inorganics

MDPI

Article

Metalation Studies on Titanocene Dithiolates

Tilmann G. Kießling and Karlheinz Sünkel *

Department of Chemistry, Ludwig-Maximilians University Munich, 81377 Munich, Germany; tilmann.kiessling@embo.org

* Correspondence: suenk@cup.uni-muenchen.de; Tel.: +49-89-2180-77773

Received: 18 July 2018; Accepted: 22 August 2018; Published: 24 August 2018

Abstract: Titanocene bis-arylthiolates $[(C_5H_4X)(C_5H_4Y)Ti(SC_6H_4R)_2]$ (X,Y = H, Cl; R = H, Me) can be prepared from the corresponding titanocene dichlorides by reacting with the thiols in the presence of DABCO as a base. They react with *n*-butyl lithium to give unstable Ti(III) radical anions. While the unsubstituted thiolates (X = Y = R = H) react with lithium Di-isopropylamide by decomposing to dimeric fulvalene-bridged and thiolate-bridged Ti(III) compounds, the ring-chlorinated compounds can be deprotonated with LDA and give appropriate electrophiles di-substituted and tri-substituted titanocene dithiolates.

Keywords: titanocene thiolates; metalation; chlorocyclopentadienyl ligands

1. Introduction

Titanocene compounds, i.e., compounds of the type "Cp_2TiX_n" where "Cp" stands for a substituted or unsubstituted cyclopentadienyl ligand and "X" for any anionic or neutral ligand and *n* = 0–2 are arguably the second-most studied metallocenes after ferrocene. Soon after the first synthesis of $(C_5H_5)_2TiCl_2$ in 1954 [1], its potential for acting as a polymerization catalyst when combined with certain aluminum compounds was discovered [2]. Further studies showed that a judicious choice of substituents on the cyclopentadienyl ring had a great influence on the stereochemistry of the produced polymers, which gave rise to an enormous number of publications and also many review articles [3–8]. However, it was also found that the titanium catalysts were rather quickly deactivated and the corresponding zirconium compounds showed much higher stability and catalytic activity. Thus, the mainstream research on metallocene catalysts stopped for titanium-based metallocenes nearly completely until recently when the concepts of "Green Chemistry" and "Sustainable Catalysis" came into play [9–12]. Another area of "applied research" opened up after the discovery that Cp_2TiCl_2 showed antitumor activity [13–15]. Here again, it turned out that the effectiveness of the titanocenes could be enhanced by introducing substituents on the cyclopentadienyl rings [16,17] as well as by modifying the "X"-ligands [17,18]. Lastly, titanocenes were the subject of purely "academic" studies, e.g. studies devoted to synthesis, isolation, and characterization of the "true" titanocenes "Cp_2Ti" [19] or of "chiral at titanium" complexes "CpCp'TiXY" [20]. In addition, in these studies, the importance of cyclopentadienyl ring substituents was well established. All of the titanocenes with substituted cyclopentadienyl rings known so-far have been prepared by a reaction of the substituted cyclopentadiene with $TiCl_n$ (*n* = 2–4). This method fails for very electronegative substituents or substituents with ligating properties. Since our group focuses on the synthesis of Cyclopentadienyl complexes with such substituents for a long time, using an approach of performing halogen-metal exchange reactions followed by electrophilic substitutions on already coordinated perhalogenated cyclopentadienyl ligands [21], we wondered if our approach was also suitable for the titanocene system. Since our synthetic protocol always involves the use of lithium organyls or lithium amides, there was also the need for a proper titanocene starting material. It has been known for a long time that titanocene

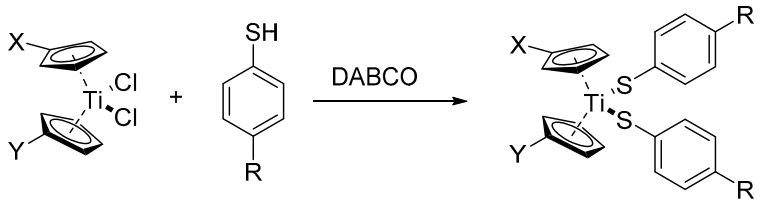
chlorides react with alkyl lithiums to thermally unstable titanocene alkyls Cp_2TiR_2, which easily decompose to titanium(III) products [22,23] and with lithium amides to mono-cyclopentadienyl titanium tris-amides $CpTi(NR_2)_3$ [24]. In addition, with the often-used base KO^tBu, a mixture of products including those of splitting off the cyclopentadienyl ligands was observed [25]. We, therefore, decided to look at the also long-known titanocene thiolates $Cp_2Ti(SR)_2$. These compounds are usually prepared either by a reaction of Cp_2TiCl_2 with thiols in the presence of the base, which were sometimes contaminated with the mixed chloride-thiolates $Cp_2Ti(SR)Cl$ [26–28] or by oxidative addition of disulfides to in-situ prepared "Cp_2Ti" [29]. Some of these thiolates showed promising antitumor properties [30,31].

In this study, we report on the synthesis of several titanocene bis(aryl thiolates) $(Cp)(Cp')Ti(SAr)_2$ and their reactivity towards lithium alkyls and amides including functionalization of the cyclopentadienyl rings. It should be mentioned here that a related approach was used for deriving the so-called "Troticenes" CpTi(Cht) [32].

2. Results

2.1. Synthesis of Starting Materials

Treatment of the known titanocene dichlorides $(C_5H_4X)(C_5H_4Y)TiCl_2$ (X = Y = H, **1a**; X = H, Y = Cl, **1b**; X = Y = Cl, **1c**) [33,34] with $HS–C_6H_4R$ (R = H, *p*-Me) in the presence of DABCO (1,4-diazabicyclo[2.2.2]octane) yields the corresponding titanocene arylthiolates $(C_5H_4X)(C_5H_4Y)Ti(S–C_6H_4R)_2$ (R = H, **2a–c**, Me: **3a–c**), respectively, in good yields (64% to 89% except for **3b**, 19%) (Scheme 1).



