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Is the trinuclear complex the true reducing species in the Cp_2TiCl_2/Mn- and Cp_2TiCl_2/Zn-promoted pinacol coupling?

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Abstract – Through a combination of kinetic, voltammetric and product analysis, it has been found that a common Ti^{III} species obtained from the metal reduction of Cp_2TiCl_2 is involved in the electron transfer to benzaldehyde. A common species in the pinacol dimerization step was also demonstrated. In neither of the two steps is it necessary to invoke trinuclear complexes as previously proposed. © 2001 Académie des sciences / Éditions scientifiques et médicales Elsevier SAS

pinacol coupling / titanium(III) / electron transfer / ketyl radical

Résumé – Le complexe trinucléaire est-il vraiment l'espèce réductrice dans le couplage pinacolique induit par Cp_2TiCl_2/Mn et Cp_2TiCl_2/Zn ? À l'aide d'une combinaison d'études cinétiques, voltamétriques et d'analyses des produits formés, il a été trouvé qu'une espèce commune Ti^{III}, obtenue par réduction métallique de Cp_2TiCl_2, est impliquée dans l'étape de transfert électronique sur le benzaldéhyde. Une espèce commune dans l'étape de dimérisation du couplage pinacolique a également été mise en évidence. Les complexes trinucléaires précédemment proposés ne sont impliqués dans aucune de ces deux étapes. © 2001 Académie des sciences / Éditions scientifiques et médicales Elsevier SAS

couplage pinacolique / titane(III) / transfert électronique / radical cétyl

1. Introduction

The pinacol coupling reaction of carbonyl compounds is an important synthetic C–C bond-forming transformation for the obtention of vicinal diols.

Various low-valent transition metal complexes have been found to promote this radical-based reaction [1–3], procedures which have become increasingly popular owing to the development of catalytic protocols with respect to the single electron reducing agent. One such reagent is bis(cyclopentadienyl)titanium chloride (Cp_2TiCl) [4], which has previously been exploited for the highly diastereoselective synthesis of *dl*-hydrobenzoin from benzaldehyde [5] and in selective reductions of epoxides [6]. The preparation of trivalent titanium species in THF may be achieved by the simple reduction of Cp_2TiCl_2 with metals such as zinc [7], aluminum [8] and manganese [9] or by electrochemical reduction [10]. Using manganese or zinc as the metal reductant, bridging trinuclear complexes $(Cp_2TiCl)_2MetCl_2$ (Met = Mn or Zn) have been identified by X-ray crystallography (*figure 1a*) [9, 11]. Subsequently, these complexes have not only been proposed to be the reacting species in THF in the generation of the ketyl radical intermediate [12], but also to be the reason for the high diastereoselectivity observed in the diol products of

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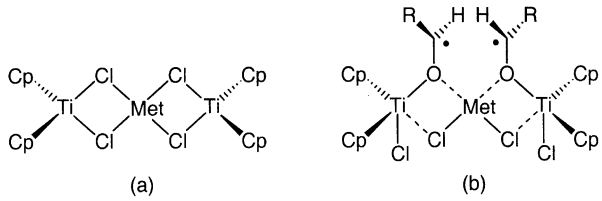

Figure 1. a. Structure of the trinuclear species obtained by reduction of Cp_2TiCl_2 using Mn [11] or Zn [9], Met = Mn or Zn. **b.** Proposed structure of the ketyl radical intermediate leading preferentially to the *dl*-isomer of the pinacol product [5].

the pinacol coupling (*figure 1b*) [5, 13]. Pivotal to this discussion is the report that replacing the central metal atom of the trinuclear complex from Zn or Mn to Mg increases the diastereoselectivity [5, 13].

In this paper, we reveal through electrochemical investigations of the reducing species obtained from Cp_2TiCl_2 with Mn or Zn, in combination with kinetic studies on the pinacol coupling of benzaldehyde, that the trinuclear complexes are not the reducing species in THF as previously proposed. In addition, we also provide evidence that such complexes are not involved in the dimerization of the ketyl radical, and that the high diastereoselectivity observed arises from simple coupling of the $Cp_2Ti^{IV}Cl$-bound ketyl radical.

