

## Weakening C–O Bonds: Ti(III), a New Reagent for Alcohol Deoxygenation and Carbonyl Coupling Olefination

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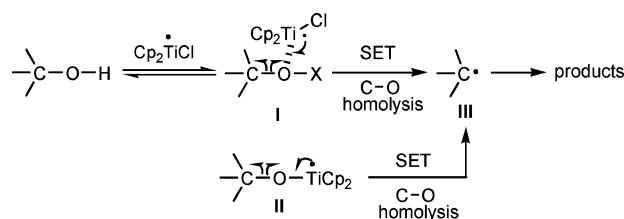
**Abstract:** Investigations detailed herein, including density functional theory (DFT) calculations, demonstrate that the formation of either alkoxy- or hydroxy-Ti(III) complexes considerably decreases the energy of activation for C–O bond homolysis. As a consequence of this observation, we described two new synthetic applications of Nugent's reagent in organic chemistry. The first of these applications is an one-step methodology for deoxygenation–reduction of alcohols, including benzylic and allylic alcohols and 1,2-dihydroxy compounds. Additionally, we have also proved that Ti(III) is capable of mediating carbonyl coupling–olefination. In this sense, and despite the fact that for over 35 years it has been widely accepted that either Ti(II) or Ti(0) was the active species in the reductive process of the McMurry reaction, the mechanistic evidence presented proves the involvement of Ti(III) pinacolates in the deoxygenation step of the herein described Nugent's reagent-mediated McMurry olefination. This observation sheds some light on probably one of the mechanistically more complex transformations in organic chemistry. Finally, we have also proved that both of these processes can be performed catalytically in Cp<sub>2</sub>TiCl<sub>2</sub> by using trimethylsilyl chloride (TMSCl) as the final oxygen trap.

### Introduction

It is well-known that Cp<sub>2</sub>TiCl (Nugent's reagent) is a mild reductant, useful through mono-electronic transfer and widely employed in organic synthesis.<sup>1</sup> Its applications arise from the interaction of titanocene dichloride, acting as a Lewis acid, with the heteroatoms of different functional groups, which behave as Lewis bases. This interaction leads to a balanced complex that may evolve into different products. Recent research revealing mechanistic details about this interaction has been reported.<sup>2</sup> In this sense, evidence showing that H<sub>2</sub>O and methanol can act, via the corresponding Ti(III) complexes, as an efficient hydrogen-atom donor has been published.<sup>2c,d</sup>

With these considerations in mind, it would be reasonable to postulate that the interaction of an alcohol and Cp<sub>2</sub>TiCl would

**Scheme 1.** Proposed Mechanism for Ti(III)-Promoted C–O Bond Homolysis



produce the alcohol complex **I**. The formation of this species, or of the titanocene alkoxide derivative **II**, could weaken the corresponding C–O bond allowing under suitable conditions and by means of mono-electronic transfer their homolytic cleavage to give rise to the C-centered radical **III**, which would finally evolve to the corresponding products (Scheme 1).

To validate this approach, we chose two synthetic transformations including C–O cleavages as key processes, namely, deoxygenation–reduction of alcohols and carbonyl coupling–olefinations.

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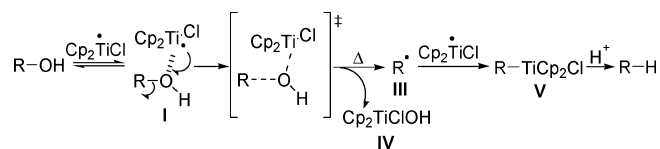
(1) The single electron transfer bis(cyclopentadienyl)-titanium(III)chloride, Nugent's reagent, can be generated in situ by stirring commercial Cp<sub>2</sub>TiCl<sub>2</sub> with dust Mn or Zn. For pioneering reports on the use of this reagent, see: (a) RajanBabu, T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1994**, *116*, 986–997 and references cited therein. For pertinent reviews on the use of this reagent, see: (b) Gansäuer, A.; Blumh, H. *Chem. Rev.* **2000**, *100*, 2771–2788. (c) Gansäuer, A.; Pierobon, M. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 2, pp 207–220. (d) Gansäuer, A.; Lauterbach, T.; Narayan, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 5556–5573. (e) Barrero, A. F.; Quílez del Moral, J. F.; Sanchez, E. M.; Arteaga, J. F. *Eur. J. Org. Chem.* **2006**, 1627–1641. (f) Cuerva, J. M.; Justicia, J.; Oller-López, J. L.; Bazdi, B.; Oltra, J. E. *Mini-Rev. Org. Chem.* **2006**, *3*, 23–35.