	X	Y
1a	H	H
1b	H	Cl
1c	Cl	Cl

X	Y	R=H	R=Me
H	H	**2a**	**3a**
H	Cl	**2b**	**3b**
Cl	Cl	**2c**	**3c**

Scheme 1. Synthesis of substituted titanocene thiolates.

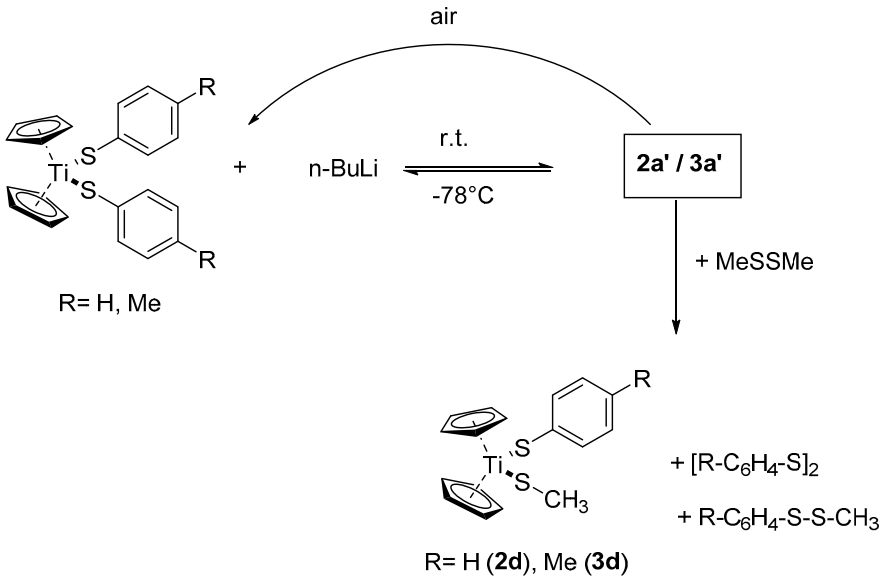
Compounds **2a** and **3a** had been reported before [26,27]. All compounds were characterized by ^{1}H-NMR and ^{13}C-NMR and mass spectroscopy including HRMS. The NMR spectra of **3b/c** show the presence of $HS–C_6H_4CH_3$ or $[S–C_6H_4–CH_3]_2$ and very weak signals (<2%) derived from **1b/c** and $(C_5H_4X)(C_5H_4Y)Ti(S–C_6H_4R)Cl$.

2.2. Reaction of Dithiolates **2a** and **3a** with Butyllithium

Treatment of a suspension of **2a** or **3a** with 1.1 equivalents of *n*-BuLi in THF at −78 °C results in the formation of yellow solutions. Warming to room temperature leads to a color change from yellow to brown within five minutes. The resulting solutions appear to be paramagnetic since it turns out impossible to obtain any good-quality ^{1}H- or ^{13}C-NMR spectra. However, the solutions resulting from **2a** show a ^{7}Li-NMR resonance at δ = 2.64 ppm while the solutions resulting from **3a** exhibit a ^{7}Li-NMR signal at δ = 2.74 ppm (Figures S5 and S6). For comparison, the ^{7}Li-NMR signals of THF

solutions of Li(C_5H_5), LiSC_6H_5, and Li$SC_6H_4CH_3$ can be found at δ = −8.37, 1.98, and 1.90 ppm, respectively). Cooling these solutions down to −78 °C leads to a color change and it turns into a violet color. Warming up to room temperature reinstates the brown color and evaporation of the solvent in vacuum leaves a brown residue, **2a′** or **3a′**, respectively. When a frozen solution made up from **3a** and four equivalents of butyl lithium in THF is gradually warmed up within a NMR spectrometer, a ^{1}H-NMR spectrum immediately taken at −80 °C shows no signals of the Li–CH_2 protons. However, a signal due to LiC_5H_5 and several signals is presumably assigned to Tol-SBu. After warming to ambient, the signals due to **3a** are re-installed and, while the LiCp signal has disappeared, the signals of Tol-SBu are still present (Figure S4).

Both solid compounds are extremely air-sensitive and yield within seconds in air violet solids, which can be identified as **2a** or **3a** by using ^{1}H-NMR spectroscopy. When the yellow solutions, obtained from **2a** or **3a** and *n*-BuLi at −78 °C, are treated with dimethyldisulfide at this temperature and the mixture is warmed to ambient, the color changes to red-violet. Evaporation of the solvent leaves violet oils that contain a mixture of various compounds where $Cp_2Ti(S–C_6H_4R)(SCH_3)$ (R = H, Me) and $(C_6H_4R)_2S_2$ can be identified as unreacted starting materials (Scheme 2).



Scheme 2. Reaction of **2a** or **3a** with *n*-BuLi and air or MeSSMe.