2. Cyclic voltammetry

In order to gain information about the reducing species obtained from the metal-based reductions of Cp_2TiCl_2, the redox properties of the Ti^{III} complexes were investigated by cyclic voltammetry in a supporting electrolyte solution of 0.2 M Bu_4NPF_6 in THF (*figure 2*). First, it is noted that the voltammogram of Cp_2TiCl_2 essentially displays a one-electron redox system, where the oxidation of the titanocene dichloride anion is detectable at –1.2 V vs Fc^+/Fc (at a sweep rate of 0.1 $V \cdot s^{-1}$) [14]. In comparison, the voltammograms of the two metal-generated titanocene chlorides show a more complicated behavior. In both cases, similar oxidation peaks are found at –0.8 and –0.4 V vs Fc^+/Fc, the electron consumption of which represents an overall one-electron oxidation. Comparison with the cyclic voltammogram of authentic $Cp_2TiCl(thf)$ (prepared from CpTl and $TiCl_3$) [15] suggests that the peak at –0.8 V vs Fc^+/Fc should be assigned to the oxidation of this species to give $Cp_2TiCl(thf)^+$ [16]. The less negative oxidation peak at –0.4 V vs Fc^+/Fc, on the other hand, originates from the corresponding titanocene cation, $Cp_2Ti(thf)_2^+$, as substantiated by the recording of a similar voltammogram when this species is generated (along with TlCl that precipitates) in the reaction between electrochemically generated $Cp_2TiCl_2^-$ and at least two equivalents of $TlPF_6$ in THF. As suggested by Laviron et al. [16], $Cp_2Ti(thf)_2^+$ as well as Cp_2TiCl_2 are formed during the sweep as the result of a father–son reaction between $Cp_2TiCl(thf)^+$ and $Cp_2TiCl(thf)$. The difference observed in the peak currents for the Zn and Mn generated titanocene chlorides is due to a competition between the abilities of $Cp_2TiCl(thf)$ and the corresponding metal chlorides to donate chloride ions to $Cp_2TiCl(thf)^+$. While $ZnCl_2$ does not donate Cl^- and a peak current ratio of ½:½ is obtained as expected when the father–son reaction is fast, $MnCl_2$ can to some extent give off Cl^-, thereby altering the peak current ratio to ¾:¼. The reduction peak appearing at –1.1 V vs Fc^+/Fc on the reverse scan is then ascribed to the reduction of Cp_2TiCl_2, even if it is shifted approximately 0.2 V in positive direction as compared to the voltammogram of pure Cp_2TiCl_2; this kinetic shift is due to a fast chloride transfer from $Cp_2TiCl_2^-$ to the metal halide.

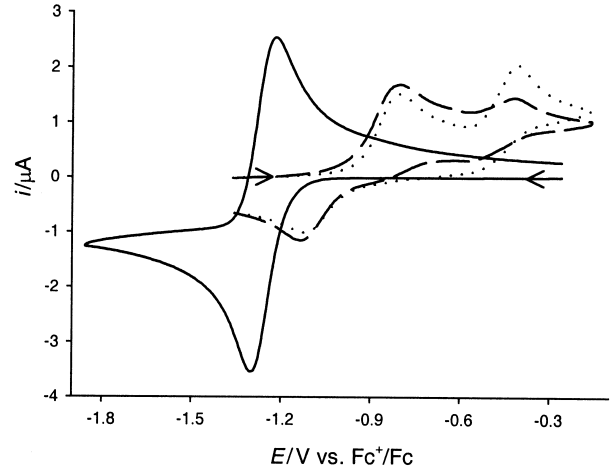

Figure 2. Cyclic voltammograms of three different titanocene chlorides (2 mM) recorded in 0.2 M Bu_4NPF_6/THF at a glassy carbon electrode (∅ = 1 mm) at a sweep rate of 0.1 $V \cdot s^{-1}$: Cp_2TiCl_2 (—), Cp_2TiCl_2/Zn (·····), Cp_2TiCl_2/Mn (– –). The arrows indicate the starting point and direction of the sweeps.

The almost identical electrochemical behavior of the two metal-generated Ti^{III} species in conjunction with our expectations that the different Lewis acid properties of Mn^{II} vs Zn^{II} ions would almost certainly have led to different oxidation peak potentials if trinuclear complexes were present in solution, suggests that the latter are not important in the electrode processes.

