

Experimental and Theoretical Studies on the Reactivity of Titanium Chelidamate Complexes: the Significant Role of the Hydroxide **Pyridine Moiety**

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Supporting Information

ABSTRACT: The reaction of $[TiCp_2Cl_2]$ with dipotassium chelidamate yields the carboxylate derivative [TiC $p_2\{(OOC)_2PyOH\}]$ (2), which is sparsely soluble in water at neutral pH but soluble in basic medium. [TiCp*Cl₃] reacts with chelidamic acid in the presence of NEt₃ to yield the dimetallic derivative $[TiCp^{*}{(OOC)_2PyOH}]_2O$ (5). The reaction of [TiCp*Cl₃] with potassium chelidamate renders the hydroxide compound $[TiCp^*(OH)\{(OOC)_2PyOH\}]$ (6). Compound 6 evolves in DMSO solution to give the trimetallic derivative $[TiCp*(DMSO){(OOC)_2PyO}]_3$ (7). Complex 6 reacts with NaOH to render the heterometallic complex [TiCp*- $\{(OOC)_2 PyONa(OH_2)_3\}$ (O) (8). The structures of complexes



7 and 8b were determined by X-ray diffraction studies. The electrostatic potential surfaces, Mulliken population analysis, and frontier molecular orbitals were determined for complex 6, allowing us to infer its reactivity.

INTRODUCTION

The synthesis of water-soluble titanium complexes is attracting considerable attention due to their potential in several fields; for example, such complexes can be designed to be nontoxic and environmentally safe precursors of titanium oxide and other inorganic materials containing titanium.¹ Moreover, titanium complexes have been the subject of interest because in some cases they show antitumor activity² or have a strong antibacterial effect.³ In both instances the stability of the complexes in water solution is a central issue.

In previous works we have found that dialkoxide or dicarboxylate pincer ligands are suitable for the synthesis of water-soluble tantalum complexes.^{4,5} Now, we seek to extend this methodology to the synthesis of water-soluble titanium complexes stabilized by carboxylate ligands. With this objective in mind, we thought that it would be useful to draw an analogy between the properties of titanium derivatives stabilized by closely related ligands such as deprotonated dipicolinic or chelidamic acids. The chelidamate anion can bond the metal in a way similar to that for the dipicolinate group, but it incorporates an OH moiety that could enhance the solubility in water of the corresponding metal derivatives. Moreover, chelidamic acid can adopt two tautomeric (Scheme 1) forms

Scheme 1



resulting from intra- or intermolecular proton transfer that can affect the coordination properties of the ligand on account of the sp³ character of the N in the keto form that can change the planarity of the ONO coordinating moiety.⁶ In addition, this multidentate ligand can be useful for the assembly of MOFs⁷ as well as in the area of medicinal chemistry.⁸

It is worth pointing out that, in spite of the interesting properties of chelidamic acid, its coordination chemistry with titanium remains so far unexplored. Taking into consideration the above comments, we have explored the behavior of two

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organometallic titanium precursors toward the mentioned chelidamic acid and its potassium salt. Herein, we report the synthesis of several chelidamate titanium complexes and compare their behavior in water solution with that of analogous dipicolinate titanium derivatives. Computational studies at B3LYP/6-31G**+LANL2DZ level of theory were also performed to understand the reactivity of one of the studied compound.

RESULTS AND DISCUSSION

The reaction of group 4 metallocene complexes with 2,6pyridinedicarboxylate ligands has been previously studied; more specifically, the complex $[TiCp_2(OOC)_2Py]$ has been synthesized by reaction of $[TiCp_2Me_2]$ with dipicolinic acid.⁹ An alternative procedure is the reaction of $[TiCp_2Cl_2]$ with the corresponding sodium carboxylate.¹⁰

Following the last synthetic procedure, we have carried out the synthesis of compound **2** by reaction of $[TiCp_2Cl_2]$ with a water solution of (KOOC)₂PyOH (prepared in situ from chelidamic acid with K_2CO_3 (Scheme 2). Complex 2 was





isolated as an air-stable yellow solid, sparsely soluble in CH2Cl2 or DMSO and insoluble in toluene or pentane. It has been spectroscopically and analytically characterized.