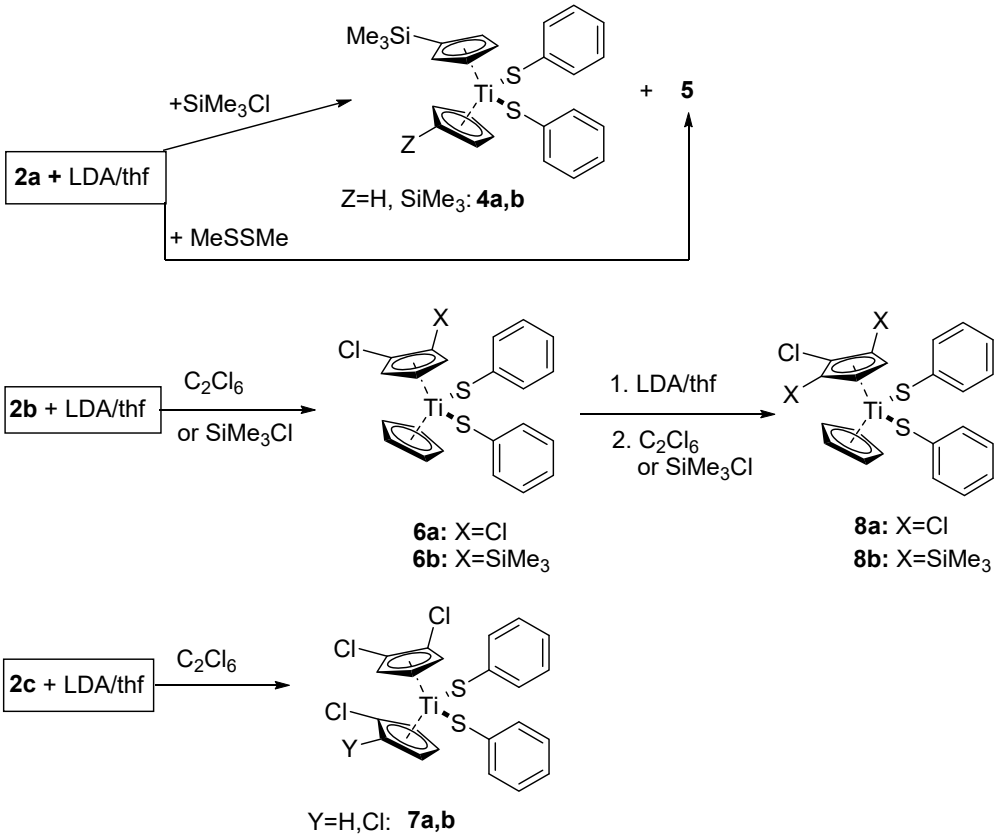
2.3. Ring Metalation of **2a**–**c** *with Lithium Diisopropylamide and Reaction with Electrophiles*

When a THF solution of **2a** is treated at −78 °C with a freshly prepared THF solution of LDA (1.2 equivalents), which is followed by the addition of an equimolar amount of $SiMe_3Cl$ and warming up to room temperature, the product isolated after work-up contains mostly apparently unreacted **2a** together with small amounts of the silylated compounds $(C_5H_4SiMe_3)(C_5H_4Z)Ti(SC_6H_5)_2$ (Z = H, **4a**; $SiMe_3$, **4b**) and a di-nuclear complex of formula $C_{32}H_{28}S_2Ti_2$ (**5**). When dimethyldisulfide was used as an electrophile, the only identifiable product was the dimer **5**. Attempts to purify the compounds by column chromatography lead only to its decomposition. However, compounds **4** and **5** could be unambiguously characterized by HRMS.

Treatment of a THF solution of **2b** with a solution of LDA at −78 °C followed by the addition of hexachloroethane leads, after a chromatographic workup, to a 72% yield of the desired 1,2-dichlorocyclopentadienyl complex $(C_5H_3Cl_2)(C_5H_5)Ti(SC_6H_5)_2$ (**6a**). Similar treatment of **2c** with LDA and C_2Cl_6 led to an inseparable mixture of $(C_5H_3Cl_2)(C_5H_3ClY)Ti(SC_6H_5)_2$ (Y = H, **7a**, Cl, **7b**) in a combined yield of ca. 40% together with a 47% yield of the olefin $C_2(SC_6H_5)_4$. Similar treatment of **2b** with LDA and chlorotrimethylsilane gave the chiral 1-chloro-2-trimethylsilyl-cyclopentadienyl

complex **6b.** While **6a**,**b** could be characterized by NMR and mass spectrometry, compounds **7a**,**b** could only be identified by HRMS. The NMR spectra of **6a** show weak signals that might be assigned to the 1,3-regio-isomer of **6a** (ca. 6%). The NMR spectra of **6b** show weak signals that might be due to PhSH or PhSSPh. The mass spectra of both compounds show peaks due to $(C_5H_3ClY)(C_5H_5)Ti(SC_6H_5)Cl$ (Y = Cl, **6a′**, $SiMe_3$, **6b′**).

If the 1,2-dichlorocyclopentadienyl complex **6a** is treated in THF solution with LDA, which is followed by hexachloroethane, chromatographic workup of the product mixture yields a 24% yield of the desired 1,2,3-trichlorocyclopentadienyl complex $(C_5H_2Cl_3)(C_5H_5)Ti(SC_6H_5)_2$ (**8a**) together with a 20% recovery of the starting material and 7% tetrakis(phenylthio)ethene. Starting from **6b**, LDA and $SiMe_3Cl$ the 1-chloro-2,5-bis(trimethylsilyl)cyclopentadienyl complex **8b** was obtained in a 75% yield (Scheme 3). **8a**,**b** could be characterized by NMR and mass spectroscopy. The ^{1}H-NMR spectrum of **8a** shows a weak signal (ca. 4%) that might be assigned to the C_5H_5 group of the 1,2,4-regio-isomer of **8a**. Signals of PhSH can be seen in NMR spectra of both compounds **8a/b**. The mass spectrum of **8a** shows the presence of $[(C_5H_2Cl_3)(C_5H_5)Ti(SC_6H_5)Cl]$ (**8a′**).



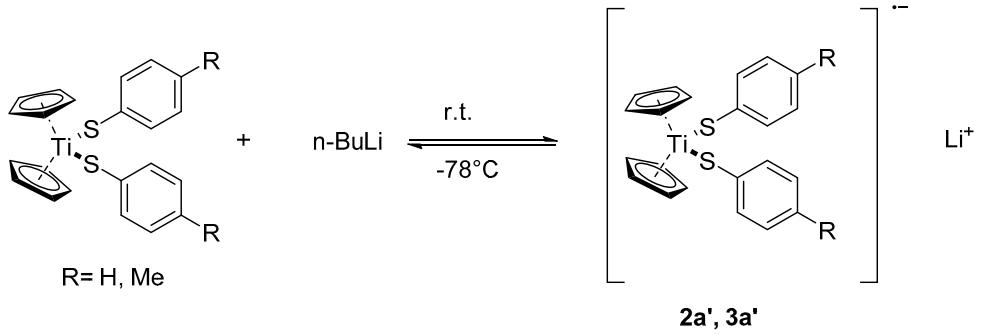
Scheme 3. Reactions of **2a**–**c** with LDA and electrophiles.

