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Syntheses and characterization of titanium malonato and amino acid complexes: $[Ti(cp^*)_2(OOCCH_2NMe_2)]$ – The first structurally characterized α-amino acid titanium(III) complex

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Abstract

The reaction of $[Ti(cp^*)_2(BTMSA)]$ (**1**) ($cp^* = \eta^5$-C_5Me_5, BTMSA = bis(trimethylsilyl)acetylene) with malonic acids ($(HOOC)_2CR_2$, R = H, Me) and *N*,*N*-dimethylglycine resulted in the formation of titanium(IV) dicarboxylato complexes $[Ti(cp^*)_2\{(OOC)_2CR_2\}]$ (R = H, **2**; R = Me, **3**) and an α-amino acid titanium(III) complex $[Ti(cp^*)_2(OOCCH_2NMe_2)]$ (**4**). The identities of complexes **2**–**4** were confirmed by microanalysis, ^1H and ^{13}C NMR spectroscopy (**2**, **3**), ESI-MS and CID experiments (**2**, **3**) as well as by ESR and magnetic measurements ($\mu_{eff} = 1.81$, 298 K) for **4**. Single X-ray diffraction analyses of **2** and **4** exhibited monomolecular complexes in which the titanium atom is distorted tetrahedrally coordinated by two η^5-C_5Me_5 rings and by the chelating bound malonato-κ^2O,O' (**2**) and *N*,*N*-dimethylglycinato-κ^2O,O' ligand (**4**).

Keywords: Titanium complexes; α-Amino acid; Malonic acid; κ^2O,O' coordination; ESI-MS; Crystal structure

1. Introduction

Titanium and its coordination compounds become ever more important in medicine especially due to the antitumor activity of some titanium complexes such as *cis*-diethoxybis(1-phenylbutane-1,3-dionato)titanium(IV) (''*Budotitane*'') [1]. Furthermore, due to the relative low toxicity of the $[Ti(cp)_2]^{2+}$ unit ($cp = \eta^5$-C_5H_5), titanocene dichloride $[Ti(cp)_2Cl_2]$ is a leading substance in the class of antitumor bis(cyclopentadienyl)metal complexes [2,3]. To understand the mode of operation it is useful to synthesize titanium complexes with bioligands.

Thus, coordination compounds of titanium with amino acid ligands came into the focus of interest [4,5]. Overall, only a few complexes could be structurally characterized, namely the complexes $[\{Ti(OEt)_2(OOCCH_2NH_2$-$\kappa^2O,N)\}_2$-$(\mu$-$EtO)_2]$ [6], $[Ti(C_5H_4Me)_2(OOCCH_2NMeH_2$-$\kappa O)_2]Cl_2$ [7] and $[Ti(cp)_2(Haa$-$\kappa O)_2]Cl_2$ (Haa = L-methionine [8], 2-methylalanine [9]). Bis(cyclopentadienyl)titanium complexes with amino acid ligands have been prepared mainly by reactions of $[Ti(cp)_2Cl_2]$ with amino acids or their alkaline salts in protic solvents [10]. To the best of our knowledge, the complex $[Ti(cp^*)_2(BTMSA)]$ (**1**) ($cp^* = \eta^5$-C_5Me_5, BTMSA = bis(trimethylsilyl)acetylene) has not yet been used as starting complex for the synthesis of dicarboxylato and amino acid complexes although complex **1** proved to be easily accessible and was found to undergo a broad variety of reactions especially C–C coupling reactions with alkynes

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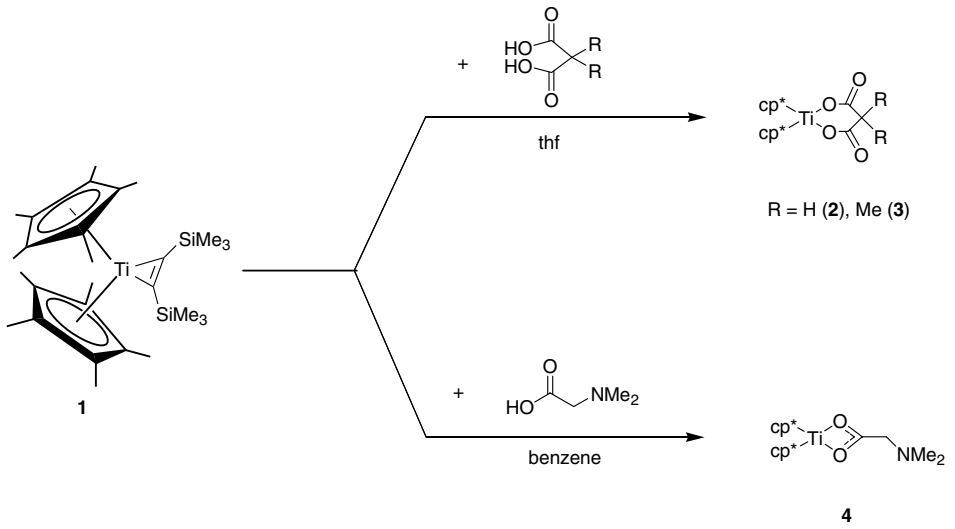

Scheme 1.

and alkenes [11,12]. Furthermore, reactions of **1** with water or methanol proceeded with the formation of hydroxy or methoxy complexes of titanium(IV) [13]. Here, we report the reactivity of [Ti(cp*)$_2$(BTMSA)] (**1**) with malonic acids $(HOOC)_2CR_2$ (R = H, Me) and with the α-amino acid *N*,*N*-dimethylglycine yielding malonato titanium(IV) complexes and, unexpectedly, a *N*,*N*-dimethylglycinato titanium(III) complex, respectively, being the first structurally characterized titanium(III) α-amino acid complex.

