use of liposomes such as in the tetranuclear species $[(Q^B)_2Ti^{IV}\text{-}\mu\text{-}O]_4$. Biological results for the antitumor water-soluble Ti agents will be reported in a separate publication.

Conclusion

A rich variety of (4-acyl-5-pyrazolonato)titanium(IV) compounds, with several nuclearities, is observed due to hydrolysis during synthesis. Avoiding moisture prevents polymerization and discriminates between mono- or polynuclear compounds. Spectroscopic data (NMR, ESI-MS) and molecular weight analysis describe the polymerization features. Isolated compounds do not show Ti−Q cleavage, in contrast with classical Ti−(β-diketones). The ESI-MS results indicate mild Ti−Q cleavage compared with the fast breaking of Ti−Cl (or Ti−alkoxy). These features may enhance antitumor properties as the two most investigated antitumor titanium compounds, budotitane, and titanocene dichloride, show fast hydrolysis for Ti−O(ethoxy) (or Ti−Cl) and slow hydrolysis for Ti−(β-diketonato) (or Ti−Cp) bonds. Ti-Q (1:1) derivatives possess novel water solubility, which is useful for antitumor drug formulation. Quantum mechanical calculations on mononuclear $Q_2Ti(OCH_3)_2$ species show (a) three different sets of Ti−O bonds and a strong *trans* influence; (b) no preference for a unique *cis* isomer, although one of the three *cis* conformers has a markedly higher energy for one compound with a bulky substituent. Voltammetry data on a mono- and a tetranuclear species show a lower tendency towards reduction to Ti^{III} in the latter.

Experimental Section

General: The Ti precursors were obtained from Aldrich and used without further purification. 1-Phenyl-3-R^3-4-R^4-(C=O)-pyrazol-5-ones HQ (Figure 2) were prepared according to the literature. Samples for microanalysis were dried in vacuo to constant weight (20 °C, about 0.1 Torr). Molecular weight (M.W.) determinations were performed at 40 °C with a Knauer KNA0280 vapour pressure osmometer calibrated with benzil. The solvent was Baker Analysed Spectrophotometric grade chloroform. The results were reproducible to ±2%. Elemental analyses (C,H,N) were performed inhouse with a Fisons Instruments 1108 CHNS-O Elemental Analyser. IR spectra were recorded from 4000 to 100 cm^{-1} with a Perkin−Elmer System 2000 FT-IR instrument. ^1H NMR spectra were recorded with a VXR-300 Varian spectrometer. Melting points were determined with an IA 8100 Electrothermal instrument. The positive and negative electrospray mass spectra were obtained with a Series 1100 MSI detector HP spectrometer, using an acetonitrile mobile phase. Solutions (3 mg/mL) for electrospray ionization mass spectrometry (ESI-MS) were prepared using reagent grade acetone or acetonitrile. For the ESI-MS data, mass and intensities were compared to those calculated using IsoPro Isotopic Abundance Simulator, version 2.1.[55] Peaks containing silver(I) ions are identified as the center of an isotopic cluster.

Synthesis and Spectroscopic Characterization

$[(Q^B)_2Ti(\mu\text{-}O)]_4$ (1): Compound **1** was prepared by treating $TiCl_4$ with HQ^B [56] (1:2 ratio) under reflux in basic (KOH, 1:1 regarding HQ^B) ethanol (10 mL). A yellow precipitate formed which was then dissolved in CH_2Cl_2 to remove KCl. After filtration, the solution was concentrated and the residue recrystallized from ethyl acetate/*n*-hexane under aerobic conditions, m.p. 195 °C (dec.). Yield 0.525 g (85%) for $TiCl_4$ (0.190 g) and of Q^B (0.556 g). F.W. = 2473.9 (a tetranuclear compound shown by X-ray diffraction[19]). M.W. ($CHCl_3$) = 2200 (0.5 10^{-2} M) (r = 0.89). $C_{34}H_{26}N_4O_5Ti$: calcd. C 66.03, H 4.24, N 9.06; found C 65.92, H 4.33, N 8.86. ^1H NMR ($CDCl_3$, 300 MHz, 293 K, ppm): δ = 1.3 m, 1.4 m, 1.6 m, 1.7 m (br) (6 H, 3-CH_3), 6.2 br, 6.5 br, 6.7 br, 7.0 br, 7.5 br, 8.0 br (20 H, C_6H_5). ^1H NMR ($CDCl_3$, 300 MHz, 324 K, ppm): δ = 1.3−1.8 (15 s, 6 H, 3-CH_3), 6.2 m, 6.3 m, 6.4 m, 6.6 m, 7.1 m, 7.2 m, 7.4 m, 7.6 m, 7.9 m, 8.0 m (20 H, C_6H_5). ^1H NMR ($CDCl_3$, 300 MHz, 218 K, ppm): 1.0−2.1 (25 s, 6 H, 3-CH_3), 6.0 m, 6.2 m, 6.3 m, 6.4 m, 6.6 m, 7.1 m, 7.2 m, 7.4 m, 7.6 m, 7.9 m, 8.0 m, 8.2 m, 8.8 d, 9.05 d br (20 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 1606 s, 1580 s, 1568 s, 1531 s (C···O, C···C and C···N), 554 m, 518 m, 504 m, 460 s, 448 vs, 410 sh, 398 s, 357 s (Ti−O). ESI-MS (MeCN) (+): *m*/*z* (%) = 301 (95) $[Na(HQ^B)]^+$, 924 (60) $[Na_4(Q^B)_3]^+$, 940 (95) $[Na_3K(Q^B)_3]^+$, 956 (60) $[Na_2K_2(Q^B)_3]^+$, 1856 (30) $[Ti_3(Q^B)_6O_3H]^+$, 1877 (30) $[NaTi_3(Q^B)_6O_3]^+$, 1894 (45) $[KTi_3(Q^B)_6O_3]^+$, 2497 (15) $[NaTi_4(Q^B)_8O_4]^+$. Alternatively, compound **1** can be obtained by treating $TiCl_4$ (1 mmol) with HQ^B (2 mmol) in CH_2Cl_2 in the presence of excess of KOH, or by direct reaction of $Ti(OR)_4$ (1 mmol, R= Me, Et or Bu) with HQ^B (at least 4 mmol).