3. Discussion

Our previous approach towards functionalization of metal-coordinated cyclopentadienyl rings needs perhalogenated cyclopentadienyl complexes as starting materials, which are not known for the titanocene system. To obtain such titanocenes with perhalogenated Cp rings, stepwise introduction of halogens via alternate metalation-electrophilic halogenation sequences might be a useful strategy, which was successfully applied by us [35–37] and others [38,39] in the ferrocene system and also in the cymantrene system [40]. For the metalation step, we used lithium bases like butyl lithium or lithium amides. As outlined in the introduction, these reagents cannot be used with titanocene chlorides but may work with the corresponding aryl thiolates. Application of the known synthetic

protocol "titanocene dichloride + aromatic thiol + base" with replacement of the usual NEt_3 by DABCO gives not only slightly better yields for the already known bis-arylthiolates **2a** and **3a** but also allows the synthesis of the new chlorocyclopentadienyl thiolates **2b**,**c** and **3b**,**c**. All chlorocyclopentadienyl compounds are air-stable and are highly viscous violet oils that withstand all attempts of crystallization. Since the used starting materials $[(C_5H_4Cl)(C_5H_4X)TiCl_2]$ are always obtained as mixtures with the unsubstituted Cp_2TiCl_2, which are extremely difficult to separate, the corresponding dithiolates were also obtained as mixtures that were easily separated by using chromatography. The lower yields of **2b**,**c** and **3b**,**c** in comparison with their unsubstituted analogs **2a**,**3a** are, therefore, probably due to losses in the purification step and not a consequence of an intrinsic instability. The particularly low yield of **3b** is probably due to an adventitious presence of moisture in the reaction mixture.

The reaction of **2a/3a** with one equivalent *n*-BuLi yields reversibly paramagnetic solutions, which are extremely air-sensitive and produce the starting materials quantitatively upon a deliberate addition of air. Treatment of the reaction solutions with dimethyldisulfide gives the mixed titanocene aryl-alkyl-thiolates **2d/3d** together with the symmetric and asymmetric disulfides ArSSAr and ArSSMe. We think that this behavior is due to a temperature dependent redox-equilibrium with the room temperature solution containing a Ti(III) radical anion, according to Scheme 4.



Scheme 4. The redox equilibrium between **2a/3a** and **2a′/3a′.**

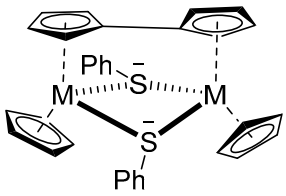
Such a redox equilibria are known from electrochemical studies of Cp_2TiCl_2 [41,42]. It was found that dependent on the cyclopentadienyl ring substituents, the intermediate radical anion might either reversibly split off a chloride anion yielding Cp_2TiCl (the so-called "Nugent-Rajanbabu-reagent" [43]) or irreversibly one of the cyclopentadienyl ligands to give $CpTiCl_2$. It was also reported that treatment of the dialkyltitanocenes Cp_2TiR_2 with organolithium compounds first produced unstable "back-onium complexes" $[Cp_2TiR_3]^-Li^+$, which decomposed at 20 °C to $CpTiR_2$, RH, and LiCp [23]. At least in the observed time and temperature frame used by us, the presumed Ti(III) thiolates **2a′/3a′** are more stable since we could not observe any LiSAr or LiCp in the reaction solution. Quite interestingly, when a *fourfold* excess of butyl lithium was used in an NMR experiment, LiCp can be detected in the cold solution, but it disappears when warming-up. At the same time, Tol-SBu can be detected. Therefore, the first reactions in this case are outlined below.

$$Cp_2Ti(SAr)_2 + BuLi \rightarrow \text{"}[Cp_2Ti(SAr)_2Bu]Li\text{"} \rightarrow \text{"}CpTi(SAr)\text{"} + ArSBu + LiCp \quad (1)$$

On warming, apparently the LiCp and the "CpTi(SAr)" fragment change back to the starting dithiolate and unidentified decomposition products. In the case of the 1:1 stoichiometric reaction, the first step might be the same, but a further reaction is different due to the absence of excessive butyl lithium.

Clearly, for the butyl lithium, the redox reaction is preferred over ring deprotonation. We, therefore, turned towards lithium diisopropylamide as a possible deprotonation agent. When **2a** was used, with $SiMe_3Cl$ as quenching reagent, small amounts of the deprotonation products could be identified together with an unexpected dinuclear compound of formula $C_{32}H_{28}S_2Ti_2$ (**5**). **5** was the only identifiable product when MeSSMe was used as a quenching reagent. We believe that this

compound is a di-titanium(III) compound triply bridged by a fulvalene-diide and two phenylthiolate ligands (Figure 1).



5

Figure 1. Proposed structure of **5** (M = Ti).

A zirconium compound of an identical structure (**5**, M = Zr) was obtained by an oxidation reaction of a Zr(II) complex and characterized by NMR spectra and crystal structure determination [44]. Similar fulvalene-bridged Ti(III) complexes with chloride, hydride, or sulfide bridges instead of the aryl thiolate bridges were obtained by a sodium reduction of Cp_2TiCl_2 [45] or thermolysis of the Ti(II) complex $Cp_2Ti(Me_3Si–C{\equiv}C–SiMe_3)$ [46]. A related mono-cyclopentadienyl Ti(III) complex without a fulvalene bridge known as $[CpTiCl]_2[\mu\text{-}SAr]_2$ was obtained from the corresponding mononuclear $CpTiCl_2(SAr)$ upon a reduction with sodium amalgam [47]. We assume that the ring-lithiated primary product of the **2a**-LDA reaction is unstable under the reaction conditions and decomposes after splitting off LiSPh first to a Ti(III) radical centered on the Cp ring, which dimerizes to form the finally observed dinuclear compound **5**.

