

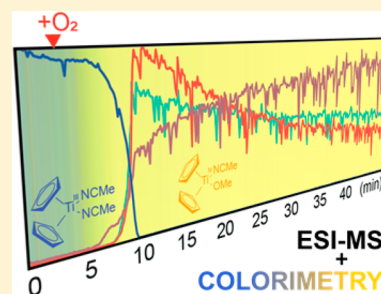
# Oxidation of Titanocene(III): The Deceptive Simplicity of a Color Change

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## S Supporting Information

**ABSTRACT:** Reduction of red  $\text{Cp}_2\text{TiCl}_2$  ( $\text{Cp}$  = cyclopentadienyl) with zinc dust in acetonitrile produces a blue solution of  $[\text{Cp}_2\text{Ti}(\text{NCMe})_2]^+$ , which when exposed to air rapidly discolors to bright yellow. This behavior makes the blue solution a handy visual indicator for the presence of oxygen, but the chemistry is considerably more complicated than the primary colors suggest at first glance. Real-time mass spectrometric and colorimetric analysis reveals that oxidation from Ti(III) to Ti(IV) produces a host of oxygen-containing complexes, whose appearance parallels the observed color changes.

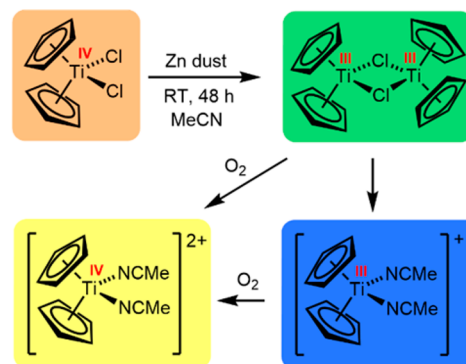


## INTRODUCTION

Titanocenes  $\text{Cp}_2\text{Ti(IV)X}_2$  ( $\text{Cp}$  = cyclopentadienyl) have been used for a wide variety of applications ranging from polymerization chemistry<sup>2</sup> to cancer research<sup>3,4</sup> to organic synthesis.<sup>5–7</sup> In situ (synthetic or electrochemical) reduction to the Ti(III) analogue has also been reported, and several examples of its use in radical-initiated catalysis have been described.<sup>8–10</sup> Because of this, the reduction of  $\text{Cp}_2\text{Ti(IV)X}_2$  to  $\text{Cp}_2\text{Ti(III)X}_y$  ( $y = 1$  or  $2$ ,  $X$  = halide or donating solvent) has been studied in detail.<sup>11–13</sup> The reverse reaction, oxidation of Ti(III) to Ti(IV), is sometimes used as an alternative to  $\text{O}_2$  sensors in gloveboxes. The oxidation of the reduced dark blue Ti(III) species,  $[\text{Cp}_2\text{TiX}_2]^+$ , to its yellow decomposition product functions as a sensitive and colorful indicator.<sup>14</sup> The transformation responsible for the various colors observed from the initial reduction of  $\text{Cp}_2\text{Ti(IV)Cl}_2$  to the Ti(III) species and back to the oxidized Ti(IV) product has been reported as a straightforward reaction. The Cl-bridged  $\text{Cp}_2\text{Ti}(\mu\text{-Cl})_2\text{TiCp}_2$  (green) and/or the cationic  $[\text{Cp}_2\text{Ti}(\text{NCMe})_2]^+$  (blue) are oxidized to form the yellow  $[\text{Cp}_2\text{Ti}(\text{NCMe})_2]^{2+}$  (Scheme 1).

Given the strong oxophilicity of titanium, the highest of all d-block elements (for the +IV oxidation state; the +III state less so), it seems likely that the oxidation of  $[\text{Cp}_2\text{Ti}(\text{NCMe})_2]^+$  is more complicated than Scheme 1 suggests.<sup>15</sup> As the presumed reactive species carries a charge, electrospray ionization mass spectrometry (ESI-MS) is well-suited for analyzing this reaction. The combination of real-time reaction monitoring methods (pressurized sample infusion)<sup>16</sup> with ESI-MS under anaerobic conditions<sup>17</sup> can conveniently be applied to study the decomposition process and product distribution. Further coupling of ESI-MS with real-time orthogonal methods would allow for a more complete picture of the occurring chemistry.<sup>18</sup> The vivid color change in this reaction offers the chance to apply a simple colorimetric analysis to match the reaction appearance and the speciation changes over time.<sup>19</sup>