$[(Q^T)_2Ti(O)(H_2O)]_n$ (2): Compound **2** was prepared by treating $Ti(OEt)_4$ with HQ^T [57] (1:4 ratio) under reflux in basic (KOH) ethanol. After 2 d, the solution was concentrated under vacuum and diethyl ether was then added. A yellow precipitate formed which was identified as compound **2**; yield 0.541 g (85%), m.p. 299−302 °C. For a monomeric unit F.W. is 636.56. $C_{32}H_{38}N_5O_6Ti$: calcd. C 61.54, H 6.46, N 8.97; found C 61.78, H 6.65, N 8.98. ^1H NMR ($CDCl_3$, 300 MHz, 293 K, ppm): δ = 1.0−1.6 (18 s, 22 H, CH_3 + CH_2), 2.4 (br m, 6 H 3-CH_3), 7.2 (br, 4 H, C_6H_5), 7.4 (br m, 2 H, C_6H_5), 7.8−8.1 (br m, 4 H, C_6H_5), 2.75 (s br, 2 H, H_2O). IR (Nujol mull, cm^{-1}): ṽ = 3176 (CH), 1602 s, 1595 sh, 1574 s, 1527 s (C···O, C···C, and C···N), 506 m, 474 s, 455 s, 411 w, 381 w, 363 w, 332 w, 287 m (Ti−O). ESI-MS (MeCN) (+): *m*/*z* (%) = 295 (95) $[Na(HQ^T)]^+$, 611 (15) $[Na_3(Q^T)_2]^+$, 629 (58) $[Na_2K(Q^T)_2]^+$, 645 (8) $[NaK_2(Q^T)_2]^+$, 1235 (30) $[Ti_2(Q^T)_4O_2H]^+$, 1257 (10) $[Ti_2(Q^T)_4O_2Na]^+$, 1274 (10) $[Ti_2(Q^T)_4O_2K]^+$, 1819 (10) $[Ti_3(Q^T)_6O_3H]^+$, 1842 (100) $[Ti_3(Q^T)_6O_3Na]^+$, 1858 (15) $[Ti_3(Q^T)_6O_3K]^+$.

$[(Q^A)_2Ti(O)(H_2O)]_n$ (3): Compound **3** was obtained by the reaction of $Ti(O\textit{n}Pr)_4$ with HQ^A [58] (1:2 ratio) in *n*PrOH, in the presence of KOH (4:1 ratio regarding Ti). The reaction mixture was stirred for 3 d. The resultant clear solution was then concentrated and the residue washed with diethyl ether and shown to be compound **3**; yield 0.566 g (81%), pale yellow, m.p. 235−238 °C. For a monomeric unit F.W. is 698.57. $C_{36}H_{34}N_4O_8Ti$: calcd. C 60.51, H 4.80, N 7.84; found C 60.32, H 5.0, N 7.51. ^1H NMR (D_2O, 200 MHz, 293 K, ppm): δ = 2.16 (s, 6 H, 3-CH_3), 3.78 (s, 6 H, OCH_3), 6.90 d, 4 H, C_6H_5), 7.19 (t, 2 H, C_6H_5), 7.23 (t, 4 H, C_6H_5), 7.5 (d, 4 H, C_6H_5), 7.58 (d, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 1603 s br, 1530 s br (C···O, C···C, and C···N), 598 s, 536 s br, 510 s, 442 m, 432 m, 422 sh, 388 w, 368 w, 325 m, 284 w.

$[(Q^N)_2Ti(O)(H_2O)]_n$ (4): The yellow compound **4** was obtained as for **3**, using HQ^N,[58] in 54% yield (0.402 g); m.p. 334 °C (dec.). For a monomeric unit F.W. is 744.52. M.W. ($CHCl_3$) = 2100 (2.1 10^{-2} M) (r = 2.82) $C_{34}H_{28}N_6O_{11}Ti$: calcd. C 54.85, H 3.79, N 11.29; found C 54.54, H 3.52, N 11.16. ^1H NMR (D_2O, 200 MHz, 293 K, ppm): δ = 2.19 (s, 6 H, 3-CH_3), 7.19 (t, 2 H, C_6H_5), 7.31 (t, 4 H, C_6H_5), 7.39 (d, 4 H, C_6H_5), 7.63 (d, 4 H, C_6H_5), 8.18 (d, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3200 br (OH) 1632 s br, 1592 s, 1500 sh br (C···O, C···C, and C···N), 566 w, 510 m, 448 m, 397 w, 376 w, 325 w, 303 w, 290 w, 279 w, 253 w, 247 w.