However, when the chlorocyclopentadienyl dithiolates **2b**,**c** were treated with LDA followed by quenching with hexachloroethane or chlorotrimethylsilane, the desired di-substituted complexes **6a**,**b** and **7a**,**b** could be isolated in moderate yields. Starting from **6b**,**b**, repeating the treatment with LDA and C_2Cl_6 or $SiMe_3Cl$ gave the corresponding tri-substituted compounds **8a**,**b** in yields of 24% and 75%, respectively. An attempt of a "one-pot" synthesis of pentachloro-titanocene thiolates using alternating additions of LDA and C_2Cl_6 gave a 52% yield of **6a** (in the case of **2b** as starting material) but no higher substituted products. Apart from the observations in the ferrocene system [35], either the reactivity towards deprotonation or the stability of the formed chlorinated products decreases with an increasing number of chlorine substituents. According to the ^{1}H-NMR spectra, both **6a** and **8a** are formed as regio-isomers with one largely dominating. By comparing results from the ferrocene system, we conclude that the major isomers are the 1,2 and 1,2,3-substituted ones. There are also weak signals in the NMR and mass spectra of **3c**, **6a**, **6b** and **8a** that might be assigned to chloride-mono(phenylthiolate) complexes, which are always accompanied by signals attributable to PhSH. Since chloroform was used as a solvent both for NMR and mass spectra, it seems possible that the complexes are unstable towards this solvent according to the equation below.

$$CpCp'Ti(SPh)_2 + CHCl_3 \rightarrow CpCp'Ti(SPh)Cl + PhSH \quad (2)$$

An alternative explanation would be that the starting materials were contaminated with the chloride-mono(thiolate) complexes. However, no signs of this can be seen in the spectra of **2b**, **2c**, **3a**.

One interesting aspect in the mass spectra of nearly all compounds is the presence of peaks assignable to $[C_{10}H_8Ti_2(SAr)_2]^{2+}$, which corresponds to the suggested structure of **5** (without the terminal C_5H_5-ligands).

4. Experimental Part

All solvents were of analytical grade and were distilled over the Na or Na/K alloy and stored over the Na wire. All reagents (*n*-BuLi: 1.6M in Hexane, thiophenol, thiocresol, Di-isopropylamine, hexachloroethane, dimethyldisulfide, and DABCO) and Cp_2TiCl_2 were obtained from commercial

suppliers and were used as such. $(C_5H_4Cl)(C_5H_4X)TiCl_2$ (X = H, Cl) were prepared according to literature procedures [33,34]. Fresh solutions of LDA were prepared from Di-isopropylamine and *n*-BuLi in THF. Chromatographic separations were performed in glass columns (30 × 7 cm^2) filled with silica 60 (Merck, 0.063 to 0.2 mm). All reactions were run under N_2 atmosphere using standard Schlenk equipment. Work-up and chromatographic purifications were performed in the air. All peaks found in the mass spectra, according to the fragmentation pattern, are included in Table S1 of the Supplementing Information.

*4.1. Preparation of $(C_5H_5)_2Ti(SPh)_2$ (**2a**)*

A suspension of Cp_2TiCl_2 (1.99 g, 8.0 mmol) in THF (50 mL) is treated with PhSH (1.64 mL, 16.0 mmol) and DABCO (1.79 g, 16.0 mmol) by stirring at r.t. After a few minutes, the color changes from red to violet. Stirring is continued for 90 min when the suspension is filtered through a glass frit. The residue on the frit is eluted with Et_2O until the filtrate is colorless. The combined filtrates are evaporated to dryness to leave a red powder, which is transferred to the top of a silica gel column (L = 30 cm) and then eluted with toluene. The eluate is evaporated to give a red powder: **2a** (2.75 g, 86%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.57 (m, 4H), 7.30 (m, 4H), 7.15 (m, 2H), 6.04 (s, 10H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.6, 132.4, 128.4, 125.6, 112.8 (C_{Cp}); MS (EI): *m*/*z* = 396 (M^+, 15%), 287 (Cp_2TiSPh, 100%), 221 (CpTiSPh–H, 14%), 218 (PhSSPh, 4%), 178 (Cp_2Ti, 80%); UV (in $CHCl_3$): λ_{max} = 539 nm, 399 nm.

*4.2. Preparation of $(C_5H_5)_2Ti(SC_6H_4CH_3\text{-}p)_2$ (**3a**)*

2b was prepared and purified in exactly the same manner as **2a** by using thiocresol (1.99 g, 16.0 mmol). A violet powder was obtained: **2b** (3.02 g, 89%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, 4H), 7.11 (d, 4H), 6.02 (s, 10H), 2.35 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 145.1, 135.2, 132.2, 129.1, 112.7 (C_{Cp}), 21.1 (C_{Me}); MS (EI): *m*/*z* = 424 (M^+, 14%), 301 ($Cp_2TiSTol$, 100%), 235 (CpTiSTol–H, 11%), 246 (TolSSTol, 7%), 178 (Cp_2Ti, 66%); UV (in $CHCl_3$): λ_{max} = 543 nm, 401 nm.

4.3. Preparation of $(C_5H_5)(C_5H_4Cl)Ti(SC_6H_5)_2$ (m/z)

A solution of $(C_5H_5)(C_5H_4Cl)TiCl_2$ (0.50 g, 1.70 mmol) in THF (15 mL) is treated with PhSH (0.39 g, 3.5 mmol) and DABCO (0.40 g, 3.50 mmol). Within a few seconds, the color changes from orange-brown to violet. Stirring is continued for 60 min when the formed suspension is filtered through a glass frit. The residue on the frit is treated with several portions of Et_2O until the extract becomes color-less. The combined filtrates are evaporated to dryness. The residue is placed on top of a silica gel column (30 × 7 cm^2) and eluted with toluene. Three fractions can be eluted, which are evaporated to dryness. The first (violet) fraction yields **2c** as a violet oil (3 mg). The second (also violet) gives **2b** as a violet oil (0.53 g, 70%) and, from the third (red) fraction, **2a** can be obtained as a red powder (32 mg). Analytical data for **2b**: ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 7.55 (m, 4H), 7.31 (m, 4H), 7.16 (m, 2H), 6.15 (t, 2H), 6.09 (s, 5H), 5.89 (t, 2H); ^{13}C-NMR (68 MHz, $CDCl_3$): δ = 148.1, 131.8, 128.3, 125.5, 116.8 ($C_{cp,i}$), 115.1 (C_{Cp}) 112.1 ($C_{cp,\alpha}$), 111.6 ($C_{Cp,\beta}$); HRMS (EI, $C_{10}H_9{}^{35}Cl^{48}Ti$): 211.9839 (calcd. 211.9873).