The ¹H NMR spectrum of 2 in deuterated DMSO shows two singlet signals at 6.18 and 7.25 ppm assigned to the Cp ligand and to the aromatic protons of the carboxylate group, respectively. In addition, the hydroxide proton appears in the spectrum as a broad singlet at 12.43 ppm. The spectroscopic data indicate that the coordination of the chelidamate ligand to the titanium is analogous to that of the previously reported dipicolinate group.

In order to study if the incorporation of the OH fragment improves the solubility of the complex in water, we have recorded the ¹H NMR spectra of saturated solutions of $[TiCp_2(OOC)_2Py]^9$ (1) and $[TiCp_2(OOC)_2PyOH]$ (2) in D₂O. The pattern of the ¹H NMR spectrum of both complexes is analogous to that found for each complex in DMSO- d_{6} , and the integral of the signal corresponding to the residual protons of the solvent in comparison to that of the titanium-bonded Cp ligands indicate that the solubility of both compounds in water is poor.

An interesting issue when studying the solubility of organometallic complexes in water is to understand how the pH affects the complex properties; with this aim in mind, we have compared the behavior of compounds 1 and 2 in basic solutions.

The addition of an NaOH solution in D₂O (pH 12) to compound 2 produces a yellow solution that has been studied by NMR; the ¹H NMR spectrum shows two singlet signals at 6.20 and 7.04 ppm corresponding respectively to the Cp groups and the aromatic protons of the carboxylate ligands. Additionally, the signal of the OH group does not appear. The ¹³C NMR spectrum shows the signal of the Cp at 119.1 ppm and the resonances of the pyridinic ring carbon atoms at 117.6,

149.5, and 180.5 ppm. The carboxylate moieties give rise to a singlet at 170.0 ppm.

Probably, the addition of a base produces the deprotonation of the OH fragment to yield a proposed ionic derivative (3)that because of its ionic charge and the possibility of hydrogen bonding with the solvent is water soluble (Scheme 3). In



agreement with this proposal, we have seen that the reaction of $[TiCp_2(OOC)_2Py]$ (1) with a solution of NaOH in D₂O under the same experimental conditions does not increase the solubility of the titanium derivative in D₂O and no additional signals in the NMR spectra appear.

Complex 3 decomposes slowly in D_2O with formation of CpH; after 5 h in D₂O solution, at room temperature, the ratio of the integral of the signal corresponding to the Cp ligands in compound 3 and those of the CpH is ca. 10/1. It is interesting to highlight the solubility and relative stability of the complex at high pH because conventional titanium compounds are stable only in strong acidic media.¹⁶

Given the interesting differences found in the reactivity of $[TiCp_2(OOC)_2Py]$ and $[TiCp_2(OOC)_2PyOH]$ with NaOH, we decided to extend the comparative study to electronically and sterically more unsaturated titanium precursors. We have previously reported the synthesis of a series of monocyclopentadienyl titanium dipicolinate derivatives such as $[TiCp*Me(OOC)_2Py]$, which reacts with water to yield the dimetallic derivative $[{TiCp*(OOC)_2Py}_2(\mu_2-O)]$ (4); compound 4 is soluble in toluene or dichloromethane and insoluble in water.¹

In order to incorporate the chelidamate ligand into the coordination sphere of the titanium center, we have followed two different synthetic approaches. The reaction of [TiCp*Cl₃] with hydrated chelidamic acid in the presence of triethylamine yields the dimetallic oxide [{TiCp*- $(OOC)_2PyOH\}_2(\mu_2-O)]$ (5) (Scheme 4).

Complex 5 was isolated as an orange solid which is soluble in dichloromethane, THF, or toluene, less soluble in Et₂O or pentane, and insoluble in water; it has been characterized spectroscopically, and the purity of the sample was established by elemental analysis. The dimetallic nature of the complex was confirmed by mass spectrometry.

The ¹H NMR spectrum of compound 5 in CDCl₃ shows a singlet signal at 1.99 ppm corresponding to the Cp* ligands and two doublet signals due to the aromatic protons of the carboxylate moiety at 7.64 and 7.74 ppm that indicate the lack of a C_{ν} symmetry plane in the ligand. The hydroxide protons appear as a singlet at 12.53 ppm. The unsymmetrical environment of the ligand is also confirmed by the ¹³C NMR spectrum. The spectroscopic data along with the structural data found for the analogous complex with the dipicolinate ligand¹¹ support the structure proposed in Scheme 4.