$[(Q^C)_2Ti(O)(H_2O)_2]_n$ (5): Compound **5** has been obtained as for **3** using HQ^C [59] and was washed with *n*-hexane to give the pale yellow product in 62% yield (0.413 g); m.p. 268 °C (dec.). For a monomeric unit F.W. is 666.61. $C_{34}H_{42}N_4O_7Ti$: calcd. C 61.26, H 6.35, N 8.40; found C 61.18, H 6.44, N 8.26. ^1H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 1.3 (br, 12 H, C_6H_{11}), 1.6−2.0 (br, 10 H, C_6H_{11}), 2.36 (s, 6 H, 3-CH_3), 2.75 (s, 4 H, H_2O), 6.90 (br, 2 H, C_6H_5), 7.20 (br, 4 H, C_6H_5), 7.53 (br, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3300 br (OH) 1624 s br, 1580 sh, 1530 s, 1500 sh br (C···O, C···C, and C···N), 511 s, 494 m, 448 s, 417 w, 381 m, 334 s, 280 w. ESI-MS (MeCN) (+): *m*/*z* (%) = 613 (10) $[Na_2H(Q^C)_2]^+$, 629 (15) $[NaKH(Q^C)_2]^+$, 920 (45) $[Na_3H(Q^C)_3]^+$, 936 (100) $[Na_2KH(Q^C)_3]^+$, 952 (80) $[NaK_2H(Q^C)_3]^+$, 1226 (10) $[Na_4H(Q^C)_4]^+$, 1241 (20) $[Na_3KH(Q^C)_4]^+$, 1257 (10) $[Na_2K_2H(Q^C)_4]^+$.

$[(Q^L)_2Ti(O)(H_2O)_2]_n$ (6): Compound **6** was obtained as described for **3** using HQ^L.[59] The residue formed was washed twice with light petroleum ether (40−60 °C) to give the pale yellow product in 49% yield (0.334 g); m.p. 80 °C (dec.). For a monomeric unit F.W. is 682.57. $C_{36}H_{34}N_4O_7Ti$: calcd. C 63.35, H 5.02, N 8.21; found C 63.18, H 4.97, N 8.32. ^1H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): 2.5 (br, 6 H, 3-CH_3), 3.85 (br, 4 H, CH_2), 6.90 (br, 8 H, C_6H_5), 7.20 (br, 8 H, C_6H_5), 7.7 (br, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3300 br (OH) 1632 s br, 1592 sh, 1500 sh br (C···O, C···C, and C···N), 591 w, 548 m, 500 m, 457 br, 327 m, 304 w. ESI-MS (MeCN) (+): *m*/*z* (%) = 315 (40) $[NaH(Q^L)]^+$, 331 (20) $[Na_2(Q^L)]^+$, 353 (25) $[NaK(Q^L)]^+$, 651 (25) $[Na_3(Q^L)_2]^+$, 667 (25) $[Na_2K(Q^L)_2]^+$, 683 $[NaK_2(Q^L)_2]^+$, 960 (35) $[Na_2KH(Q^L)_3]^+$, 976 (100) $[NaK_2H(Q^L)_3]^+$, 991 (22) $[K_3H(Q^L)_3]^+$, 1273 (10) $[Na_3KH(Q^L)_4]^+$, 1593 (55) $[Na_6(Q^L)_5]^+$, 1610 (75) $[Na_5K(Q^L)_5]^+$, 1626 (100) $[Na_4K_2(Q^L)_5]^+$, 1641 (80) $[Na_3K_3(Q^L)_5]^+$; (−): *m*/*z* (%) = 291 (100) $[Q^L]^-$, 605 (15) $[Na(Q^L)_2]^-$, 913 (5) $[Na_2(Q^L)_3]^-$, 1233 $[Na_3(Q^L)_4]^-$.

$[(Q^E)_2Ti(O)(H_2O)]_n$ (7): Compound **7** was obtained as described for **3** using HQ^E.[56] It was recrystallized as a colorless compound from $CHCl_3$/*n*-hexane (1:1) in 50% yield (0.335 g); m.p. 260−270 °C (dec.). For a monomeric unit F.W. is 670.54. $C_{34}H_{46}N_4O_7Ti$: calcd. C 60.89, H 6.91, N 8.35; found C 61.12, H 6.87, N 8.45. ^1H NMR (D_2O, 200 MHz, 293 K, ppm): δ = 0.73 (t, 6 H, CH_3), 1.17 (br, 12 H, CH_2), 1.46 (m, 4 H, CH_2), 2.21 (s, 6 H, 3-CH_3), 2.79 (pt, 4 H, CH_2), 7.16 (t, 2 H, C_6H_5), 7.22 (t, 4 H, C_6H_5), 7.33 (d, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3300 br (OH) 1624 s br, 1591 s, 1580 sh, 1500 sh br (C···O, C···C, and C···N), 512 m, 490 w, 464 w, 437 w, 390w, 386 w, 372 w, 330 w. ESI-MS (MeCN) (+): *m*/*z* (%) = 309 (100) $[NaH(Q^E)]^+$, 325 (40) $[NaK(Q^E)]^+$, 639 (20) $[Na_3(Q^E)_2]^+$, 926 (50) $[Na_3H(Q^E)_3]^+$, 942 (75) $[Na_2KH(Q^E)_3]^+$, 958 (50) $[NaK_2H(Q^E)_3]^+$, 1233 (5) $[Na_4H(Q^E)_4]^+$, 1249 (10) $[Na_3KH(Q^E)_4]^+$, 1267 (10) $[Na_2K_2H(Q^E)_4]^+$, 1845(65) $[Na_4KH_2(Q^E)_6]^+$, 1861 (80) $[Na_3K_2H_2(Q^E)_6]^+$.