*4.4. Preparation of $(C_5H_5)(C_5H_4Cl)Ti(SC_6H_4CH_3\text{-}p)_2$ (**3b**)*

A solution of $(C_5H_5)(C_5H_4Cl)TiCl_2$ (0.459 g, 1.60 mmol) in THF (20 mL) is treated with *p*-TolSH (0.397 g, 3.20 mmol) and DABCO (0.359 g, 3.20 mmol). Work-up was performed in exactly the same manner as for **3a**. Chromatography yielded two fractions. **3b** was obtained as a violet oil (0.135 g, 19%) from the first fraction while the second gave **3a** as a red powder (13 mg). Analytical data for **3b** include: ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.42 (m, 4H), 7.11 (m, 4H), 6.16 (t, 2H), 6.07 (s, 5H), 5.87 (t, 2H), 2.36 (s, 6H). Additional weak peaks are assigned to **1b** (at 6.63 and 6.45 ppm) and to **3b′** (6.34 and 6.29 ppm); ^{13}C-NMR (68 MHz, $CDCl_3$): δ = 144.7, 135.3, 131.7, 129.1, 116.7 ($C_{cp,i}$), 115.1 (C_{Cp}), 112.9 ($C_{cp,\alpha}$), 111.5 ($C_{Cp,\beta}$), 21.1 (C_{Me}); HRMS (EI, $C_{24}H_{23}{}^{35}Cl^{48}Ti^{32}S_2$): 458.0421 (calcd. 458.0409).

*4.5. Preparation of $(C_5H_4Cl)_2Ti(SC_6H_5)_2$ (**2c**)*

A suspension of $(C_5H_4Cl)_2TiCl_2$ (0.636 g, 2.00 mmol) in THF (30 mL) was treated with PhSH (0.41 mL, 4.0 mmol) and DABCO (0.449 g, 4.0 mmol). Within a few seconds, the color of the suspension changed from orange to violet. Stirring was continued for 60 min. Work-up was performed as described for **2b**. (for a 30 × 7 cm^2 column, a maximum of 0.25 crude product can be separated by using a total of 3.0 L of toluene). Three fractions can be collected. The first (violet) fraction yields **2c** as a violet oil (0.205 g, 70%). The second (violet) fraction gives **2b** as a violet oil (25 mg) and the third (red) fraction contains **2a** obtained as a red powder (11 mg). Analytical data for **2c**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.55 (m, 4H), 7.33 (m, 4H), 7.17 (m, 2H), 6.10 (t, 4H), 6.02 (t, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.0, 131.8, 128.4, 125.8, 118.1 ($C_{cp,i}$), 115.7 ($C_{cp,\alpha}$), 112.8 ($C_{Cp,\beta}$); HRMS (EI, $C_{22}H_{18}{}^{35}Cl_2{}^{48}Ti^{32}S_2$): 463.9710 (calcd. 463.9707).

*4.6. Preparation of $(C_5H_4Cl)_2Ti(SC_6H_4–CH_3\text{-}p)_2$ (**3c**)*

A suspension of $(C_5H_4Cl)_2TiCl_2$ (0.30 g, 0.94 mmol) in THF (25 mL) was treated with TolSH (0.234 g, 1.88 mmol) and DABCO (0.211 g, 1.88 mmol). Within a few seconds, the color of the suspension changed from orange to violet. Stirring was continued for 60 min. A work-up was performed as described for **2b**. Three fractions could be collected. The first yielded **3c** as a violet oil (0.294 g, 64%), the second yielded **3b** as a violet oil (20 mg), and the third yielded **3a** as a red powder (14 mg). Analytical data for **3c**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, 4H), 7.11 (d, 4H), 6.10 (t, 4H), 6.01 (t, 4H), 2.36 (s, 6H). An additional, very weak signal at 6.48 ppm could be assigned to **1c**: ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 144.6, 135.5, 131.6, 129.2, 117.8 ($C_{cp,i}$), 115.6 ($C_{cp,\alpha}$), 112.7 ($C_{Cp,\beta}$), 21.1 (C_{Me}); HRMS (EI, $C_{17}H_{15}{}^{35}Cl^{37}Cl^{48}Ti^{32}S$): 370.9727 (calcd. 370.9718).

*4.7. Preparation of $(C_5H_5)(C_5H_3Cl_2)Ti(SC_6H_5)_2$ (**6a**)*

A deep violet solution of **2b** (0.413 g, 0.96 mmol) in THF (25 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.14 mL, 0.96 mmol) and *n*-BuLi (0.60 mL of a 1.6 M solution in hexane) in THF (15 mL) at 0 °C). After stirring for 10 min, hexachloroethane (0.341 g, 1.44 mmol) is added and the cooling bath is removed. When the solution has reached r.t., the solvent is evaporated in vacuo. The residue is placed on top of a silica gel column. Toluene elutes three fractions (the first one is yellow, the second one is violet, and the third one is reddish). The second fraction yields **6a** as a violet oil (0.317 g, 72%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.53 (m, 4H), 7.30 (m, 4H), 7.15 (m, 2H), 6.39 (t, 1H), 6.10 (s, 5H), 6.01 (d, 2H). Additional weak signals at 6.17 (s), 6.30 (d), 5.79 (t) with significantly smaller coupling constants can be assigned to the 1,3-regio-isomer. ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 147.9, 131.8, 128.4, 125.8, 117.5 (C_{cp}), 116.6 ($C_{Cp,Cl}$), 115.6 ($C_{cp,\alpha}$), 112.5 ($C_{Cp,\beta}$); HRMS (EI, $C_{22}H_{18}{}^{35}Cl_2{}^{48}Ti^{32}S_2$): 463.9727 (calcd. 463.9707).