Scheme 4



As an alternative procedure for the incorporation of the chelidamate group into the coordination sphere of the titanium, we have carried out the reaction of $[TiCp*Cl_3]$ with a water solution of $(KOOC)_2PyOH$ prepared in situ with the expectation of obtaining compound 5 by a more direct procedure (Scheme 5).



However, the reaction takes place with formation of an orange solid, [TiCp*(OH){(OOC)₂PyOH}] (6), which, in contrast with the properties found for compounds 4 and 5, is insoluble in THF, CH₂Cl₂, or water but soluble in DMSO. It has been analytically and spectroscopically characterized. The ¹H NMR spectrum of **6** in DMSO- d_6 shows two singlets at 1.81 and 7.19 ppm that can be assigned to the Cp* ligand and to the aromatic protons of the carboxylate ligand. Moreover, the spectrum shows two broad signals at 3.39 and 12.89 ppm that can be assigned to the OH protons bonded to the titanium and to the pyridine moiety, respectively. The structure proposed is in agreement with the spectroscopic data as well as with the structural features found for comparable pentamethylcyclopentadienyl titanium complexes with the dipicolinate ligand.¹¹ It is noteworthy that under these experimental conditions the condensation process to give the dimetallic oxide species does not take place and a titanium hydroxide can be isolated.

Metal hydroxide complexes are interesting precursors for the synthesis of heterometallic derivatives,¹² and their reactivity can also serve as models of enzyme active sites.¹³ Moreover, hydroxides are proposed to play a crucial role in the formation of metal oxides.

Although discrete titanium hydroxide derivatives are not common, a number have been described¹⁴ and are known to easily suffer condensation reactions to yield the corresponding oxides.¹⁵ In the case of compound **6** we can consider two different intermolecular condensation reactions: (1) the condensation of two Ti–OH units to yield a μ -oxide dimetallic complex (eq 1) or (2) the condensation of the Ti–OH moiety with the HOAr group of a second molecule that would render an oligometallic titanium aryloxide derivative (eq 2).

$$2\mathrm{Ti}-\mathrm{OH} \xrightarrow{-\mathrm{H}_{2}\mathrm{O}} \mathrm{Ti}-\mathrm{O}-\mathrm{Ti}$$
(1)

$$Ti-OH + ROH \xrightarrow{-H_2O} Ti-OR$$
(2)

Complex 6 is particularly interesting because it incorporates both a Ti-OH and a ROH function and it evolves according to reaction 1 or 2 depending on the experimental conditions. In fact, complex 6 is unstable in DMSO- d_6 solution and its evolution has been monitored by ¹H NMR. After 3 h at room temperature the transformation is complete and the spectrum shows a broad signal at 3.34 ppm that has a relative integral corresponding to two protons assigned to the water molecule eliminated in the condensation process. Moreover, the spectrum shows a set of signals corresponding to the new titanium compound $[TiCp*(DMSO){(OOC)_2PvO}]_3$ (7) resulting from the condensation process shown in eq 2. The most outstanding feature of the spectrum is the high field of the signals attributed to the ring protons (6.08 ppm). The low shift of the latter, in comparison to the values found for 5 or for 6, could indicate that in the new complex the chelidamate fragment adopts the keto form (Scheme 6).



In order to unequivocally establish the coordination environment of the titanium center in complex 7, we have studied the structure by X-ray diffraction. Suitable crystals were obtained by slow diffusion of Et₂O into a saturated solution of 6 in wet DMSO. Figure 1 shows an ORTEP drawing of the molecule, and some important bond distances and angles are shown in Table 1. The crystals consist of discrete trimetallic units with a triangular shape in which the titanium atoms are placed at the vertex and the chelidamate ligands that bridge two titanium atoms form the edge. Each titanium atom adopts the geometry of a distorted octahedron with the Cp* ligand and the pyridine nitrogen placed in apical positions while the equatorial plane is formed by four oxygen atoms, three from the chelidamate ligand and one from the DMSO that, presumably, has been incorporated into the coordination sphere of the metal in the crystallization process.