## Scheme 1. Synthesis and Subsequent Oxidation of $[\text{Cp}_2\text{Ti(III)(NCMe)}_2]^+$



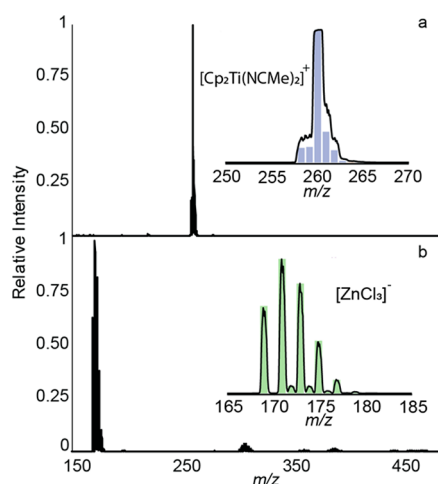
<sup>a</sup>Species colored as proposed by ref 14.

## RESULTS AND DISCUSSION

The synthesis of  $[\text{Cp}_2\text{Ti(III)(NCMe)}_2]^+$  is straightforward via zinc dust reduction of  $\text{Cp}_2\text{TiCl}_2$  in acetonitrile.<sup>14</sup> Because of the high sensitivity of  $[\text{Cp}_2\text{Ti(III)(NCMe)}_2]^+$ , concentration was kept as high as possible (5 mM) while avoiding saturation effects in ESI-MS. The positive-ion ESI-MS spectrum shows just one Ti-containing signal, which can be assigned to the  $[\text{Cp}_2\text{Ti(III)(NCMe)}_2]^+$  ion (Figure 1a). Two sodium adducts of acetonitrile,  $[\text{Na}(\text{NCMe})_n]^+$ ,  $n = 2$  or  $3$ , appear at low mass and are a common feature in the ESI-MS spectra of acetonitrile solutions.<sup>20</sup> Previous studies of this system have described the formation of a bimetallic chloro-bridged Ti - Zn species  $\text{Cp}_2\text{Ti}(\mu\text{-Cl})_2\text{Zn}(\mu\text{-Cl})_2\text{TiCp}_2$  upon zinc reduction of  $\text{Cp}_2\text{TiCl}_2$ , which we do not observe.<sup>11,21</sup> The negative-ion

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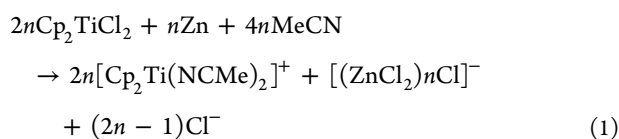
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**Figure 1.** Full spectrum of the acetonitrile solution generated by reduction of  $\text{Cp}_2\text{TiCl}_2$  with zinc dust in positive (top) and negative (bottom) ion modes.

spectrum shows zincate anions of the form  $[(\text{ZnCl}_2)_n\text{Cl}]^-$  ( $n = 1, 2, 3$ , Figure 1b). These results concur with the work reported by Stephan and co-workers.<sup>22a</sup> Daasbjerg and Skrydstrup have examined  $\text{Cp}_2\text{TiX}_2$  reduction by Zn in tetrahydrofuran (THF) by cyclic voltammetry and kinetic studies, and found a mixture of  $\text{Cp}_2\text{TiX}$ ,  $(\text{Cp}_2\text{TiX})_2$ , and  $[\text{Cp}_2\text{Ti}]^+$  to be present, though detected none of the cation for  $\text{X} = \text{Cl}$ .<sup>22b</sup> However, when the more coordinating hexamethylphosphoramide (HMPA) solvent was added, the dimeric species broke up, and we suspect something similar is operative in these acetonitrile studies.<sup>22c</sup>

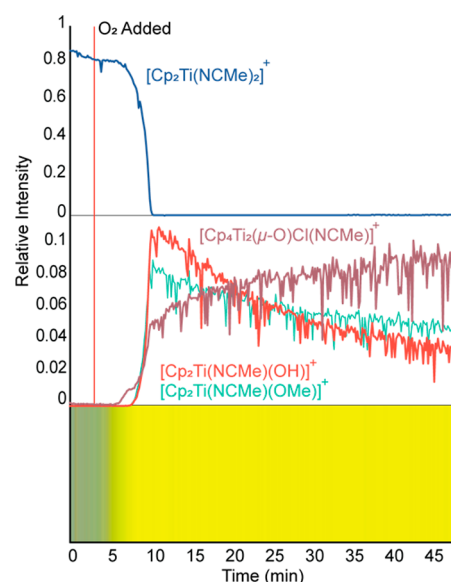
This observation is readily explicable, as the zinc is not only responsible for the reduction of Ti(IV) to Ti(III), but the resulting  $\text{Zn}^{2+}$  ions can also sequester some of the chloride ions produced in the process; that is, the overall reaction can be written as shown in eq 1.