$[(Q^P)_2Ti(O)(H_2O)]_n$ (8): Compound **8** was prepared by reaction of $Ti(OMe)_4$ with HQ^P [59] (1:4 ratio) in refluxing benzene. The resultant clear solution was concentrated under vacuum and the residue recrystallized twice from $CHCl_3$/*n*-hexane to give a colorless compound with an m.p. of 289−291 °C (dec.). For a monomeric unit F.W. is 786.68, yield 0.700 g (89%). $C_{46}H_{34}N_4O_6Ti$: calcd. C 70.23, H 4.36, N 7.12; found C 70.09, H 4.46, N 6.92. ^1H NMR ($CDCl_3$, 300 MHz, 293 K, ppm): 6.4−7.8 (m, 30 H, C_6H_5), 2.75 (s br, 2 H, H_2O). IR (Nujol mull, cm^{-1}): ṽ = 3400 br (OH) 1611 s br, 1565 s, 1514 s (C···O, C···C, and C···N), 562 m, 544 m, 522 m, 474 s, 443 s, 430 sh, 377 w, 340 m, 326 m, 305 m, 298 m, 280 m.

$(Q^B)_2Ti(OnPr)_2$ (9): The pale yellow compound **9** was prepared by treating $Ti(OnPr)_4$ with HQ^B [56] (1:2 ratio) in refluxing benzene under nitrogen. F.W. = 720.66; yield 0.612 g (85%), m.p. 97−105 °C (dec.). $C_{40}H_{40}N_4O_6Ti$: calcd. C 66.67, H 5.59, N 7.77; found C 67.00, H 5.89, N 7.52. M.W. ($CHCl_3$) = 450 (1.0 10^{-2} M) (*r* = 0.62). Λ_m (CH_2Cl_2, 1.0 10^3 M) = 0.3 $\Omega^{-1}\cdot mol^2\cdot cm^{-1}$. ^1H NMR ($CDCl_3$, 300 MHz, 293 K, ppm): δ = 0.9 (m, 6 H, CH_3), 1.3 (m, 4 H, CH_2), 1.95 (s, 6 H, 3-CH_3), 4.5 (t, 4 H, OCH_2), 7.0−8.0 (m, 20 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 1598 s, 1560 s, 1534 s, 1526 s, 1506 s (C···O, C···C, and C···N), 550 m, 513 m, 499 m, 462 s, 446 s, 410 w, 400 w, 360 m, 340 w, 320 w, 300 w (Ti−O).

$(Q^T)_2Ti(OMe)_2$ (10): The colorless compound **10** was prepared as described for **9**, using HQ^T,[57] in 85% yield (0.552 g), F.W. = 652.63, m.p. 190 °C (dec.). $C_{34}H_{44}N_4O_6Ti$: calcd. C 62.57, H 6.80, N 8.58; found C 62.73, H 6.89, N 8.79. ^1H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 0.6−1.3 (14 s, 18 H, CH_3), 1.8−2.6 (25 s, 10 H, 3-CH_3 + CH_2), 4.0−4.6 (10 s, 6 H, OCH_3), 6.7−8.3 (m, 10 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 1607 s, 1576 s, 1530 s (C···O, C···C, and C···N), 595 s, 581 s, 514 s, 506 s, 465 s, 394 w, 361 m, 335 m, 316 m, 284 m (Ti−O).

$(Q^T)_2Ti(OnPr)_2$ (11): Compound **11** was prepared by treating $Ti(OnPr)_4$ with HQ^T [57] (1:2 ratio) in refluxing benzene. After 24 h of stirring, the solution was completely concentrated under vacuum. No precipitate formed when a 1:1 diethyl ether/propyl alcohol solution was added, so the solution was again concentrated and the residue washed with *n*-hexane. A colorless oil formed that was identified as compound **11**; yield 0.604 g (85%). F.W. = 710.75; M.W. ($CHCl_3$). = 380 (1.0·10^{-2} M) (*r* = 0.53). Λ_m (CH_2Cl_2, 1.0·10^3 M), 1.0 10^3 M) = 0.2 $\Omega^{-1}\cdot mol^2\cdot cm^{-1}$. $C_{38}H_{54}N_4O_6Ti$: calcd. C 64.22, H 7.66, N 7.88; found C 63.80, H 7.52, N 7.76. ^1H NMR ($CDCl_3$, 300 MHz, 293 K, ppm): δ = 0.9 (m, 24 H, CH_3), 1.3 (br m, 6 H, CH_2), 1.6 (m, 4 H, CH_2), 2.4 (s, 3 H, 3-CH_3), 2.5 (s, 3 H, 3-CH_3), 4.5 (m, 4 H, OCH_2), 7.2 (t, 2 H, C_6H_5), 7.4 (t, 4 H, C_6H_5), 8.0 (d, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3193 w, 3060 m, 3048 m (CH), 1625 s, 1614 s, 1574 s, 1531 s (C···O, C···C, and C···N), 509 m, 471 s, 412 w, 394 m, 362 m, 339 sh, 314 w, 281 w.