The Ti(1)–O(3) bond length of 1.919(5) Å is longer than those normally found in titanium aryloxide compounds,¹⁶



Figure 1. ORTEP drawing of the trimetallic chelidamate complex 7. Hydrogen atoms are omitted for clarity.

Table 1. Selected Bond Lengths (Å) and Angles (deg) for Complexes 7 and 8b

7		8b		
Bond Lengths				
Ti(1) - O(3)	1.919(5)	Ti(1) - O(11)	1.814(1)	
Ti(1) - N(1)	2.117(5)	Ti(1) - N(1)	2.085(2)	
Ti(1) - O(1)	2.018(4)	Ti(1) - O(1)	2.035(1)	
Ti(1) - C(9)	2.388(5)	Ti(1) - O(3)	2.036(1)	
C(3)-C(4)#2	1.408(6)	C(4) - C(5)	1.442(3)	
C(2) - C(3)	1.370(7)	C(5) - C(6)	1.364(3)	
N(1)-C(2)	1.310(5)	N(1) - C(6)	1.351(2)	
O(3) - C(4)	1.283(8)	O(5) - C(4)	1.258(2)	
Ti(1) - O(4)	2.10(1)	Na(1) - O(5)	2.325(2)	
		Na(1) - O(14)	2.276(2)	
Bond Angles				
C(4) - O(3) - Ti(1)	151.6(4)	C(4) - O(5) - Na(1)	127.0(1)	
O(1)-Ti(1)-O(4)	85.1(2)	Ti(2)-O(11)-Ti(1)	175.01(9)	

while the O(3)-C(4) bond distance (1.283(8) Å) is shorter than the C–O bond lengths found in aryloxide ligands bonded to titanium.¹⁷ These geometrical features point to an important contribution of the keto form to the bonding of the chelidamate fragment to the metal (Scheme 7b). Moreover,

Scheme 7

the Ti(1)–N(1) bond distance is somewhat shorter than those found in titanium dipicolinate derivatives.¹¹

Remarkably, the addition of pyridine to a suspension of compound 6 in $CDCl_3$ gives rise to the formation of 5 (Scheme 8). It is conceivable that, in deuterated chloroform,



the addition of a base favors the condensation reaction of the titanium-bonded hydroxide 6 (according to eq 1) to render compound 5.

The deprotonation of a titanium-bonded hydroxide ligand to yield an anionic derivative has been previously observed,¹⁸ but in most cases the reaction of a terminal metal hydroxide with a base results in condensation reactions that yield dimeric oxide-bridged species.¹⁴

As we have mentioned above, compound 6 is insoluble in water; in order to increase its solubility and following the procedure used for complex 2, we have carried out the reaction of the titanium hydroxide 6 with a water solution of NaOH. The reaction was carried in a 1:1 molar ratio by addition of a solution of NaOH in water to a suspension of 6 in THF (Scheme 9). The heterometallic derivative [TiCp*- $\{(OOC)_2 PyONa(OH_2)_3\}_2$ (8) was isolated as an intense orange solid that is soluble in water or DMSO and insoluble in pentane, Et₂O, or THF. Complex 8 is the result of both a condensation process of two Ti-OH moieties to give the expected Ti-O-Ti unit and the appropriate deprotonation of pyridine-containing OH groups. Additionally, three H₂O molecules are proposed to be coordinated to both sodium centers (see Scheme 9). The ¹H NMR of compound 8 in DMSO- d_6 shows a broad singlet at 3.34 ppm with an integral corresponding to 12 protons that can be assigned to the proposed six water molecules in the molecule. Moreover, the spectrum indicates that the complex in solution is C_s symmetric.

Slow diffusion of Et_2O into a saturated solution of 8 in DMSO yields orange crystals of 8b that have been characterized by X-ray diffraction. Figure 2 shows an



Scheme 9



Figure 2. (a) ORTEP drawing of the asymmetric unit of complex 8b. Hydrogen atoms are omitted for clarity. (b) Representation of the polymeric arrangement of 8b.

Scheme 10



ORTEP drawing of the molecules, and some selected bond distances and angles can be found in Table 1.

