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Cp_2TiCl: An Ideal Reagent for Green Chemistry?

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ABSTRACT: The development of Green Chemistry inevitably involves the development of green reagents. In this review, we highlight that Cp_2TiCl is a reagent widely used in radical and organometallic chemistry, which shows, if not all, at least some of the 12 principles summarized for Green Chemistry, such as waste minimization, catalysis, safer solvents, toxicity, energy efficiency, and atom economy. Also, this complex has proved to be an ideal reagent for green C−C and C−O bond forming reactions, green reduction, isomerization, and deoxygenation reactions of several functional organic groups as we demonstrate throughout the review.

1. INTRODUCTION

Green Chemistry, also called sustainable chemistry, is a term coined in the early 1990s by Anastas et al.[1] of the US Environmental Protection Agency (EPA). It is an area of chemical engineering and chemistry centered on the chemical methodologies and design of components that minimize the use and formation of hazardous substances. The 12 principles of Green Chemistry reported by Anastas et al.[1] are listed in Scheme 1.

This new concept allowed change from the traditional concepts of reaction efficiency and selectivity focused on chemical yield, to one that assigns value, among others, waste prevention, atom economy, and elimination of hazardous and/or substances.

For decades in the area of chemical synthesis, great efforts were made to develop newer methodologies and reagents without considering the sustainability of chemical processes.

The development of Green Chemistry inevitably involves the development of new methodologies and green reagents which have experienced significant growth over the past two decades while contributing to the development of sustainable chemistry. Many of these reagents largely comply with the principles set for Green Chemistry. Some examples of these reagents were reported by P. Tundo and V. Esposito[2] and have involved the design of new synthetic pathways which allow chemical methodologies to be performed in a very controlled way, so as to minimize drastically, or even eliminate, all the environmental impact. In this context, new green reagents are of paramount importance in the development of alternative methodologies in chemical synthesis that catalyze several efficient transformations, under mild reaction conditions, with simple experimental procedures, safer solvents, and avoiding toxic wastes. In this way, after the seminal works reported by Nugent and Rajanbabu in the radical opening of epoxides,[3] titanocene monochloride (Cp_2TiCl) has proved to be a mild single-electron transfer (SET) which has found wide use in organometallic and radical[4] chemistry, which include, if not all, at least some of the 12 principles reported for Green Chemistry.

In this review, we highlight that Cp_2TiCl can be considered an ideal reagent for green C−C and C−O bond forming reactions, green reduction, isomerization, and deoxygenation reactions of several functional organic groups.

The content of the review aims to demonstrate that Cp_2TiCl is a reagent which evaluates the chemical yield, selectivity, solvents, catalysis, toxicity, and efficiency according to the atoms economy principle established by Trost.[5]

2. Cp_2TiCl AS A GREEN CHEMISTRY REAGENT

2.1. Synthesis and Properties of Cp_2TiCl. Cp_2TiCl is a single-electron-transfer (SET) complex that can be easily prepared from commercial and nontoxic Cp_2TiCl_2 (Scheme 2) by using economic and nontoxic reductants such as Mn or Zn.[6a,b] In solution, Cp_2TiCl is in an equilibrium between mononuclear and dinuclear species (Scheme 2).[7] It has recently been reported that the stoichiometric metal reductant can be replaced by an organic reducing agent.[6c]

The structures of these species of titanium(III) show an unpaired *d* electron, giving them mild electron-reducing character ($E°$= −0.8 vs Fc^+/Fc).[8] This reducing character together with the presence of a vacant site allows the coordination of a heteroatom with free valence electrons, thus initiating the monoeletronic transfer through an inner-sphere mechanism.[9]

In the seminal works reported by Nugent and Rajanbabu,[3] it was observed that Cp_2TiCl was a novel single-electron transfer species capable of generating a radical from an epoxide, which under different experimental conditions could give cyclization reactions, intermolecular additions, reductions, and deoxygenation reactions. From this moment, this SET was widely used in

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