Close inspection of the low-abundance, high-mass anionic species also reveals small quantities of  $[(\text{ZnO})_4\text{Cl}]^-$  and  $[(\text{ZnCl}_2)_2(\text{ZnO})\text{Cl}]^-$  (see Supporting Information Figure S1), with the ZnO presumably coming from surface oxidation of the zinc dust.

To follow the oxygenation of  $[\text{Cp}_2\text{Ti}(\text{III})(\text{NCMe})_2]^+$   $[(\text{ZnCl}_2)_n\text{Cl}]^-$  ( $n = 1-3$ ), the acetonitrile solution was connected to the ESI-MS via PEEK tubing, pressurized with argon, and monitored in the positive ion mode until a stable signal was obtained. An oxygen-saturated acetonitrile solution was infused (1 equiv over 15 min), resulting in changes in speciation (Figure 2). The  $[\text{Cp}_2\text{Ti}(\text{III})(\text{NCMe})_2]^+$  signal has fully disappeared 7 min after  $\text{O}_2$  addition, as half an equivalent is required to fully oxidize the complex. The expected color change also occurred, with the solution changing from blue to bright yellow.

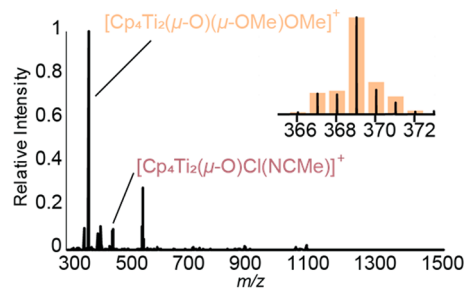
Three low-mass Ti(IV) derivatives were the most abundant products of the reaction, and their masses could be assigned to  $[\text{Cp}_2\text{Ti}(\text{NCMe})(\text{OH})]^+$ ,  $[\text{Cp}_2\text{Ti}(\text{NCMe})(\text{OMe})]^+$ , and  $[\text{Cp}_4\text{Ti}_2(\mu\text{-O})\text{Cl}(\text{NCMe})]^+$ . No sign of the putative oxidized  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})_2]^{2+}$  ion was observed, either as the 2+ ion



**Figure 2.** Real-time oxidation of  $[\text{Cp}_2\text{Ti}(\text{III})(\text{NCMe})_2]^+$ : parent Ti(III) cation (top), traces of main oxidation products formed as obtained by ESI-MS (middle), and colorimetric trace (bottom).  $\text{O}_2$  added as 1 equiv in solution over a time period of 15 min.

itself or as the charge-reduced ion pair with an anion (e.g.,  $\{[\text{Cp}_2\text{Ti}(\text{NCMe})_2]^{2+} + [(\text{ZnCl}_2)_n\text{Cl}]^-\}$ ). The lack of this observation does not rule out its participation; rather, if it does form, its existence is fleeting due to very high reactivity. Its reactivity is so high that it scavenges even trace levels of water and methanol, deprotonating them and leading to hydroxy and methoxy complexes as observed in the most abundant product species. Any decomposition process that leads to a neutral or insoluble byproduct will *not* be detected by ESI-MS, but if such processes are active it means that our analysis is underestimating the complexity of the product mixture. There is evidence that the reaction does generate insoluble byproducts, as a yellow precipitate eventually settles out of solution. The precipitate was later analyzed by redissolution in methanol, revealing only  $[\text{ZnCl}_3]^-$  in the negative ion mode but no titanium-containing species in the positive ion mode (see Supporting Information Figure S2). These results suggest the yellow solid is predominantly a complex mixture of high molecular weight species and/or neutral species.