$(Q^T)_2Ti(OnBu)_2(H_2O)$ (12): Compound **12** was prepared as described for **11**, using $Ti(OnBu)_4$ and HQ^T [57] to furnish a colorless oil in 80% yield (0.600 g), F.W. = 754.80. $C_{40}H_{58}N_4O_7Ti$: calcd. C 63.65, H 7.75, N 7.42; found C 64.00, H 7.89, N 7.52. ^1H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 0.5−1.7 (m, 34 H, CH_2 + CH_3), 2.0−2.7 (br m, 10 H, CH_2 +3-CH_3), 4.5 (m, 4 H, OCH_2), 7.2 (m, 2 H, C_6H_5), 7.4 (m, 4 H, C_6H_5), 7.7 (d, 2 H, C_6H_5), 8.0 (d, 2 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3430 br (OH), 3192 w, 3070 m, 3036 m (CH), 1625 s, 1615 s, 1593 s, 1574 s, 1531 s (C···O, C···C, and C···N), 509 m, 470 s, 410 w, 392 m, 364 m, 334 sh, 312 w, 281 w.

$[(Q^A)Ti(OH)_3(H_2O)]_n$ (13): This compound was obtained by treating $Ti(OEt)_4$ with HQ^A [58] (1:1 ratio) in EtOH, in the presence of KOH (4:1 ratio regarding Ti), for 4 h. After concentration of the resultant clear solution, a residue was obtained that was washed with *n*-hexane and shown to be compound **13**; pale yellow, m.p. 84−86 °C, yield 0.385 g (95%). For a monomeric unit F.W. is 406.23. $C_{18}H_{18}N_2O_6Ti$: calcd. C 53.22, H 4.47, N 6.90; found C 53.51, H 4.44, N 6.96. ^1H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 2.10 (s br, 3 H, 3-CH_3), 2.9 (br, 3 H, OH), 3.74 (br s, 3 H, OCH_3), 6.68 (t, 4 H, C_6H_5), 6.96 (d, 4 H, C_6H_5), 7.00 (d, 4 H, C_6H_5), 7.4 (t, 2 H, C_6H_5), 7.5 (d, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): ṽ = 3400−3100 br (OH), 1620 s br, 1600−1500 s br (C···O, C···C. and C···N), 539 m, 508 m, 480 m, 467 m, 362 w, 326 w.

$[(Q^C)Ti(OH)_3]_n$ (14]): This compound was obtained as described for **13**, using HQ^C,[57] as a colorless, m.p. 95−98 °C, in 73% yield (0.278 g). For a monomeric unit F.W. is 382.25. $C_{17}H_{22}N_2O_5Ti$:

calcd. C 53.42, H 5.80, N 7.33; found C 53.46, H 5.93, N 7.23. ^{1}H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 1.2 (br, 6 H, C_6H_{11}), 1.65 (br, 5 H, C_6H_{11}), 2.37 (s, 3 H, 3-CH_3) 2.74 (br, 2 H, O*H*), 7.0 (br, 3 H, C_6H_5), 7.6 (br, 2 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 324 K, ppm): δ = 1.2 m, 6 H, C_6H_{11}), 1.65 (br, 5 H, C_6H_{11}), 2.37 (br, 3 H, 3-CH_3) 2.8 (br, 1 H, O*H*), 4.0 (br, 2 H, OH), 7.0 (br, 2 H, C_6H_5), 7.1 (br, 1 H, C_6H_5), 7.6 (br, 2 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 273 K, ppm): δ = 1.2 (br, 5 H, C_6H_{11}), 1.67 (br, 5 H, C_6H_{11}), 2.34 (br, 3 H, 3-CH_3) 2.8 (br, 1 H, C_6H_{11}), 3.5 (br, 1 H, O*H*), 4.3 (br, 1 H, O*H*), 7.1 (br, 3 H, C_6H_5), 7.6 (br, 2 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 218 K, ppm): δ = 1.0 (m, 2 H, C_6H_{11}), 1.2 (m, 4 H, C_6H_{11}) 1.53 (m, 3 H, C_6H_{11}), 1.82 (s, 2 H, C_6H_{11}), 2.19, 2.24, 2.34, 2.39, 2.1, 2.47 (6 s, 3 H, 3-CH_3) 2.8, 2.9 (2 s br, 1 H, O*H*), 3.6 (br, 1 H, 3-CH_3), 6.6−7.6 (br, 3 H, C_6H_5), 7.9 (br, 2 H, C_6H_5). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 3400−3000 br (OH), 1620 s br, 1600−1550 s br, 1530 s (C···O, C···C, and C···N), 509 m, 470 m, 449 m, 361 w, 330 m, 281 w.

[(Q^B)Ti(OH)$_2$(O*n*Pr)](H$_2$O) (15): Compound **15** was obtained from the reaction of HQ^B [56] and Ti(O*n*Pr)$_4$ (1:1 ratio) in *n*PrOH at room temperature. After 12 h, a colorless precipitate (TiO_2) formed which was filtered off, and the resulting clear solution was concentarted and the residue extracted with $CHCl_3$. A green gel then formed which slowly converted into a green-black precipitate that was identified as compound **15**; F.W. = 436.30, yield 0.237 g (55%), m.p. 135−145 °C. $C_{20}H_{24}N_2O_6Ti$: calcd. C 55.06, H 5.54, N 6.43; found C 55.22, H 5.63, N 6.74. ^{1}H NMR (D_2O, 200 MHz, 293 K, ppm): 0.78 (t, 3 H, CH_3), 1.37 (m, 2 H, CH_2), 2.14 (s, 3 H, 3-CH_3), 3.48 (t, 2 H, CH_2), 7.1−7.6 (m, 5 H, C_6H_5). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 3400−3000 br (OH), 1621 s br, 1590 sh, 1530 s (C···O, C···C, and C···N), 543 m, 504 m, 418 m, 397 m, 374 w, 352 m, 326 br, 279 m. ESI-MS (MeCN) (+): *m*/*z* (%) = 323 (10) $[Na_2(Q^B)]^+$, 617 (15) $[NaKH(Q^B)]^+$, 917 (40) $[Na_2KH(Q^B)_3]^+$, 933 (100) $[NaK_2H(Q^B)_3]^+$, 1196 (10) $[Na_2KH_2(Q^B)_4]^+$, 1512 (100) $[Na_2K_2H_2(Q^B)_5]^+$, 1528 (45) $[NaK_3H_2(Q^B)_5]^+$, 1813 (60) $[Na_3K_2H_2(Q^B)_6]^+$, 1828 (45) $[Na_2K_3H_2(Q^B)_6]^+$.