2. Results and discussion

2.1. Syntheses and characterization

[Ti(cp*)$_2$(BTMSA)] (**1**) was found to react with malonic acid and dimethylmalonic acid in tetrahydrofuran at room temperature yielding the malonato titanium(IV) complexes **2** and **3**, respectively (Scheme 1). Complexes **2** and **3** were obtained in good yields as brown-reddish small crystals that can be handled on air for a short time. On the other hand, the reaction of [Ti(cp*)$_2$(BTMSA)] (**1**) with *N*,*N*-dimethylglycine in benzene at room temperature yielding the *N*,*N*-dimethylglycinato titanium(III) complex **4** (Scheme 1). Complex **4** was obtained in 60% yield as grass-green powder that underwent decomposition on air within seconds forming a yellowish-brown powder. As revealed by GC–MS experiments of the reaction solutions, the BTMSA ligand is not only simply cleaved off yielding $Me_3SiC{\equiv}CSiMe_3$ (**5**) but also the corresponding alkenes (*E*)- and (*Z*)-$Me_3SiCH{=}CHSiMe_3$ (**6**). Forming complexes **2** and **3**, the ratios **5**:(*Z*)-**6** ≈ 6–8:10 were found, whereas in reaction solution of **4** ratio **5**:(*Z*)-**6**:(*E*)-**6** ≈ 10:1:0.3 was found.

The identities of the complexes **2** and **3** were confirmed by microanalysis, thermogravimetry, ESI mass spectrometry, NMR and IR spectroscopy as well as by single-crystal X-ray diffraction analysis (**2**). Both in the ^{1}H and ^{13}C NMR spectra, the cp* ligands exhibited singlet resonances in the expected range [14]. The intensities of the cp* protons and those of the malonato ligands gave evidence for the 2:1 stoichiometry of the complexes that indicates the chelate bonding (κ^2O,O') of the malonato ligands as it was definitely proved by the structural investigation of **2**. The coordination of the malonato ligands is also reflected in the shift of the ν_{CO} vibrations of the malonato ligands from 1740/1717 cm^{-1} to 1655/1628 cm^{-1} for complex **2** and from 1705/1696 cm^{-1} to 1595/1562 cm^{-1} for **3**.

Thermogravimetric investigations on **2** and **3** exhibited a different thermal stability. The decomposition starts at ca. 190 °C (**2**) and 100 °C (**3**) in an exothermic step likely with the loss of the cp* ligands. Mass spectra of the two malonato complexes **2** and **3** were obtained by ESI-MS analyses using solutions of the complexes in methanol. In both cases the mass peaks of the protonated molecular cations $[Ti(cp^*)_2\{(OOC)_2CR_2\}]H^+$ (R = H, **2**; R = Me, **3**) were detected as the most intensive peaks in the spectra[1], showing an isotopic envelope characteristic of monocations containing one titanium atom [natural isotopic composition: ^{46}Ti (8.0%), ^{47}Ti (7.3%), ^{48}Ti (73.8%), ^{49}Ti (5.5%) and ^{50}Ti (5.4%)]. The observed values are in good agreement with the calculated ones. Furthermore, collision-induced dissociation (CID) experiments of the isolated parent ions (see Fig. 1 for **3** as an example) showed a stepwise fragmentation by the loss of malonic acid anhydride and water yielding the daughter ions **7** and **8** (Scheme 2). The further dissociation of the daughter ion **7** (*m*/*z* 335) to the product ion **8** (*m*/*z* 317) was confirmed by independent MS^3 experiments, showing the exclusive formation of **8** from isolated **7** under CID conditions. Most likely, complex cation **8** is a η^5:η^1-(tetramethylfulvene)titanium(IV) cation $[Ti(cp^*)(\eta^5{:}\eta^1\text{-}C_5Me_4CH_2)]^+$. Complexes of this type are well known, both of titanium(III) ($[Ti(cp^*)(\eta^5{:}\eta^1\text{-}C_5Me_4CH_2)]$ [15]) and titanium(IV) ($[Ti(cp^*)(\eta^5{:}\eta^1\text{-}C_5Me_4CH_2)Cl]$ [16]).

[1] Cations of type $[M+Na]^+$ and clusters ($[2M+H]^+$, $[2M+Na]^+$) were also detected.