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

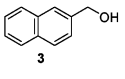



Alcohol deoxygenation constitutes a powerful synthetic tool especially used in complex natural product synthesis.<sup>3</sup> Most of the known synthetic procedures take place via a number of steps, the Barton–McCombie methodology being the most commonly used, mainly for secondary alcohols, due to its compatibility with different functional groups.<sup>4</sup> Few procedures involving one-step deoxygenations have been described,<sup>5</sup> which in our opinion makes necessary further efforts in this subject.

On the other hand, the reductive coupling of carbonyls into olefins by use of low-valent titanium species (LVT), known as the McMurry reaction, has been extensively used in organic synthesis, and both inter- and intramolecular couplings have been described to proceed with remarkable efficiency.<sup>6</sup> This kind of reaction is usually carried out in two consecutive steps, namely, reduction of TiCl<sub>4</sub> or TiCl<sub>3</sub> followed by addition of the carbonyl compound. In this regard, a number of reducing agents such as Li, Na, K, Mg, Zn, KC<sub>8</sub>, Zn(Cu), LiAlH<sub>4</sub>, and others were used, in an attempt to overcome the reproducibility problems usually associated with this reaction. To this end, different improved protocols have been reported.<sup>7</sup> From a mechanistic point of view, there are three main features to consider: formation of the LVT species, coupling reaction, and finally, deoxygenation of the intermediates leading to the olefin. In the coupling step, the involvement of acyl radical and/or carbenoid intermediates in the metallopinnacolate formation is accepted, although their structure is claimed to be influenced by the nature of the carbonyl group, the titanium species, and the reducing agent.<sup>6g</sup> In this sense, even more uncertainties exist about the actual mechanism of the deoxygenation of these metallopinnacolate intermediates, although it has been widely

**Scheme 2.** Proposed Mechanism for Ti(III)-Mediated Alcohol Deoxygenation–Reduction



**Table 1.** Calculated<sup>a</sup>  $\Delta G^\ddagger$  and  $\Delta G_{\text{rxn}}$  Values for C–O Bond Homolytic Cleavage of Different Alcohols

substrate	$\Delta G^\ddagger$	$\Delta G_{\text{rxn}}$
	30.0	2.3
	29.0	2.7
	29.9	4.9
	31.7	6.3
	41.7	19.8
	52.3	36.7

<sup>a</sup> Calculated via UM05/Ahlich-VZD.

accepted that species with low valence states of Ti, either Ti(II) or Ti(0), were required in this reductive process.

## Results and Discussion

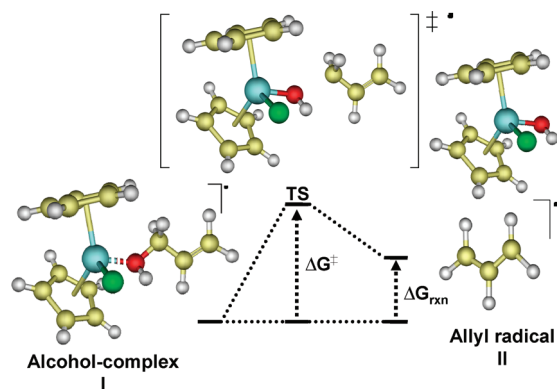
**A. Deoxygenation–Reduction of Alcohols. i. Mechanistic Proposal and DFT Calculations.** The mechanistic proposal for deoxygenation–reduction of alcohols is depicted in Scheme 2. Thus, the C-centered radical **III**, originating from homolysis of the corresponding C–O bond, could evolve to the corresponding hydrocarbon after being trapped by another molecule of Cp<sub>2</sub>TiCl, generating alkyltitanium **V**, which would then be protonated easily to afford the alkane. In this regard, the direct reduction of the radical **III** by species such as **I**, **IV**, or the solvent should not be ruled out.