The structural study shows that complex **8b** crystallizes in DMSO to render a linear polymer in which Ti_2Na_2 tetrametallic units are brought together by DMSO bridging ligands. The titanium centers display a pseudo-square-planar pyramidal geometry in which the metal is bonded to the Cp* ligand placed in an apical position to an oxide bridging ligand and to the chelidamic fragment that bonds the metal as an ONO pincer ligand. Moreover, the chelidamic group is bonded to a sodium ion through the aryloxide moiety. The sodium shows a trigonal-bipyramidal geometry with the equatorial plane for the oxygen atoms of the chelidamic ligand, one

terminal and one bridging DMSO molecule, and apical positions occupied by the oxygens of one terminal and one bridging DMSO ligands.

The titanium–O bond distances (Ti(1)-O(11) 1.814(1) Åand Ti(2)-O(11) 1.806(1) Å) are in the range expected for di- μ -oxo-dititanium bridging systems.¹⁹ In contrast, the Ti(1)-O(11)-Ti(2) bond angle $(175.01(9)^{\circ})$ is greater than that found in complex 4 $(129.6(1)^{\circ})$.¹¹

The geometrical parameters within the pyridinic ring are close to those in 7, indicating an important participation of the keto form B (Scheme 10). In this way, the C(4)–C(5) bond length (1.442(3) Å) is longer than the C(5)–C(6) distance (1.364(3) Å): moreover, the O(5)–C(4) bond length

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(1.258(2) Å) is intermediate between those expected for C–O single and double bonds. The Na(1)–O(5) and Na(2)–O(10) bond distances (2.325(2) and 2.281(2) Å, respectively) are long for terminal sodium aryloxides.²⁰

THEORETICAL CALCULATIONS

Quantum chemical calculations at the DFT level were performed to gain further insight into the reactivity of complex **6**. The optimized structure of **6** in the gas phase shows a distorted-trigonal-bipyramidal geometry of the titanium atom²¹ and reveals that the chelidamate moiety is not totally planar (Figure 3). The orientation of the hydroxypyridine ring can be



Figure 3. Geometry of the stationary point for **6** in the gas phase in the electronic ground state computed at the B3LYP/6-31g**+LANL2DZ level.

defined by the torsion angles C(8)-C(7)-C(6)-O(3)(-174.3°) and C(32)-C(31)-C(30)-O(28) (174.2°) that reflect an slight deviation from the planarity due to the coordination with the titanium atom. The calculated Ti(1)-O(3), Ti-O(28), and Ti-N(2) bond lengths (2.018, 2.011, and 2.155 Å, respectively) are in the range expected for pyridine carboxylate titanium complexes¹¹ and the Ti-O(38) bond length (1.840 Å) is close to the values obtained theoretically (1.812 Å) for Ti(OH)₄²² or experimentally (1.810(2) Å) for terminal titanium hydroxide complexes.^{15,18}

The bulk solvent effect of a low-polarity solvent $(CHCl_3)$ and a polar solvent (DMSO) on the molecular geometry and charge densities of **6** was investigated by the solvation model based on density (SMD).²³

Geometrical parameters are close to those obtained in the gas phase, but it is noticeable that, in DMSO, Ti(1)–O(28), Ti(1)–O(3), O(5)–H(40), and O(38)–H(39) bond lengths slightly increase (0.019, 0.014, 0.005, and 0.004 Å, respectively) in comparison to those values in the gas phase or using CHCl₃ as solvent. The observed variations in O–H bond lengths could be correlated with a diminishing of the pK_a values.²⁴

The molecular electrostatic potential (MEP) is a good guide for the purpose of assessing the reactivity related with the molecular charge distribution and other related properties. Molecular recognition between molecules can be also studied through MEP, as it is through their potentials that the two molecules first interact with each other.²⁵ MEP maps show different colors that represent the different values of the electrostatic potential on a molecular surface. A deep blue color indicates the highest electrostatic potential energy and deep red the lowest. The color code of the obtained maps for **6** is in the range -0.031 to +0.011 au (Figure 4). Negative



Figure 4. Molecular electrostatic potential maps of **6** computed at the B3LYP/6-31G**+LANL2DZ level in the gas phase and in the bulk solvents CHCl₃ and DMSO using the SMD model: (A) top view of **6**; (B) rotated 90° view. The deepest red color corresponds to the lowest electrostatic potential energy value in atomic units (hartree) and blue to the highest.