[(Q^B)Ti(OH)$_2$(O*n*Bu)](H$_2$O) (16): Compound **16** was prepared in similar fashion to **15**, using HQ^B [56] and Ti(O*n*Bu)$_4$ to give a pale green gel in 95% yield (0.410 g); F.W. = 432.21, m.p. 88−92 °C (dec.). $C_{21}H_{24}N_2O_5Ti$: calcd. C 58.34, H 5.60, N 6.48; found C 58.22, H 5.78, N 6.38. ^{1}H NMR (D_2O, 200 MHz, 293 K, ppm): 0.78 (t, 3 H, CH_3), 1.37 (m, 2 H, CH_2), 1.41 (m, 2 H, CH_2), 2.16 (s, 3 H, 3-CH_3), 3.53 (t, 2 H, CH_2), 7.3−7.6 (m, 10 H, C_6H_5). ^{1}H NMR (D_2O, 200 MHz, 353 K, ppm): δ = 0.78 (t, 3 H, CH_3), 1.37 (m, 2 H, CH_2), 1.41 (m, 2 H, CH_2), 2.16 (s, 3 H, 3-CH_3), 3.53 (t, 2 H, CH_2), 7.3−7.6 (m, 10 H, C_6H_5).^{1}H NMR ($CDCl_3$, 300 MHz, 323 K): δ = 0.9 (t, 3 H, CH_3), 1.24 (br m, 2 H, CH_2), 1.49 (m, 2 H, CH_2), 2.11 (s, 3 H, 3-CH_3), 3.42 (t, 2 H, CH_2), 7.1 t, 7.4 t, 7.5 m, 7.6 d (br, 10 H, C_6H_5). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 3400−3000 br (OH), 1650 br (OH), 1624 s br, 1594 sh (C···O, C···C, and C···N), 545 m, 505 m, 4417 w, 407 w, 373 w, 357 w, 331 s, 279 m. ESI-MS (MeCN) (+): *m*/*z* (%) = 339 (18) $[NaK(Q^B)]^+$, 617 (10) $[NaKH(Q^B)]^+$, 917 (35) $[Na_2KH(Q^B)_3]^+$, 933 (100) $[NaK_2H(Q^B)_3]^+$, 949 (15) $[K_3H(Q^B)_3]^+$, 1512 (75) $[Na_2K_2H_2(Q^B)_5]^+$, 1528 (100) $[NaK_3H_2(Q^B)_5]^+$, 1544 (20) $[K_4H_2(Q^B)_5]^+$, 1813 (40) $[Na_3K_2H_2(Q^B)_6]^+$, 1828 (80) $[Na_2K_3H_2(Q^B)_6]^+$, 1846 (40) $[NaK_4H_2(Q^B)_6]^+$, 1861 (40) $[K_5H_2(Q^B)_6]^+$, 2128 (10) $[Na_3K_3H_2(Q^B)_6]^+$.

[(Q^L)Ti(O)(OH)]$_n$ (17): Compound **17** was obtained by the method described for **15**, using HQ^L,[59] and was recrystallized from $CHCl_3$/*n*-hexane as a pale-green compound in 80% yield (0.297 g), m.p. 100−110 °C (dec.). For a monomeric unit F.W. is 372.22. $C_{18}H_{16}N_2O_4Ti$: calcd. C 58.08, H 4.33, N 7.53; found C 57.80, H 4.45, N 7.43. ^{1}H NMR (D_2O, 200 MHz, 293 K, ppm): δ = 2.19 (s, 3 H, 3-CH_3), 4.16 (s, 2 H, CH_2), 7.21 (m, 6 H, C_6H_5), 7.3 (m, 4 H, C_6H_5). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 3400−3000 br (OH), 1650 br (OH), 1628 s br, 1594 sh, 1580 s (C···O, C···C, and C···N), 545 m, 501 m, 458 m, 446 w, 419 w, 398 m, 375 w, 357 w, 328 m, 311 m, 289 w, 276 m.