To verify this hypothesis, density functional theory (DFT; UM05/Ahlich-VZD)<sup>8</sup> calculations were carried out. Thus, the energy barriers ( $\Delta G_{\text{rxn}}$  and  $\Delta G^\ddagger$ ) for homolytic cleavage of the C–O bond in the alcohol complex **I** were calculated for different type of alcohols (Table 1 and Figure 1).

Although the calculated values were endothermic for all compounds studied (**1–6**), the allylic and benzylic alcohols showed, as expected, lower activation and reaction energies

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**Figure 1.** Energy diagram for C–O bond homolytic cleavage in allylic alcohol **1** (activation energy  $\Delta G^\ddagger$  and reaction energy  $\Delta G_{\text{rxn}}$ ).

(Table 1). In any case, when these data were compared with those calculated theoretical and experimentally for the uncomplexed homolytic C–O bond dissociation,<sup>9</sup> significant higher values were found for the uncomplexed species, which clearly show that this homolytic cleavage is strongly affected by coordination to Ti(III).

In light of these observations, we surmised that the necessary energy for this homolysis could be obtained by simply heating organic solutions of the corresponding alcohol– $\text{Cp}_2\text{TiCl}$  complexes. Thus, a solution of benzyl alcohol **4** in THF (0.2 M) was treated with 2.1 equiv of  $\text{TiCp}_2\text{Cl}_2$  and 8.0 equiv of Mn in THF. After the mixture was refluxed for 45 min, the reaction was proven to be completed, and gratifyingly, only toluene was obtained in an excellent yield of 93%.

Variations on the quantities of Nugent's reagent were carried out in order to gain further insight into the course of the reaction. Thus, when only 1.1 equiv of  $\text{Cp}_2\text{TiCl}_2$  was used, the reaction stopped when approximately half the starting material **4** remained unaltered, toluene being obtained in a 47% yield. This fact suggests that the C-centered radical (**III**) is efficiently trapped by a second equivalent of Ti(III) leading to the formation of a benzyl–titanium intermediate (**V**). Consequently, 2.0 equiv of Ti(III) is required to drive the reaction to completion. With respect to the reducing agent, its quantity can be lowered up to 1.5 equiv, and the transformation still remains efficient (92%).

**ii. Scope of the Reaction.** We devoted our efforts to investigate the scope of this transformation (Table 2). Ti(III) (2.0 equiv), 1.5 equiv of reducing agent, and tetrahydrofuran (THF) as solvent were used, except for entry 19, where toluene was employed. Thus, different benzylic alcohols were transformed efficiently into the corresponding deoxygenated–reduced compounds (Table 2, entries 1–5). Allylic alcohols reacted in a similar way producing the expected deoxygenated–reduced products (Table 2, entries 6–12). Thus, farnesol **19** gave rise mainly to hydrocarbon **20** (Table 2, entry 7). In this case, the absence of cyclization products resulting from an intermediate allylic radical also supports the fast reduction of this species (Scheme 2). This result is in good accordance with previous results by some of us, which reported the high tendency of allylic radicals to evolve to allyltitanium species in presence of excess

**Table 2.** Ti(III)-Mediated Deoxygenation–Reduction of Alcohols<sup>a</sup>

entry	substrate	product	<i>t</i> (min)	yield (%)
1			60	79 <sup>a</sup>
2			60	91 <sup>a</sup>
3			50	90 <sup>a</sup>
4			90	60 <sup>a</sup>
5			55	83 <sup>a</sup>
6			50	91 <sup>a</sup>
7			60	80 <sup>a</sup>
8			55	92 <sup>b</sup>
9		-	240	-
10			60	70 <sup>a</sup>
11			50	87 <sup>a</sup>
12			120	38 <sup>a</sup>
13			240	85 <sup>b</sup>
14			65	94 <sup>a</sup>
15			60	79 <sup>a</sup>
16			90	86 <sup>b</sup>
17			90	68 <sup>a</sup>
18			90	92 <sup>a</sup>
19			120	90 <sup>c</sup>

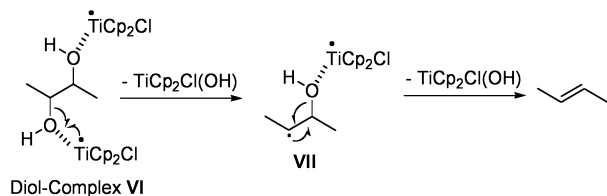
<sup>a</sup> 2.0 equiv of Ti(III) and 1.5 equiv of reducing agent per mole of starting material were used; THF was used as solvent. <sup>b</sup> 0.3 equiv of Ti(III), 4.0 equiv of TMSCl equiv, and 8 equiv of reducing agent per mole of starting material were used; THF was used as solvent. <sup>c</sup> Toluene was used as solvent.