To further confirm the identity of the aforementioned low-mass ions as well as the less-abundant high-mass ions, high-resolution Orbitrap mass spectrometric analysis was conducted (Figure 3). As the orbitrap instrument is not kept under anaerobic conditions, additional species appeared that were not



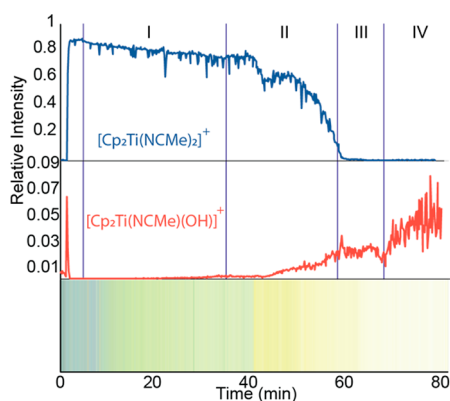
**Figure 3.** High-resolution orbitrap mass spectrum of oxidized titanocene species 300–1500 Da region.

observed in the anaerobic triple quadrupole detector mass spectrometer (TQD) environment. The orbitrap spectrum is dominated by  $[\text{Cp}_2\text{Ti}(\text{NCMe})(\text{OR})]^+$  ( $\text{R} = \text{H}$  or  $\text{Me}$ ; see Supporting Information Figure S8). Both species are also observed during the TQD experiments, but their enhanced presence is most likely due to the regular exposure of air,  $\text{H}_2\text{O}$ , and methanol of the orbitrap. Indeed, if  $\text{H}_2\text{O}$  or  $\text{MeOH}$  are added during oxidation formation of Ti-OR complexes is increased (see Supporting Information Figure S3). The formation is not unexpected, as Ti-OR compounds are well-known, and these types of interactions are important in the free-radical chemistry of Ti(III) complexes.<sup>23</sup>

All the high-mass species observed in both instruments are titanocene clusters containing bridging oxygen, and none of them exceeded 10% of the abundance of the Ti(III) complex from which they are derived (see Supporting Information Table T1). The formation of Cp-titanium oxide species is in line with the wide variety of titanium oxide-based clusters that have been reported over the years. Examples of this include the oxo-bridged  $\text{Cp}_2\text{Ti}(\mu\text{-O})\text{TiCp}_2$ ,<sup>24</sup>  $\text{Cp}_2(\text{Cl})\text{Ti}(\mu\text{-O})\text{Ti}(\text{Cl})\text{Cp}(\mu\text{-O})\text{Ti}(\text{Cl})\text{Cp}_2$ ,<sup>25</sup>  $\{[\text{Cp}^*\text{Ti}(\mu\text{-O})]_3(\mu_3\text{-N})\}$ ,<sup>26</sup>  $[\text{CpTiCl}(\mu\text{-O})]_4$ ,<sup>27</sup>  $(\text{Cp}^*\text{Ti})_4(\mu\text{-O})_6$ ,<sup>28</sup>  $(\text{CpTi})_6(\mu_3\text{-O})_8$ ,<sup>29</sup>  $(\text{CpTi})_8(\mu\text{-O})_{12}$ ,  $6\text{MeCN}$ ,<sup>30</sup> among many others.<sup>31</sup>

Aside from  $[\text{Cp}_4\text{Ti}_2(\mu\text{-O})\text{Cl}(\text{NCMe})]^+$  (presumably arising from trace chloride) all the abundant monocationic product species contain one or more OR ( $\text{R} = \text{H}$  or  $\text{Me}$ ) groups and have a  $[\text{Cp}_v\text{Ti}(\text{IV})_w\text{O}_x(\text{OR})_y(\text{NCMe})_z]^+$  type of molecular formula. Because of the instrument maintenance and cleaning protocols trace amounts of methanol cannot be excluded, and these may account for the  $-\text{OMe}$  groups observed, although that seems unlikely, as no OR species are observed before oxidation. All attempts to reduce the formation of OMe-containing species through extra drying and rinsing steps were unsuccessful. To test if trace amounts of  $\text{H}_2\text{O}$  and methanol were themselves primarily responsible for the observed OR-containing species we intentionally hydrolyzed  $[\text{Cp}_2\text{Ti}(\text{III})(\text{NCMe})_2]^+$  (Figure 4).

