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Note

Synthesis of substituted titanocene dichloride derivatives by hydrosilylation

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ABSTRACT

Substituted titanocene complexes have been prepared by hydrosilylation of organic substrates containing a terminal double bond by cyclopentadienyl complexes of titanium bearing a Si–H functional group. This new synthetic protocol is demonstrated by synthesis of mono-, bi- and trihomonuclear complexes. The structures of prepared compounds have been characterized by standard methods (NMR, IR, and HRMS).

Introduction

Metallocenes of group 4 transition metals, in particular titanocenes, have received special attention among the cyclopentadienyl complexes and over the last few decades have become a well-established class of compounds, for which numerous applications have been found. Cyclopentadienyl complexes of titanium also play an important role in catalysis of many chemical transformations [1]. Syntheses of new titanocene-based catalysts for polymerization and hydrogenation still remain an attractive field of research [2]. Titanocene dichloride (TDC) has been shown to have antiproliferative activity but due to the low efficacy in the clinical trials its further investigation were abandoned. Since then various methods have been developed to modify the structure of titanocenes to improve its antitumour activity [3].

In contrast to ferrocene, functionalization of the cyclopentadienide ring in titanocene is difficult because of the electrophilic nature of the $[TiCl_2]$ fragment which renders most synthetic strategies inapplicable. Standard methods for the preparation of ring-substituted titanocenes are based on modification of the cyclopentadiene ligand prior its deprotonation and metallation, or on carbolithiation or hydrolithiation of suitably modified fulvenes and transmetallation [4]. Preparation of a larger number of derivatives such as homological series by these multistep methods is tedious and time-consuming. An elegant modular strategy, developed by Gansäuer for ester-substituted as well as cationic amide-substituted titanocene dichlorides, is based on the reaction of the titanocene acyl chloride building block with various alcohols or primary or secondary amines to afford the corresponding products. This modular synthesis allows introducing polar functional groups which are incompatible with the strongly basic and nucleophilic conditions of the traditional procedures [5].

Here we wish to report another approach based on hydrosilylation of a terminal double bond of different substrates by titanocene bearing an Si–H group in its molecule. Recently Gómez-Ruiz's studied the reactivity of an *ansa*-bridge Si–H bond in the hydrosilylation of unsaturated silane substrates in order to modify the ligand framework of robust *ansa*-metallocene complexes of the group 4 [6]. Cuenca introduced the Si–H unit to the Cp ring by reaction of $Na(C_5H_5)$ with an appropriate chlorosilane reagent, and subsequently, synthesis of silyl substituted mono- and di-cyclopentadienyl zirconium derivatives was described [7]. Alt used this ligand, among others, for synthesis of unsymmetrical titanium complex $Ti(C_5H_5)[C_5H_4(SiMe_2H)]Cl_2$. Nevertheless the intention to utilize this complex as a component in hydrosilylation reaction failed [8]. To avoid the slightly unstable bond between silicon and a cyclopentadiene ring we synthesized precursors of a cyclopentadienyl ligand with an alkyl spacer between the SiH fragment and cyclopentadiene as it is described in our previous

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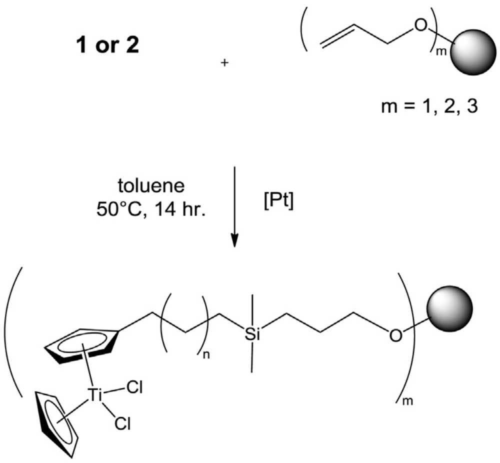
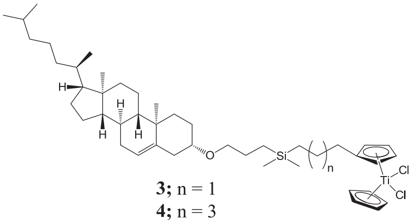
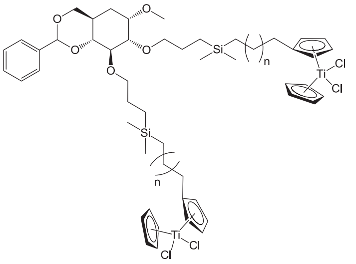
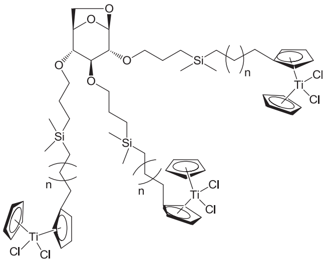
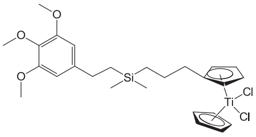