$\text{Cp}_2\text{TiCl}$ .<sup>10</sup> The conversion of 4-hydroxy-3-methylbut-2-enyl benzoate **22** to isopentenyl benzoate **23** (Table 2, entry 10) deserved to be emphasized, since it mimicks the function of

(9) Complementary calculations on nonmediated homolytic C–O bond cleavages gave values larger than 56 kcal mol<sup>-1</sup> in any case. The reported experimental value for MeOH is 102 kcal mol<sup>-1</sup>; Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465–500. For supplementary data, see Supporting Information.

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**Scheme 3.** Proposed Mechanism for Ti(III)-Promoted Deoxygenation of 1,2-Diols

the IspH enzyme in the natural biosynthesis of C5 units of the terpenoids through the deoxyxylulose phosphate pathway.<sup>11</sup> With respect to 1,2-diols, treatment of 1,2-diphenylethane-1,2-diol **28** with 2.1 equiv of  $\text{TiCp}_2\text{Cl}_2$  and 1.5 equiv of Mn led almost quantitatively to *trans*-stilbene **29** (Table 2, entry 14). Other 1,2-diols such as tetradecane-1,2-diol **32** and pinanediol **34** were easily deoxygenated to **33** and  $\beta$ -pinene **35**, respectively, in high yield (Table 2, entries 17 and 18). The stoichiometry of the reagents and good yield seem to indicate that the double bond would be formed via an initial deoxygenation from the diol complex **VI** leading to the C-centered radical **VII** (Scheme 3). The presence of this first radical would facilitate the second C–O cleavage to lead to the corresponding olefin.

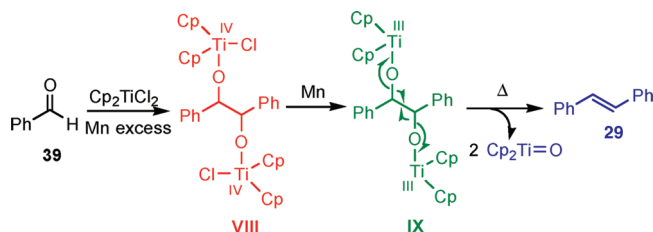
When nonactivated alcohols such as octadecanol **36** were used as starting material, no reaction was observed (see  $\Delta G_{\text{rxn}}$  in Table 1). To overcome this unreactivity, other solvents with higher boiling point were tested. Thus, when a mixture of Nugent's reagent and **36** were heated in toluene at reflux, **37** and **38** (1:1) were obtained as result of deoxygenation–reduction and dehydration processes, respectively (Table 2, entry 19).

When we focused our attention on the presence of different functional groups in the alcohols to be deoxygenated, good yields of the corresponding deoxygenation products were also obtained in the presence of hydroxyls protected as methyl ethers (Table 2, entries 3 and 4), although the acid-labile silyl ethers did not tolerate the reaction conditions. Other hydroxyl protecting groups such as acetate also decompose under the reaction conditions. However, most robust esters such as the benzoate or, even more efficiently, the pivalate proved to be appropriate protecting groups in our deoxygenation protocol (Table 2, entries 10 and 11). Furthermore, alcohols containing carboxylic acids protected as methyl esters, as well as chloro derivatives, also deoxygenated in acceptable yields (Table 2, entries 5 and 15). Finally, although in a low-yield, nonoptimized process, a primary allylic alcohol was deoxygenated in the presence of a carbonyl group (Table 2, entry 12), which in our opinion widens promisingly the possibilities of this transformation.