An acetonitrile solution of water (2 mM) was added to the titanocene solution in the same manner as for the oxygenation. A slow color change could be observed indicating slow transformation of the Ti(III). Further addition of water and addition of oxygen accelerated the oxidation and the formation



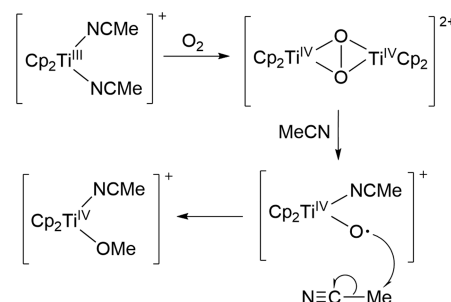
**Figure 4.** ESI-MS reaction trace for the hydrolysis of  $[\text{Cp}_2\text{Ti}(\text{NCMe})_2]^+$ . (I) addition of 0.1 equiv of  $\text{H}_2\text{O}$ ; (II) addition of 125 equiv of  $\text{H}_2\text{O}$ ; (III) addition of 10 000 equiv of  $\text{H}_2\text{O}$ ; (IV) sparging of reaction mixture with  $\text{O}_2$ . Note that some of the color change observed is actually dilution, due to the large volume of added solvent.

of the singly charged, Ti(IV) species  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})(\text{OH})]^+$ . The abundance of water suppressed formation of other product species. Figure 4 demonstrates clearly the relative insensitivity of the Ti(III) species to water. It takes almost 125 equiv before  $[\text{Cp}_2\text{Ti}(\text{III})(\text{NCMe})_2]^+$  signal has completely disappeared, and there is only limited  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})(\text{OH})]^+$  formation before  $\text{O}_2$  addition. Interestingly, more  $[\text{Cp}_2\text{Ti}(\text{NCMe})(\text{OH})]^+$  is formed after  $\text{O}_2$  addition, even though no Ti(III) precursor remains.

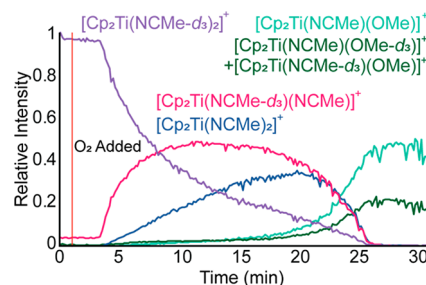
Presumably the presence of oxygen enables a plethora of other reaction pathways leading to the formation of OH- and OMe-containing clusters. This observation stands in stark contrast to the rapidity of the reaction with oxygen. Experimentalists using the Ti(III) complex as an indicator of a poor atmosphere are probably aware it probes only the presence of  $\text{O}_2$ , and these experiments are a graphic confirmation of this suspicion.

The formation of methoxide complexes could also arise through a different route than trace contamination: radical abstraction of a methyl group from acetonitrile by a radical intermediate.<sup>32</sup> Titanocenes are known to facilitate radical-initiated catalysis.<sup>1,13,23</sup> Therefore, a possible hypothesis for the formation of  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})(\text{OMe})]^+$  is a radical  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})(\text{O}\cdot)]$  intermediate that could abstract  $\text{CH}_3$  from the acetonitrile (Scheme 2).

#### Scheme 2. Proposed Radical Generation of Methoxide Ligand



A deuterium labeling experiment was performed to test this hypothesis.  $\text{Cp}_2\text{Ti}(\text{NCMe-}d_3)_2$  was synthesized and oxidized in the same manner as described earlier. As soon as the oxygen-saturated acetonitrile solution was added, exchange of NCMe- $d_3$  by NCMe in the coordination sphere of the metal center was observed (Figure 5). Two main mass spectrometric signals were detected upon oxidation corresponding to  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})(\text{OMe})]^+$  and  $[\text{Cp}_2\text{Ti}(\text{IV})(\text{NCMe})(\text{OMe-}d_3)]^+$  or



**Figure 5.** Real-time oxidation of  $[\text{Cp}_2\text{Ti}(\text{III})(\text{NCMe-}d_3)_2]^+$ : traces of parent Ti(III) cation and main oxidation products formed.  $\text{O}_2$  added as 1 equiv in solution over a time period of 15 min.

$[\text{Cp}_2\text{Ti(IV)(NCMe-}d_3\text{)(OMe)}]^+$ , respectively. MS/MS data confirmed the presence of both  $\text{NCMe-}d_3$  (loss of that neutral molecule) and  $\text{OMe-}d_3$  (loss of unlabeled  $\text{NCMe}$ ) indicating that the reaction proceeds, at least partially, via radical formation, because any trace methanol present would not generate any  $-\text{OMe-}d_3$  ligands.

That the reaction to form  $-\text{OMe}$  ligands does not seem to proceed at an appreciable rate until nearly all of the  $\text{NCMe-}d_3$  was substituted is a curious feature, and we plan to investigate this radical chemistry in more detail in the near future. The fact that ESI-MS is unperturbed by the existence of radical species is an advantageous property when it comes to the examination of these systems.

