Mechanistic Studies on Reactions Employing Bis(cyclopentadienyl)titanium Halides as Single Electron Transferring Agents

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The extensive use of the mild reducing agent bis(cyclopentadienyl)titanium chloride (titanocene chloride, Cp_2TiCl) in diastereoselective pinacol couplings,[1] epoxide openings[2] and reductions of alkyl halides[3] has stimulated a great interest in clarifying the mechanism of these reactions. The interest is further stimulated by the conflicting literature reports on the exact nature of the reactive species in a THF solution of titanocene chloride.[1-4]

Titanocene halide (X = Cl, Br and I) can be prepared in a number of different ways from titanocene dihalide (**I**) by electrochemical reduction or by using metals such as Zn, Mn or Al as reductants (eq 1).

$$\underset{\mathbf{I}}{Cp_2TiX_2} + Met \xrightarrow[THF,\ r.t.]{} Cp_2TiX + {}^{1}/_{y}\ MetX_y \qquad (1)$$

In the present work these titanocene halides have been studied by means of cyclic voltammetry and reaction kinetics involving a number of different substrates such as benzyl chloride, benzyl bromide and benzaldehyde. Furthermore the product distribution (*dl:meso* ratios) obtained in the pinacol coupling of benzaldehyde was investigated.

Cyclic voltammetry studies

Cyclic voltammograms of the titanocene halides generated by reduction of **I** using Zn show two oxidation peaks in the range -0.9 to -0.3 V *vs.* Fc^+/Fc, fig. 1. The first peak at the lower potentials is attributed to the oxidation of titanocene halide, the peak potential of which increases going from X = Cl to Br and I. The second peak is assigned to the oxidation of the titanocene cation, since its position is unaffected by the nature of X. The same pattern is observed for all metal generated titanocene halides.

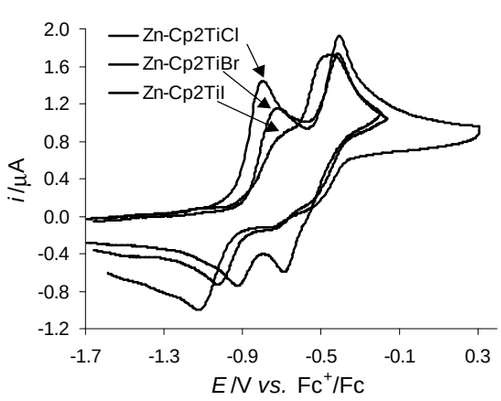

Figure 1. Cyclic voltammograms of 2 mM Zn-Cp_2TiX at a glassy carbon electrode in 0.2 M $TBAPF_6$/THF solution. The sweep rate is 0.1 V s^{-1}.

Kinetic measurements

The kinetics of the reaction between titanocene halides and benzyl chloride, benzyl bromide and benzaldehyde was followed by UV spectroscopy, table 1. Surprisingly, the observed rate constants were found to be practically independent of the X in Cp_2TiX and the method used for its preparation, the exception being for the electrochemically generated titanocene chloride.

On this basis, we propose that the reactive species in the titanocene based reductions is the common titanocene cation, even if it is a relatively poor electron donor as deduced from the measured peak potentials.

Table 1. Observed rate constants in $M^{-1}\ s^{-1}$ for the reactions between titanocene halides and three different substrates.

	BnCl	BnBr	PhCHO [b)]
Zn-Cp_2TiCl	0.48	11	30
Zn-Cp_2TiBr	0.45	12	25
Zn-Cp_2TiI	0.46	10	20
Mn-Cp_2TiCl	0.48	11	25
Mn-Cp_2TiBr	0.44	11	25
Mn-Cp_2TiI	0.5	11	22
Al-Cp_2TiCl	0.48	12	30
Al-Cp_2TiBr	0.50	13	25
Al-Cp_2TiI	0.55	15	20
$Cp_2TiCl_2^-$ [a)]	0.05	1.2	≈ 1
$Cp_2TiBr_2^-$ [a)]	0.33	9	15
$Cp_2TiI_2^-$ [a)]	0.48	12	17

[a)] Electrochemically generated; the effect of the presence of supporting electrolyte is not yet fully clarified.
[b)] Recent measurements on the kinetics of the reaction between titanocene halide and benzaldehyde indicate that the electron transfer step may be reversible.

Diastereoselectivity in the pinacol coupling of benzaldehyde

A systematic investigation of the diastereoselectivity in the pinacol coupling of benzaldehyde promoted by titanocene halide revealed that the *dl:meso* ratios were practically independent of the method used for generating (chemically or electrochemically) the titanocene halide. However, the nature of the halogen atom now plays an important role as the diastereomeric excess is lowered when going from Cl to Br and I.

On the basis of these results we conclude that the metal halides formed in the metal reduction of the titanocene dihalides do not have any influence on the diastereoselectivity as suggested in literature[1,4] and that the most likely species to undergo radical coupling is a $Cp_2Ti^{IV}X$-bound ketyl radical.

References

1) Handa, Y.; Inanaga, J. *Tetrahedron Lett.* **1987**, *28*, 5717.
2) Rajanbabu, T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1994**, *116*, 986
3) Cavallaro, C. L.; Schwartz, J. *J. Org. Chem.* **1995**, *60*, 7055.
4) Gansäuer, A.; Bauer, D. *Eur. J. Org. Chem.* **1998**, 2673.