### B. Carbonyl Coupling–Olefination. i. Mechanistic Proposal.

On the basis of the above findings, namely, the dramatic decrease in the calculated homolytic C–O bond dissociation energy for  $\text{RH}_2\text{C–OH}$  compared to that calculated for the complex  $\text{Cp}_2\text{Ti}^{\text{III}}(\text{Cl})\text{HO–CH}_2\text{R}$  and the observed double-bond formation upon treatment of diols **28**, **30**, **32**, and **34** with titanocene(III), we surmised that the Nugent's reagent ( $\text{Cp}_2\text{TiCl}$ ) would be able to promote carbonyl olefinations via homolysis of the carbon–oxygen bonds present in the Ti(III) pinacolates (**IX**, Scheme 4). Species **IX** would originate after reduction of the corresponding Ti(IV) pinacolates (**VIII**, Scheme 4), which are described as intermediates in Ti(III)-mediated pinacol coupling of carbonyls.<sup>12</sup>

To test the validity of this hypothesis, we began by examining whether homolytic cleavage of the C–O bond in the species  $\text{PhCH}_2\text{OTi}^{\text{III}}\text{Cp}_2$  could be obtained by treating sodium benzoxide

**Scheme 4.** Proposed Mechanism for Ti(III)/Mn-Promoted Carbonyl Olefination

with  $\text{Cp}_2\text{TiCl}$  in refluxing THF.<sup>13</sup> Gratifyingly, after this mixture was heated for 3 h, gas chromatographic (GC) analysis of the crude product proved the generation of toluene, which seemed to confirm the first premise of our hypothesis.<sup>2d</sup> Encouraged by this result, we made benzaldehyde **39** react with 2 equiv of titanocene(III) in THF at reflux. Stilbene **29** was thus obtained with high efficiency (93% yield) after 1 h (Table 3, entry 1). Considering that the system  $\text{Cp}_2\text{TiCl}_2/\text{Mn}$  was previously reported to mediate pinacol coupling of aldehydes and ketones,<sup>12</sup> we focused our efforts to gain an insight into the real species participating in the deoxygenation step.

To this end, we subjected benzaldehyde **39** to the same experimental conditions described above but now maintained the temperature at 25 °C. After 10 min of stirring at this temperature, analysis of an aliquot taken from the green reaction mixture revealed complete consumption of the starting material, benzopinacol being the only product formed. Excess Mn was then removed from the remaining reaction mixture, and the filtrate was heated at reflux for 1 h to afford again stilbene **29**. It is worth noting the progressive color change, from green to blue, during the heating. At this point, it was reasonable to assume the involvement of a Ti(III) pinacolate in this olefination process, according to the mechanistic proposal depicted in Scheme 4. The excess Mn present in the reaction medium would reduce the initially generated Ti(IV) pinacolate species<sup>12</sup> to the corresponding Ti(III) species. The fact that, to the best of our knowledge, Mn is not able to reduce Ti to a valence lower than 3 at room temperature, together with the green color of the solution, constitutes a strong hint to confirm the presence of this Ti(III) metalpinacol.<sup>14</sup>

A final piece of evidence to denote the involvement of Ti(III) pinacolates in the deoxygenation step was derived from the following experience. Thus, addition of only 0.5 equiv of Zn or Mn to a solution of 1 equiv of  $\text{Cp}_2\text{TiCl}_2$  in THF at room temperature, after 5 min of stirring, caused the expected color change in the solution, which turned from red to green, thus confirming the reduction of the Ti(IV) species to Ti(III). Addition at this point of 1 equiv of benzaldehyde **39** caused the solution to show an orange hue within a few minutes, most likely due to the presence of Ti(IV) pinacolates. NMR analysis of an aliquot confirmed the disappearance of benzaldehyde and

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(14) Villiers and Ephritikhine postulated the involvement of U(III) analogues in the reductive coupling of ketones: Villiers, C.; Ephritikhine, M. *Chem.—Eur. J.* **2001**, *14*, 3043–3051.