*4.8. Preparation of $(C_5H_5)(C_5H_3ClSiMe_3)Ti(SC_6H_5)_2$ (**6b**)*

A deep violet solution of **2b** (0.139 g, 0.32 mmol) in THF (20 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.06 mL, 0.40 mmol) and *n*-BuLi (0.25 mL of a 1.6 M solution in hexane) in THF (10 mL) at 0 °C). After stirring for 10 min, chlorotrimethylsilane (0.05 mL, 0.40 mmol) is added and the cooling bath is removed. When the solution has reached r.t., the solvent is evaporated in vacuo. The residue is placed on top of a silica gel column and eluted with toluene. The first two fractions (yellow and grey) are discarded. The third fraction yields **6b** as a violet oil (0.068 g, 44%) and the fourth is apparently unreacted with **2b** (0.011 g, 9%). ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 7.53 (m, 4H), 7.29 (m, 4H), 7.14 (m, 2H), 6.54 (m, 2H), 6.03 (s, 5H), 5.65 (t, 1H), 0.33 (s, 9H). An additional very weak peak (<2%) at 6.30 ppm is assigned to **6b′**. ^{13}C-NMR (68 MHz, $CDCl_3$): δ = 148.9, 148.2, 131.8, 131.7, 128.28, 128.24, 127.48, 127.12, 121.8, 118.9, 115.9 (C_5H_5), 108.5, −0.1 (SiCH). HRMS (EI, $C_{25}H_{27}{}^{35}Cl^{28}Si^{48}Ti^{32}S_2$): 502.0493 (calcd. 502.0491).

*4.9. Preparation of $(C_5H_5)(C_5H_2Cl_3)Ti(SC_6H_5)_2$ (**8a**)*

A deep violet solution of **6a** (0.25 g, 0.50 mmol) in THF (10 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.07 mL, 0.50 mmol) and *n*-BuLi (0.31 mL of a 1.6 M solution in hexane) in THF (10 mL) at 0 °C). After stirring for 10 min, hexachloroethane (0.176 g, 0.75 mmol) is added and the cooling bath is removed. When the solution has reached r.t., the solvent is evaporated in vacuo. The residue is placed on top of a silica gel column. Toluene elutes three fractions (the first one is yellow, the second one is violet, and the third one is reddish). The first fraction yields tetrakis(phenylthio)ethane (8 mg), the second gives **8a** as a violet oil (59 mg, 24%), and unreacted **6a** can be recovered from the third fraction (25 mg, 10% recovery). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.56 (m, 4H), 7.32 (m, 4H), 7.17 (m, 2H), 6.46 (s, 2H), 6.11 (s, 5H). An additional weak singlet at 6.13 ppm is assigned to the 1,2,4-regio-isomer. ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 147.9, 131.8, 128.5, 125.9, 118.6 (C_{Cp}), 116.0 ($2C_{cp,Cl}$), 113.5 ($C_{cp,H}$), 111.2 ($C_{Cp,Cl}$); HRMS (EI, $C_{10}H_7{}^{35}Cl_3{}^{48}Ti^{32}$): 279.9076 (calcd. 279.9093).

*4.10. Preparation of $(C_5H_5)[C_5H_2Cl(SiMe_3)_2]Ti(SC_6H_5)_2$ (**8b**)*

A deep violet solution of **6b** (0.040 g, 0.08 mmol) in THF (10 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.02 mL, 0.13 mmol) and *n*-BuLi (0.08 mL of a 1.6 M solution in hexane) in THF (10 mL) at 0 °C). After stirring for 10 min, trimethylchlorosilane (0.02 mL, 0.16 mmol) is added and the cooling bath is removed. When the solution has reached r.t., the solvent is evaporated in vacuo. The residue is placed on top of a silica gel column. ^{tert}BuOMe elutes two fractions of which only the first one is collected. **8b** is obtained as a violet oil (37 mg, 75%), ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.55 (m, 4H), 7.29 (m, 4H), 7.12 (m, 2H), 6.75 (s, 2H), 6.03 (s, 5H), 0.30 (s, 18H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.9, 131.7, 128.2, 125.2, 123.9($C_{Cp,Cl}$), 121.7 ($C_{cp,H}$), 120.7($C_{Cp,Si}$), 116.2 (C_{Cp}), 0.03 (SiCH); both ^{1}H- and ^{13}C-NMR spectra also show signals of the starting compound **8b**. HRMS (EI, $C_{28}H_{35}{}^{35}Cl^{48}Ti^{32}S_2{}^{28}Si_2$): 574.0891 (calcd. 574.0887).

4.11. Reaction of **2a** *with LDA and $SiMe_3Cl$*

A violet solution of **2a** (0.199 g, 0.50 mmol) in THF (15 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.085 mL, 0.60 mmol) and *n*-BuLi (0.38 mL of a 1.6 M solution in hexane) in THF (15 mL) at 0 °C). After stirring for 10 min, $SiMe_3Cl$ (0.063 mL, 0.50 mmol) is added and is continually stirred at this temperature for 10 min. Then the cooling bath is removed. After the solution has reached r.t., the solvent is evaporated in vacuo. The residue is extracted with benzene (10 mL). Evaporation of the violet extract in vacuo yields a violet oil (0.217 g). ^{1}H-NMR analysis shows that it mainly consists of the starting material **2a**. MS-analysis shows the presence of small amounts of $(C_5H_5)(C_5H_4SiMe_3)Ti(SPh)_2$ (**4a**) together with $(C_5H_4SiMe_3)Ti(SPh)_2$ (**4b**) and a compound **5** analyzed as "$C_{32}H_{28}S_2Ti_2$". Compounds **4b** and **5** can be separated and isolated by chromatography in trace amounts. EI-MS-data: for **4a**: *m*/*z* = 359 (M^+-SPh), 250 (M^+-2 SPh), for **4b**: *m*/*z* = 431 (M^+-SPh, 53%), 357 (M^+-SPh-$SiMe_3H$, 20%), 322 (M^+-2 SPh, 100%), for **5**: *m*/*z* = 572 (M^+, 4%), 463 (M^+-SPh, 5%), 396 ($Cp_2Ti(SPh)_2$, 7%), 333 ($C_{10}H_8Ti_2SPh$, 38%), 287 (Cp_2TiSPh, 58%), 224 ($C_{10}H_8Ti_2$, 39%), 178 (Cp_2Ti, 100%). HRMS: **4a**: $C_{19}H_{23}{}^{32}S^{28}Si^{48}Ti$: 359.0744 (calcd: 359.0746); **4b**: $C_{22}H_{31}{}^{32}S^{28}Si_2{}^{48}Ti$: 431.1162 (calcd. 431.1164); **5**: $C_{32}H_{28}{}^{32}S_2{}^{48}Ti_2$: 572.0591 (calcd. 572.0591).