[(Q^E)Ti(O)(OH)]$_n$ (18): Compound **18** was also obtained as described for **15**, using HQ^E,[56] and was recrystallized from $CHCl_3$/*n*-hexane as the colorless product in 96% yield (0.350 g), m.p. 225−230 °C (dec.). For a monomeric unit F.W. is 366.25. $C_{17}H_{22}N_2O_4Ti$: calcd. C 55.75, H 6.05, N 7.65; found C 56.00, H 6.30, N 7.67. ^{1}H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 0.8−2.0 (m, 11 H, CH_3 + CH_2), 2.42 (m, 3 H, CH_3), 3.70 (m, 2 H, CH_2), 7.0−7.6 (m, 5 H, C_6H_5). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 3400−3000 br (OH), 1650 br (OH), 1624 s br, 1594 sh, 1580 s, 1518 s (C···O, C···C, and C···N), 512 m, 495 m, 464 m, 438 w, 397 w, 387 w, 349 w, 331 m. ESI-MS (MeCN) (+): *m*/*z* (%) = 309 (100) $[NaH(Q^E)]^+$, 325 (40) $[NaK(Q^E)]^+$, 639 (20) $[Na_3(Q^E)_2]^+$, 655 (10) $[Na_2K(Q^E)_2]^+$, 671 (10) $[NaK_2(Q^E)_2]^+$, 926 (10) $[Na_3H(Q^E)_3]^+$, 942 (20) $[Na_2KH(Q^E)_3]^+$, 958 (10) $[NaK_2H(Q^E)_3]^+$, 1233 (5) $[Na_4H(Q^E)_4]^+$, 1249 (10) $[Na_3KH(Q^E)_4]^+$, 1266 (10) $[Na_2K_2H(Q^E)_4]^+$, 1927 (50) $[NaTi_3(Q^T)_6O_3]^+$, 1943 (100) $[KTi_3(Q^T)_6O_3]^+$.

(Q^B)$_2$TiCl$_2$ (19): Compound **19** was obtained from the reaction between $TiCl_4$·$(THF)_2$ and NaQ^B [56] in anhydrous MeOH. A yellow precipitate formed that was filtered off, washed with MeOH, and shown to be compound **19**. F.W. = 673.39, yield 0.470 g (70%); M.W. ($CHCl_3$) = 650 ($1.0\cdot10^{-2}$ M) (r = 0.96), yellow-orange, m.p. 165−166 °C. $C_{34}H_{26}Cl_2N_4O_4Ti$: calcd. C 60.64, H 3.89, N 8.32; found C 60.83, H 4.0, N 8.07. ^{1}H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 1.0−2.2 (m, 6 H, 3-CH_3), 7.0−8.0 (m, 20 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 293 K, ppm): δ = 1.1−2.1 (14 m, 6 H, 3-CH_3), 6.9−7.4 (br m, 6 H, C_6H_5), 7.5 (3 t, 2 H, C_6H_5), 7.8 (t, 1 H, C_6H_5), 8.0 (m, 1 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 327 K, ppm): δ = 1.5−2.0 (br m, 6 H, 3-CH_3), 6.9−7.6 (br m, 8 H, C_6H_5), 8.0 (br, 2 H, C_6H_5). ^{1}H NMR (C_6D_6, 300 MHz, 283 K, ppm): δ = 1.5−2.0 (7 s, 6 H, 3-CH_3), 6.6−7.4 (br m, 6 H, C_6H_5), 8.0 d, 8.1 d, 8.4 t, 8.5 d, 8.6 d (4 H, C_6H_5). ^{1}H NMR (C_6D_6, 300 MHz, 303 K, ppm): δ = 1.5−2.0 (4 s, 6 H, 3-CH_3), 6.6−7.3 (br m, 6 H, C_6H_5), 8.0 br, 8.1 br, 8.4 br, 8.5 br, 8.6 br (4 H, C_6H_5). ^{1}H NMR (C_6D_6, 300 MHz, 328 K, ppm): δ = 1.6−1.9 (br, 6 H, 3-CH_3), 6.6−7.4 (br, 6 H, C_6H_5), 8.0 br, 8.3 br, 8.4 br (4 H, C_6H_5). ^{1}H NMR (C_6D_6, 300 MHz, 347 K, ppm): δ = 1.73 (s, 6 H, 3-CH_3), 6.9 (br, 6 H, C_6H_5), 7.2 (br, 2 H, C_6H_5), 8.2 (br, 2 H, C_6H_5). ^{13}C NMR (C_6D_6, 300 MHz, 293 K, ppm): δ = 15.91, 16.0, 16.3 (3 s, CH_3), 120.0, 121.0, 121.3, 121.4, 122.0, 122.1, 125.9, 126.7, 127.2, 127.7, 128.0, 128.1, 128.3, 128.7, 128.8, 128.9, 129.1, 129.5, 130.1, 131.0, 131.3, 131.9, 132.1, 132.6 (C_{arom}). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 3060 sh (CH), 1599 s br, 1584 s, 1574 s, 1561 s, 1553 s, 1552 s, 1518 s (C···O, C···C, and C···N), 567 br, 552 s, 517 s, 497 s, 462 m, 455 s, 376 m, 357 m, 321 w. ESI-MS (MeCN) (+): *m*/*z* (%) = 323 (10) $[Na_2(Q^B)]^+$, 623 (20) $[Na_3(Q^B)_2]^+$, 923 (10) $[Na_4(Q^B)_3]^+$, 1223 (10) $[Na_4(Q^B)_3]^+$, 1856 (30) $[Ti_3(Q^B)_6O_3H]^+$, 1878 (100) $[NaTi_3(Q^B)_6O_3]^+$, 1894 (45) $[KTi_3(Q^B)_6O_3]^+$, 2497 (40) $[NaTi_4(Q^B)_8O_4]^+$, 2514 (25) $[KTi_4(Q^B)_8O_4]^+$.