**Table 3.** Titanocene(III)-Mediated Reductive Carbonyl Coupling<sup>a</sup>

entry	substrate	product	yield (%)
1			93 <sup>a</sup>
2			87 <sup>a</sup>
3			94 <sup>a</sup>
4			93 <sup>a</sup>
5			74 <sup>a</sup>
6			95 <sup>b</sup>
7			65 <sup>a</sup>
8			76 <sup>a</sup>
9			74 <sup>a</sup>
10			73 <sup>a</sup>
11			71 <sup>a</sup>
12			62 <sup>a</sup>
13			65 <sup>c</sup>
14			77 <sup>c</sup>

<sup>a</sup> 1.2 equiv of Ti(III) and 2.4 equiv of reducing agent per mole of starting material were used; THF was used as solvent. <sup>b</sup> 0.3 equiv of Ti(III), 4.0 equiv of TMSCl equiv, and 8 equiv of reducing agent per mole of starting material were used; THF was used as solvent. <sup>c</sup> For details, see text.

the sole presence of benzopinacol as reaction product. This orange solution remained unaltered for hours, in both color and composition. At this point, addition of a further 0.5 equiv of Zn or Mn led the reaction mixture to recover its former green color (15 min), which was rationalized by assuming a new reduction from the corresponding Ti(IV) to Ti(III) pinacolate (Scheme 4). At this moment, benzopinacol was again proven to be the only component of the reaction mixture. As happened previously, no change in the color or composition was observed after several hours of stirring. However, gentle heating until refluxing temperature was reached produced the formation of stilbene **29**, as well as a last color change, in this case, from green to dark blue, which was attributed to the production of titanocene oxide as a result of the deoxygenation step.

**ii. Scope of the Reaction.** Once we obtained conclusive evidence confirming the involvement of Ti(III) species in the

deoxygenation process, we devoted our effort to investigate the scope of this transformation. Thus, excellent to good yields and reproducibility were also found with other aromatic and conjugated aldehydes (Table 3, entries 1–10). This protocol proved also to be applicable, less efficiently, to aromatic and aliphatic ketones (Table 3, entries 11 and 12), where longer reaction times were necessary to complete the reductive coupling.<sup>15</sup> Different aliphatic and aromatic aldehydes bearing additional functional groups led efficiently to the coupling products, which increases substantially the potential of this transformation. Thus, aldehydes containing hydroxyl groups protected as ethers or esters, and even unprotected hydroxyl derivatives, coupled efficiently (Table 3, entries 2, 4, and 10). Methoxycarbonyl and halogen derivatives also reacted with acceptable yields (Table 3, entries 3 and 5).

With the aim of widening the scope of this transformation, we checked the ability of titanocene(III) to promote intermolecular cross-coupling reaction between dissimilar ketones. Thus, we submitted benzophenone **60** and excess (4 equiv) cyclohexanone **59** to the standard reaction conditions to obtain the intermolecular cross coupling adduct **61** at 65% yield (Table 3, entry 13). Similar results were obtained with a mixture of citral **49** and benzaldehyde **39** in excess (Table 3, entry 14). It was thus proven that unsymmetrical olefins can be generated by reaction of aromatic and aliphatic carbonyls.

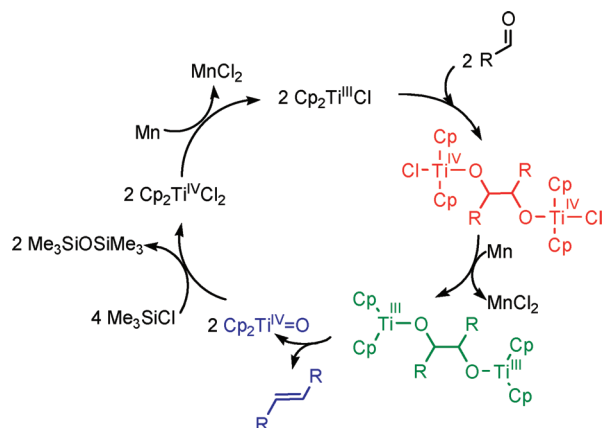
**C. Catalytic Processes in Titanium.** Our final efforts were devoted to render these processes catalytic. Among the types of reagents that have been described to regenerate Cp<sub>2</sub>TiCl<sub>2</sub> from species of oxygen-bonded titanium,<sup>16</sup> chlorosilanes were claimed to promote carbonyl coupling reactions catalytic in titanium by regenerating TiCl<sub>3</sub> from the corresponding titanium oxide, namely, ClTi=O, and accumulating the corresponding hexamethyldisiloxane, which is finally removed in vacuum. Since we propose the formation of titanocene oxides or hydroxytitanocene derivatives in the deoxygenation step of these processes, we decided to make farnesol **19** react with 0.3 equiv of Cp<sub>2</sub>TiCl<sub>2</sub> (2 equiv is required in the noncatalytic route) in the presence of excess Mn and 4 equiv of trimethylsilyl chloride (TMSCl). To our delight, the deoxygenation product was obtained after 55 min in an exceptional 92% yield (Table 2, entry 8). The deoxygenation of diol **30** could also be achieved by employing substoichiometric quantities of Ti and TMSCl as regenerator. The yield of the corresponding alkene (86%) was again higher than that obtained in the stoichiometric version (Table 2, entry 16).