potential regions are related to reactions with electrophiles and positive potential regions to reactions with nucleophiles. Figure 4A shows a top view of the MEP maps for **6**, and they reveal that the most negative potential regions are on the oxygen atoms of the dicarboxylate moieties and on O(38) linked to a titanium atom. Analyzing the maximum MEP values obtained around the hydroxyl group atoms of **6**, we observed an increase in the nucleophilic character around O(38) as the polarity increases (Table 2). On the other hand, no significant effect

Table 2. MEP Values, in Atomic Units (hartree), Obtained around Atoms of Hydroxyl Groups of 6

atom	gas phase	CHCl ₃	DMSO
O(38)	-0.203	-0.236	-0.311
H(39)	+0.054	+0.059	+0.057
O(5)	-0.008	-0.0006	-0.004
H(40)	+0.090	+0.102	+0.110

was observed around O(5), which possesses a less significant nucleophilic character. In contrast, the most electrophilic region was found on H(40) in DMSO, while H(39) has a substantially less electrophilic character with no significant solvent polarity effect (Table 2). In addition, a side view of the MEP maps (Figure 4B) reveals that the size of the electrophilic area around H(40) (deepest blue) increases as the polarity of the solvent increases. Therefore, we can assert that that, in DMSO, the titanium OH moiety is basic enough and the pyridine OH is acidic enough to react with each other to give 7 plus water.

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Finally, it is also worth noting that the molecular moiety with MEP values closer to zero (yellow-green) corresponds to the pyridine ring (Figure 4B), indicating that this is the less polar region of the molecule.

The electrostatic potential properties of **6** described above can lead to intense antiparallel interactions between the most electrophilic region (H(40)) of a chelidamate ligand and the most nucleophilic region (O(38)) located in another ligand. These interactions are expected to be more intense in polar solvents such as DMSO, and they could be the driving force of the molecular recognition that precedes the formation of compound 7. Antiparallel interactions between some chelidamate derivatives have been previously reported.²⁶

Finally, the molecular orbital plots reveal that both HOMO and LUMO orbitals have participation of d orbitals of the Ti atom. They are mainly π type orbitals with a significant contribution of the Cp* to the former and of the hydroxypyridine moiety to the latter (Figure 5).



Figure 5. Shapes of the HOMO and LUMO of compound 6 computed at the B3LYP/6-31G**+LANL2DZ level in the gas phase.

CONCLUSION

In this study we compare the properties of bis-(cyclopentadienyl) and mono(cyclopentadienyl) titanium chelidamate complexes with the behavior of previously reported titanium dipicolinate derivatives. We have seen that the OH moiety in the chelidamate ligand does not increase the solubility of the titanocene complex in neutral D₂O but allows its solubilization in basic media. In the case of monocyclopentadienyl complexes we have been able to isolate a titanium hydroxide compound (6) that evolves in DMSO solution to render a neutral trimetallic cyclic architecture in which the chelidamate ligand behaves as an organic linker. Moreover, in the presence of a base, in CDCl₃, compound 6 reacts to yield a dimetallic oxide. The hydroxide compound 6 can be deprotonated with NaOH to render a water-soluble Ti-Na heterometallic complex that crystallizes as a linear polymer. The theoretical calculations reveal that the two hydroxyl groups of 6 show significant differences in their nucleophilic and electrophilic character that can justify the reactivity of 6 in polar media.

EXPERIMENTAL DETAILS

General Procedures. The experimental procedures reported here were carried out, unless otherwise mentioned, under an argon atmosphere using standard vacuum line and Schlenk techniques. All organic solvents were dried and distilled under an argon atmosphere. Water was distilled and deoxygenated. [TiCp*Cl₃] was prepared according to literature procedures.²⁷

The commercially available compounds dipicolinic acid and chelidamic acid were used as received from Aldrich. ¹H and ¹³C NMR spectra were recorded on a 400 MHz Avance Bruker Fourier transform spectrometer. Trace amounts of protonated solvents were

used as references, and chemical shifts are reported in units of parts per million relative to SiMe₄.