Further evidence for the absence of such trimetallic species was supported by kinetic studies on the pinacol coupling of benzaldehyde in combina

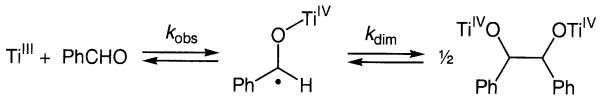

Figure 3. Reaction mechanism for the Ti^{III}-promoted pinacol coupling of benzaldehyde.

tion with measurements made on the diastereoselectivities of the hydrobenzoins obtained from the reduction with the three different Ti^{III} reducing agents. The pinacol coupling reaction is composed of two distinct steps, as illustrated in *figure 3*, involving an initial electron transfer to the carbonyl group followed by a dimerization of the intermediate Ti^{IV} bound ketyl radical. As the first step is the rate-controlling, comparative information concerning the Ti^{III} species in solution may be obtained by the rate constants measured. On the other hand, analysis of the diol obtained provides details about the Ti^{IV} bound ketyl radical.

3. Kinetic measurements

The relevant rate constants k_{obs} were extracted from the exponential decay of the Ti^{III} species observed under pseudo-first-order conditions, i.e. in the presence of excess benzaldehyde, at a wavelength of 780 nm in UV–vis spectroscopy. As can be seen from the *table*, the Zn- or Mn-generated titanocene chloride afforded essentially identical rate constants for the reduction of benzaldehyde to its corresponding ketyl radical, implying that the same metal generated Ti^{III} species is responsible for the reduction in the rate-controlling step. For a trinuclear complex the rate constants for the reduction of benzaldehyde with the Zn- vs the Mn-generated Ti^{III} reducing agents would most likely have been different. On the other hand, a 20 fold rate decrease was observed using the electrochemically reduced Cp_2TiCl_2, suggesting that another reducing agent is in play or that the rate-controlling step is different in this case, e.g. the dissociation of $Cp_2TiCl_2^-$ to give Cp_2TiCl and Cl^-.

Table. Rate constants k_{obs} for the reaction between benzaldehyde and titanocene chlorides generated by different procedures together with the *dl:meso* ratio of the pinacol coupling products. All measurements were carried out at 20 °C.

Reducing agent	k_{obs} ($mol^{-1}\cdot s^{-1}$)	*dl:meso*
Cp_2TiCl_2/Zn	30 ± 5	97:3
Cp_2TiCl_2/Mn	30 ± 5	97:3
Cp_2TiCl_2/e^-	1.5 ± 0.5	96:4
Cp_2TiCl [a]	–	98:2

[a] From ref. [17], where Cp_2TiCl is prepared from reduction of Cp_2TiCl_2 using Al. This reaction was run at –78 °C.

4. Diastereoselectivities

Examination of the diastereoselectivities of the pinacol coupling product obtained employing the three differently prepared Ti^{III} agents (*table*), led to essentially the same *dl:meso* ratios of approx. 97:3, a similar value which was also noted by Schwartz employing the salt free Cp_2TiCl_2 in THF [17]. In other words, the presence or the absence of the metal halides does not have an apparent effect on the diastereoselectivities of the diol product, suggesting that the $Cp_2Ti^{IV}Cl$-bound ketyl radical is the most likely intermediate undergoing radical coupling.

Clearly, the above results are not in favor of trinuclear complexes in either of the two steps of the pinacol coupling reaction. The previous results by Inanaga and Gansäuer, demonstrating that diastereoselectivities of the pinacol coupling of aryl aldehydes are significantly improved upon the addition of $MgBr_2$ [5, 13], do not necessarily imply that trinuclear complexes are involved. However, what role this Lewis acid may play on either the reducing species or the ketyl radical intermediate is not certain.

In conclusion, we have shown that trinuclear complexes need not to be invoked in the mechanism for the reductive dimerization of benzaldehyde by Cp_2TiCl prepared by the reduction of Cp_2TiCl_2 with zinc or manganese. Further work is now in progress in our laboratories to identify the true reducing species in these and other Cp_2TiCl promoted reductions, the results of which will be published in a subsequent paper.

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