## CONCLUSION

In conclusion, real-time orthogonal ESI-MS/colorimetric analysis of  $[\text{Cp}_2\text{Ti(NCMe)}_2]^+$  reactivity allowed the distinctive color changes to be mapped to changes in speciation as established by ESI-MS. The supposedly simple oxidation of the titanium(III) complex turns out to generate an array of oxygen-containing di- and trimeric products, and if the solvated mononuclear dicationic Ti(IV) complex does form, it is reactive and immediately reacts with either trace protic solvents to provide species of the form  $[\text{Cp}_2\text{Ti(IV)(OR)(NCMe)}]^+$  or by a reaction in which an oxygen radical abstracts a methyl group from acetonitrile (the existence of this pathway was proved by isotopic labeling and MS/MS studies). Reactivity of  $[\text{Cp}_2\text{Ti(NCMe)}_2]^+$  with water was slow and required many equivalents of  $\text{H}_2\text{O}$  to be added to cause appreciable decomposition.

## EXPERIMENTAL SECTION

**General Considerations.** All experiments were performed under an inert atmosphere using standard Schlenk and glovebox techniques. Acetonitrile (reagent grade, Caledon Laboratories) was dried over  $\text{CaH}_2$  and distilled prior to use. Acetonitrile- $d_3$  (Sigma-Aldrich) was used without further purification.  $\text{Cp}_2\text{TiCl}_2$  (Sigma-Aldrich) and zinc dust (325 mesh, Anachemia) were used without further purification. Glass fiber syringe filters (0.45  $\mu\text{m}$ , Whatman) were dried prior to use.

The colorimetric chronograph was constructed using an in-house built software "ColorPixel", whereby time-lapse photography of the reaction captured via smartphone was processed to get the final chronograph.

All ESI-MS spectra were recorded using a Waters Acquity Triple Quadrupole Detector equipped with a Z-Spray electrospray ionization source. The capillary voltage was held at 3.1 kV, cone voltage at 5.0 V, and extraction cone at 1.0 V. The following settings were used to obtain optimal desolvation conditions: desolvation gas flow rate 300 L/h, cone gas flow rate 150 L/h, source temperature 85 °C, desolvation temperature 180 °C. The detector gain was set to an optimal voltage of 470 V. Scan time was set to 1 s, with an interscan time of 0.1 s. MS/MS experiments were performed with a collision energy between 2 and 50 V with an argon collision gas flow rate of 0.1 mL/h.

**Preparation of Solutions for Analysis.**  $\text{Cp}_2\text{Ti(III)(NCMe)}_2$  was prepared using a modified literature synthesis in which  $\text{Cp}_2\text{TiCl}_2$  (32 mg, 0.13 mmol) was dissolved in 60 mL of MeCN. Zinc dust was added (2 g, 30.6 mmol), and the solution was stirred for 2 d at room temperature. Filtration of the solution enables a final  $\text{Cp}_2\text{Ti(III)(NCMe)}_2$  concentration of 5 mM that could be used directly in the ESI-MS experiments without significant decomposition.

**ESI-MS Details.** Oxidation: In a typical experiment 4 mL of a 5 mM stock solution of  $[\text{Cp}_2\text{Ti(III)(NCMe)}_2]^+$  was taken and filtered through a glass fiber syringe filter into an 8 mL sample vial enclosed with a septum. This system was connected to the ESI-MS and used for the initial data collection. In a separate vial, oxygen was sparged into 10 mL of acetonitrile for 2 min to ensure saturation. After data

collection had started, this solution was infused into the vial via a syringe pump at 0.200 mL/min to start the oxidation. The speciation was monitored until no more changes were observed (~20 min).

**Hydrolysis:** In a typical experiment 4 mL of a 5 mM stock solution of  $[\text{Cp}_2\text{Ti(III)(NCMe)}_2]^+$  was taken and filtered through a glass fiber syringe filter into an 8 mL sample vial enclosed with a septum. This system was connected to the ESI-MS and used for the initial data collection. Separately different solutions of water in acetonitrile were prepared volumetrically and introduced to the main solution via a stepper motor pump at 0.200 mL/min. Where applicable  $\text{O}_2$  was sparged into the main solution to induce oxidation.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.7b02705.

Experimental information, detailed orbitrap data, MSMS spectra (PDF)

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### Notes

The authors declare no competing financial interest.

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