Synthesis of [TiCp₂{(OOC)₂PyOH}] (2). To a solution of [TiCp₂Cl₂] (0.515 g, 2.07 mmol) in THF (5 mL) was added a water solution of (HOOC)₂PyOH (0.378 g, 2.06 mmol) and K₂CO₃ (0.285 g, 2.06 mmol), and the mixture was stirred, at room temperature, for 1 h. Afterward, the solvent was removed under vacuum and the residue was washed with water (2 × 5 mL) and dried under vacuum. The yellow solid obtained was identified as [TiCp₂{(OOC)₂PyOH}] (2). Yield: 0.565 g, 76%. ¹H NMR (DMSO-*d*₆, room temperature): δ (ppm) 6.18 (s, 10H, Cp), 7.25 (s, 2H, Ar), 12.43 (br, 1H, OH). ¹H NMR (D₂O, room temperature): δ (ppm) 6.25 (s, 10H, Cp), 7.09 (s, 2H, Ar). Anal. Calcd for C₁₇H₁₃O₅NTi: C, 56.84; H, 3.64; N, 3.89. Found: C, 56.57; H, 3.84; N, 3.71.

Reaction of [TiCp₂{(OOC)₂PyOH}] (2) with NaOH. To a sample of compound 2 (10 mg) was added a solution of NaOH in D₂O (0.6 mL, 0.01 M), and the yellow solution that formed was characterized by NMR. ¹H NMR (D₂O, room temperature): δ (ppm) 6.20 (s, 10H, Cp), 7.04 (s, 2H, Ar). ¹³C NMR (D₂O, room temperature): δ (ppm) 117.6 (Cp), 119.1 (Ar), 149.5 (Ar), 170.0 (COO), 180.5 (Ar).

Synthesis of [{TiCp*(OOC)₂PyOH}₂(μ₂-O)] (5). To a solution of [TiCp*Cl₃] (0.212 g, 0.73 mmol) in THF were added [(HOOC)₂PyOH].H₂O (0.147 g, 0.73 mmol) and NEt₃ (0.204 mL, 1.46 mmol), and the mixture was stirred, at room temperature, for 72 h. The solvent was removed under vacuum, and the residue was extracted with toluene. The orange solid obtained upon evaporation of the solvent was washed with pentane and identified as 5 (0.164 g, 60%). ¹H NMR (CDCl₃, room temperature): δ (ppm) 1.99 (s, 30H, Cp*), 7.64 (d, J = 1.8 Hz, 2H, Ar), 7.74 (d, J = 1.8 Hz, 2H, Ar), 12.53 (s, 2H, OH). ¹³C NMR (CDCl₃, room temperature): δ (ppm) 12.1 (Cp*), 112.8 (Ar), 114.9 (Ar), 131.8 (Cp*), 149.9 (Ar), 152.4 (Ar), 167.3 (COO), 169.7 (COO), 173.7 (Ar). Anal. Calcd for C₃₄H₃₆N₂O₁₁Ti₂: C, 54.85; H, 4.87; N, 3.76. Found: C, 54.61; H, 5.04; N, 3.53. ESI-MS (electrospray ionization/mass spectrometry; *m/z*): calculated for C₃₄H₃₆N₂O₁₁Ti₂, 744.4; found, 744.9.

Synthesis of [TiCp*(OH){(OOC)₂PyOH}] (6). To a solution of [TiCp*Cl₃] (0.248 g, 0.86 mmol) in THF (10 mL) was added a solution of chelidamic acid (0.157 g, 0.86 mmol) and K₂CO₃ (0.118 g, 0.86 mmol) in 1 mL of H₂O, and the mixture was stirred at room temperature for 1 h. Afterward, the solvent was removed under vacuum and the solid washed with water (3 × 5 mL). The orange compound was identified as [TiCp*(OH){(OOC)₂PyOH}] (6). Yield: 0.281 g, 86%. ¹H NMR (DMSO-*d*₆, room temperature): δ (ppm) 1.81 (s, 15H, Cp*), 3.39 (br, 1H, OH), 7.19 (s, 2H, Ar), 12.89 (br, 1H, OH). ¹³C NMR (DMSO-*d*₆, room temperature): δ (ppm) 1.9 (Me-Cp*), 112.5 (Ar), 129.7 (Cp*), 151.4 (Ar), 166.0 (COO), 172.7 (Ar). Anal. Calcd for C₁₇H₁₉NO₆Ti: C, 53.56; H, 5.02; N, 3.67. Found: C, 54.07; H, 5.21; N, 3.43.