Additionally, this catalytic protocol could also be used to promote the reductive coupling of benzylic aldehydes, and thus, by using only 0.3 mmol of Cp<sub>2</sub>TiCl<sub>2</sub> and 4 equiv of TMSCl, **46** was transformed into **31** in 95% yield (Table 3, entry 6), which again meant an increase in the efficiency of transformation when compared to the stoichiometric version.

The catalytic protocol for this McMurry reaction can be rationalized as depicted in Scheme 5. Thus, the titanium oxo species resulting from the deoxygenation step would react with TMSCl in view of the pronounced oxophilicity of silicon. Consequently, hexamethyldisiloxane, which can be easily removed, would be the final acceptor of oxygen. In this sense, the fact that TMSCl, a known regenerator of titanium chloride from titanium oxides, is capable of regenerating the final

(15) Although in these cases, other reductive coupling mechanisms possibly coexist, it should be noted that the corresponding pinacols deriving from acetophenone **55** and geranylketone **57** could be isolated.

(16) Fürstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468–4475.

**Scheme 5.** Proposed Catalytic Cycle for Reductive Carbonyl Olefination

titanium species produced in this transformation strongly supports the proposed formation of  $\text{Cp}_2\text{Ti}=\text{O}$  in the deoxygenation process.

A final piece of evidence of the potential of this protocol was obtained when the keto alcohol **26** was subjected to catalytic conditions, giving an excellent 85% yield of the deoxygenated compound. The yield improved significantly on that obtained in the stoichiometric version, an increase that was noticed in all cases where both versions were compared.

## Conclusion

We describe two new synthetic applications of Nugent's reagent in organic chemistry as a direct consequence of the dramatic decrease in homolytic C–O bond dissociation energy for  $\text{RH}_2\text{C}-\text{OH}$  compared to that for the complex  $\text{Cp}_2\text{Ti}^{\text{III}}(\text{Cl})\text{HO}-\text{CH}_2\text{R}$ . The first of these applications is an easy and reproducible deoxygenation–reduction procedure for alcohols and 1,2-diols. This method complements alternative previously reported deoxygenations and is of general interest to organic synthesis. Its application on the allylic terpenoid alcohol **22** deserved to be emphasized, since it mimicks the

function of the IspH enzyme in the natural biosynthesis of C5 units of the terpenoids through the deoxyxylulose phosphate pathway.<sup>11</sup>

We have also described that Nugent's reagent has the capability to induce reductive carbonyl coupling in reasonable short reaction times and with total reproducibility. The mechanistic evidence presented, proving the involvement of Ti(III) pinacolates in the deoxygenation step of this McMurry olefination, is particularly noteworthy since, in our opinion, it casts some light on one of the mechanistically more obscure transformations in organic chemistry.

Additionally, we have proven how these processes can be performed catalytically in  $\text{Cp}_2\text{TiCl}_2$  by using TMSCl as the final oxygen trap. In this sense, we should underscore the fact that keto alcohol **26** was efficiently transformed into the corresponding deoxygenated compound **27** by using the catalytic protocol, a process where the less reactive aliphatic keto group was completely discriminated in favor of the allylic alcohol.

Our current interest is focused to gain a comprehensive understanding of the overall reactions and to widen the scope of these innovative processes. We are also engaged in testing the applicability of these processes in the synthesis of bioactive natural products.

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**Supporting Information Available:** Computational details, experimental procedures, spectroscopic data, and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra for compounds **8**, **10**, **12**, **14**, **16**, **18**, **20**, **23**, **25**, **27**, **29**, **31**, **33**, **41**, **43**, **45**, **48**, **50**, **52**, **54**, **56**, **58**, **61**, and **62** and complete ref 8a. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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