(Q^T)$_2$TiCl$_2$ (20): Compound **20** was obtained as described for **19**, using NaQ^T [57] to give the orange product in 55% yield (0.363 g). F.W. = 661.46, m.p. 189−192 °C. $C_{32}H_{38}Cl_2N_4O_4Ti$: calcd. C 58.11, H 5.79, N 8.47; found C 58.09, H 6.0, N 8.24. ^{1}H NMR ($CDCl_3$, 200 MHz, 293 K, ppm): δ = 0.7−1.3 (m, 18 H, CH_3), 1.7 (m, 4 H, CH_2), 2.5 (m, 6 H, 3-CH3), 6.4−8.2 (m, 10 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 218 K, ppm): δ = 0.2−1.2 (br m, 18 H,

CH_3), 1.3−1.8 (br m, 4 H, CH_2), 2.0−2.8 (br m, 6 H, 3-CH_3), 6.6−8.4 (m, 10 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 273 K, ppm): δ = 0.4−1.2 (21s, 18 H, CH_3), 1.4−2.0 (20s, 4 H, CH_2), 2.0−2.7 (18s, 6 H, 3-CH_3), 6.4−8.2 (m, 10 H, C_6H_5). ^{1}H NMR ($CDCl_3$, 300 MHz, 323 K, ppm): δ = 0.4−1.1 (15 s, 18 H, CH_3), 1.6 (br, 4 H, CH_2), 2.0−2.7 (10 s, 6 H, 3-CH_3), 6.6−8.1 (5 m br, 10 H, C_6H_5). IR (Nujol mull, cm^{-1}): $\tilde{\nu}$ = 1604 s br, 1569 s, 1525 s (C···O, C···C, and C···N), 507 s, 473 s, 455 s, 412 br, 377 s br, 361 m, 331 m, 287 m. ESI-MS (MeCN) (+): *m/z* (%) = 295 10) $[Na(HQ^T)]^+$, 629 (60) $[Na_2K(Q^T)_2]^+$, 1211 (50) $[Na_2K_2H(Q^T)_4]^+$, 1235 (45) $[Ti_2(Q^T)_4O_2H]^+$, 1257 (10) $[Ti_2(Q^T)_4O_2Na]^+$, 1274 (10) $[Ti_2(Q^T)_4O_2Na]^+$, 1820 (30) $[Ti_3(Q^T)_6O_3H]^+$, 1842 (100) $[Ti_3(Q^T)_6O_3Na]^+$, 1858 (15) $[Ti_3(Q^T)_6O_3K]^+$.

Theoretical Calculations: The structural features of Q_2TiX_2 compounds were analyzed as follows. Starting coordinates were obtained from the X-ray molecular structure of the tetranuclear compound[19] $[(Q^B)_2Ti\text{-}\mu\text{-}O]_4$; three $(Q^B)_2TiO$ units were eliminated and the two former O(oxo) atoms were converted into two OH groups by adding two H atoms. Calculations on this mononuclear molecule, $(Q^B)_2Ti(OH)_2$, were preformed with the Mulliken program[60] package using an IBM/SP2 supercomputer. The MB3LYPDFT (Density Functional Theory)[61] method was used and the basis set was 6-31G*. For the titanium atom an ECP approximation[62−70] was applied, as implemented within MULLIKEN, using a double zeta basis. The starting structure was very far from that of the energy minimum reached because of the strain in the original tetranuclear molecule,[19] where *trans* O−Ti−O bond angles were as low as 163°, *cis* O(oxo)−Ti−O(oxo) bond angles were about 100° and Ti−O(oxo)−Ti bond angles were as wide as 154° − very far from the regular angle subtended at an oxygen atom. Consequently, the minimization process took about 45 d. After convergence, the H atoms in the two OH groups were replaced by methyl groups, and the two Ph groups (R^4) were replaced by neopentyl groups. This conformer, *cis*-$[(Q^T)_2Ti(OCH_3)_2]$, named CIS1, was minimized with the Accelrys program Cerius 2.4.6, subroutine DMol3,[71] using an Octane SGI computer. Standard local density was the VWN[72] functional and full geometric optimization was performed using a double numeric basis set with polarization functions (DNP)[73] on all atoms. The two other feasible *cis* isomers were analyzed after modifying the Q^T positions accordingly, and energy-minimized; these two conformers are named CIS2 and CIS3. The structure of $(Q^B)_2Ti(OH)_2$, converged with MULLIKEN, was also minimized with DMol3 and gave the same structural parameters in the coordination sphere. A related process was performed to study (a) $(Q^T)_2TiCl_2$ conformers, i.e., replacement of methoxy groups by Cl atoms in $(Q^T)_2Ti(OCH_3)_2$; (b) $(Q^B)_2Ti(OCH_3)_2$ replacing neopentyl groups by Ph groups in $(Q^T)_2Ti(OCH_3)_2$; (c) the anion $[(Q^T)_2Ti(OCH_2CH_2CH_3)_2]^-$, whose coordinates were obtained from $(Q^T)_2Ti(OCH_3)_2$ by replacing a H with a CH_2CH_3 group in each methoxy group.

Voltammetry: Electrochemical measurements were performed in a conventional three-compartment cell with three electrodes. The working electrode was vitreous carbon, the counter electrode was a platinum wire, and the reference electrode was saturated calomel. Ferrocene was used as an internal reference potential. The complex concentration was $1\cdot10^{-3}$ M, the solvent was *N*,*N*-dimethylformamide (Merck), used without further purification, and the support electrolyte was $1\cdot10^{-1}$ M tetraethylammonium perchlorate. The cyclic voltammograms were recorded with a PAR173 potentiostate/galvanostate coupled to a PAR175 universal potential programmer and a Graphtec WX4301 XY recorder.

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