Synthesis of [TiCp*(DMSO){(OOC)₂PyO}]₃ (7). The evolution of a solution of 6 (20 mg) in DMSO- d_6 was monitored by ¹H and ¹³C NMR. After 3 h at room temperature the transformation was complete and indicated the formation of the new compound 7 along with the stoichiometric amount of water. ¹H NMR (DMSO- d_6 , room temperature): δ (ppm) 1.98 (s, 15H, Cp*), 3.34 (br, 2H, H₂O), 6.08 (s, 2H, Ar). ¹³C NMR (DMSO- d_6 , room temperature): δ (ppm) 12.6 (Me-Cp*), 112.8 (Ar), 132.8 (Cp*), 148.1 (Ar), 168.2 (COO), 177.9 (Ar).

Crystals of 7 were obtained by slow diffusion of Et_2O into a saturated solution of **6** in DMSO.

Synthesis of [TiCp*{(OOC)₂PyONa(OH₂)₃]₂(O) (8). To a suspension of compound 6 (0.977 g, 2.56 mmol) in THF was added NaOH (2.35 mL, 1.09 M in H₂O), and the resulting suspension was stirred at room temperature for 1 h. The solvent was removed by filtration; the orange solid was dried under vacuum and was characterized as 8. Yield: 1.003 g, 87%. ¹H NMR (DMSO- d_{6} , room temperature): δ (ppm) 1.68 (s, 30H, Cp*), 3.34 (s, 12H, H₂O), 6.18 (s, 4H, Ar). ¹³C NMR (DMSO- d_{6} , room temperature): δ (ppm) 11.6 (Me-Cp*), 115.2 (Ar), 126.9 (Cp*), 150.7 (Ar), 169.4 (COO),

181.6 (Ar). Anal. Calcd for $C_{34}H_{46}N_2O_{17}Ti_2Na_2$: C, 45.55; H, 5.17; N, 3.12. Found: C, 45.66; H, 5.00; N, 3.01.

Crystals of **8b** can be obtained by slow diffusion of Et_2O into a saturated solution of **8** in DMSO.

¹H NMR (D₂O, room temperature): δ (ppm) 1.74 (s, 30H, Cp*), 2.58 (DMSO), 6.68 (s, 4H, Ar). ¹³C NMR (D₂O, room temperature): δ (ppm) 11.1 (Me-Cp*), 116.2 (Ar), 131.3 (Cp*), 149.5 (Ar), 171.2 (COO), 182.4 (Ar).

X-ray Crystallography. A summary of crystal data collection and refinement parameters for all compounds is given in the Supporting Information. The single crystals for 7.4.5Me₂SO and 8b were mounted on a glass fiber and used for data collection on a Bruker X8 APEX II CCD-based diffractometer equipped with a graphitemonochromated Mo K α radiation source ($\lambda = 0.71073$ Å). Data reduction was performed with the APEX3²⁸ software, and an absorption correction was performed with the program SADABS.²⁹ Crystal structures were solved by direct methods using the SIR97 program³⁰ and refined by full-matrix least squares on F^2 , including all reflections using anisotropic displacement parameters by means of the WINGX crystallographic package.³¹ All non-hydrogen atoms were refined anisotropically, and all hydrogen atoms were geometrically placed and refined using a riding model. The structure of the compound 7.4.5Me₂SO is highly disordered, and the Squeeze procedure was necessary to eliminate the contribution of the electron density from the intensity data³² probably due to uncoordinated Me₂SO. One Me₂SO group of compound 8b showed disorder, which was modeled over three positions.

Computational Methods. Ground states of 6 were optimized at the DFT level with the B3LYP³³ functional using the Gaussian 09 Rev.D.O1 program.³⁴ The titanium element was characterized by the pseudopotential LanL2DZ,³⁵ and the 6-31G(d,p) basis set was used for other atoms.³⁶

The determination of the stationary points and the full geometry optimizations was carried out with Schlegel's gradient optimization algorithm.²³ The bulk effect of the solvent was calculated, with chloroform ($\varepsilon' = 4.81$) and dimethyl sulfoxide ($\varepsilon' = 47.24$) as solvents, by means of the solvation model based on density (SMD).³⁷

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organo-met.8b00209.

Crystallographic data for 7.4.5Me₂SO and **8b** (PDF)

Accession Codes

CCDC 1835890–1835891 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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