Scheme 1. General Scheme for preparation of titanium complexes by hydrosilylation.

Table 1
Functionalized titanocenes dichloride prepared by hydrosilylation.

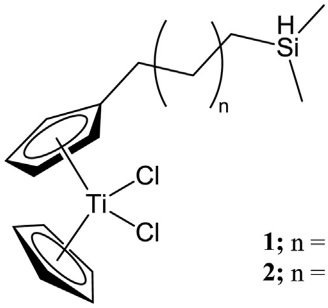
Product	Yield %
 **3;** n = 1 **4;** n = 3	65, 68
 **5;** n = 1 **6;** n = 3	46, 57
 **7;** n = 1 **8;** n = 3	63, 72
 **9;** n = 1	56

works [9]. Three substituted cyclopentadienes with a variable length of the spacer between the Si—H moiety and the cyclopentadiene ring were designed and synthesized. Then unsymmetrically substituted titanocene dichlorides bearing those ligands were prepared. In the last step, metallodendrimers were constructed by anchoring the prepared titanium complexes to the periphery of vinylated carbosilane dendrimers by hydrosilylation. This process was optimized towards obtaining a series of new carbosilane metallodendrimers with dicyclopentadienyl complexes on their periphery.

We have been interested in utilization of this method in a more general manner. To this objective we prepared two-component molecules, which consist of a titanocene unit and a second functional unit which varies within the series. The general synthetic protocol is illustrated in Scheme 1. We prepared a series of titanocene dichloride conjugates possessing from one to three metallic cores attached by hydrosilylation to terminal double bonds (Table 1). A changeable spacer between the organic and the metallic part can modify properties of the target molecules. Structures of the prepared compounds have been characterized by standard methods (NMR, IR, and HRMS).

Result and discussion

Preparations of titanocene dichlorides with three- and five-carbon spacers between the Si—H functionality and the Cp ring (Fig. 1) were described in the preceding papers [9]. Organic substrates were modified to obtain the suitable non-metallic partner for hydrosilylation. Their hydroxyl group(s) were allylated by reaction with allyl bromide to introduce terminal double bonds into the molecules as shown for 1,6-anhydro-β-D-glucopyranose (Scheme 2). Hydrosilylation of allylic molecules with complexes **1** and **2** used in a slight excess gave the products **3**–**9** (Table 1). The Karstedt catalyst was used in toluene at 50 °C, and the course of the reactions was monitored by ^{1}H NMR. A characteristic feature of the starting complex is the presence of Si—H functionality which is easily recognized by NMR spectroscopy (Si*H*: δ_H = 3.84 ppm; δ_{Si} = −13.1 ppm for **1** resp. δ_H = 3.72 ppm; δ_{Si} = −13.1 ppm for **2**). The presence of the Si—H group led to a splitting of the signals corresponding to Si(CH_3)$_2$ (δ_H = 0.09 ppm) into doublets with a low coupling constant ($^3J_{HH}$ = 3.3 Hz), which is typical for vicinal coupling through the silicon atom. Infrared spectroscopy is also useful for detection of the Si—H group: band (ν(Si—H) = 2110 cm^{-1} for **1** resp. 2109 cm^{-1} for **2**). Characteristic for the formation of the product is the change of multiplicity of methyls connected to the silicon. Due to the addition of the Si—H bond to the allyl group the methyl doublet disappears and a new singlet with a typical shift about zero ppm is formed. At the same time we observe disappearance of the signals of the double bond. If the signals of the



1; n = 1
2; n = 3

Fig. 1. Structure of titanium complexes with a variable length of spacer between Si—H moiety and cyclopentadienyl ring.