4.12. Reaction of **2a** *with LDA and MeSSMe*

A violet solution of **2a** (0.199 g, 0.50 mmol) in THF (15 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.085 mL, 0.60 mmol) and *n*-BuLi (0.38 mL of a 1.6 M solution in hexane) in THF (15 mL) at 0 °C). After stirring for 10 min, MeSSMe (5 drops) is added and continuously stirred at this temperature for 15 min. Then the cooling bath is removed. After the solution has reached r.t., the solvent is evaporated in vacuo. The residue is extracted with benzene (20 mL). Evaporation of the violet extract in vacuo yields a violet oil. MS analysis of this oil shows the

presence of **5** as the only identifiable product. Attempts of chromatographic purification lead only to complete decomposition.

4.13. Reaction of **2c** *with LDA and Hexachloroethane*

A deep violet solution of **2c** (0.200 g, 0.43 mmol) in THF (20 mL) is treated at −78 °C with a freshly prepared THF solution of LDA (from HN(*i*-Pr)$_2$ (0.13 mL, 0.90 mmol) and *n*-BuLi (0.56 mL of a 1.6 M solution in hexane) in THF (20 mL) at 0 °C). After stirring for 5 min, hexachloroethane (0.407 g, 1.72 mmol) is added and the cooling bath is removed. When the solution has reached r.t., the solvent is evaporated in vacuo. The residue is placed on top of a silica gel column. Toluene elutes two fractions. Evaporation of the first brown fraction leaves tetrakis(phenylthio)ethene as a brown oil (47 mg). The second violet fraction yields an inseparable mixture of $(C_5H_4Cl)(C_5H_3Cl_2)Ti(SPh)_2$ (**7a**) and $(C_5H_3Cl_2)_2Ti(SPh)_2$ (**7b**) as a violet oil (0.114 g). Due to strongly overlapping signals of the two compounds, no NMR data can be attributed to the single components. However, identification is possible via HRMS: **7a**: $C_{22}H_{17}{}^{35}Cl_3{}^{32}S_2{}^{48}Ti$: 497.9349 (calcd. 497.9319); **7b**: $C_{22}H_{16}{}^{35}Cl_4{}^{32}S_2{}^{48}Ti$: 531.8946 (calcd. 531.8927).

5. Conclusions

The unsubstituted titanocene arylthiolates $Cp_2Ti(SAr)_2$ cannot be ring-functionalized either by a *n*-BuLi/electrophile or an LDA/electrophile sequence. In both cases, unstable Ti(III) radicals are formed, which either form the starting materials, dimerize to fulvalene bridged dititanocenes, or decompose completely. With chloro-substituted (^{Cl}Cp)(^{X}Cp)Ti(SPh)$_2$ (X = H, Cl), α-deprotonation can be achieved with LDA and Di-substituted and *tri*-substituted-cyclopentadienyl complexes can be obtained. However, the stability of the chloro-substituted titanocene thiolates decreases with an increasing degree of ring-substitution and, thus, the desired perchlorotitanocenes could not be obtained.

Supplementary Materials: The following are available online at http://www.mdpi.com/2304-6740/6/3/85/s1, Figure S1: VT-1H-NMR of compound **3a**. Figure S2: 1H-NMR of a THF/hexane-solution of *n*-butyl lithium at −90 °C; Figure S3: 1H-NMR of a freshly prepared THF solution of LiC_5H_5 at −80 °C, Figure S4: VT-1H-NMR of the reaction of 3a with 4 eqiv. BuLi in THF, mixed at −120 °C. Figure S5: ^{7}Li-NMR of the reaction mixture of 2a with 1.1 equiv BuLi, measured at r.t. Figure S6: 7Li-NMR of the reaction mixture of 3a with 1.1 equiv BuLi, measured at r.t. Figures S7, 9, 11, 13, 15, 17, 19, 21, 23: ^{1}H-NMR spectra in $CDCl_3$ of **2b**, **2c**, **3b**, **3c**, **6a**, **6b**, **7ab**, **8a**, **8b**. Figures S8, 10, 12, 14, 16, 18, 20, 22, 24: ^{13}C-NMR spectra in $CDCl_3$ of **2b**, **2c**, **3b**, **3c**, **6a**, **6b**, **7ab**, **8a**, **8b**. Figures S25–33: EI-mass spectra of **2b**, **2c**, **3b**, **3c**, **6a**, **6b**, **7ab**, **8a**, **8b**. **Table S1** contains the EI-mass spectral data of **2**, **3**, **6**, **8**.

Author Contributions: T.G.K. performed the preparative and analytical work in the course of his Ph.D. thesis. K.S. supervised the work and wrote the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Wilkinson, G.; Birmingham, J.M. Bis-cyclopentadienyl Compounds of Ti, Zr, V, Nb and Ta. *J. Am. Chem. Soc.* **1954**, *76*, 4281–4284. [CrossRef]
2. Natta, G.; Pino, P.; Mazzanti, G.; Giannini, U. A Crystallizable Organometallic Complex Containing Titanium and Aluminum. *J. Am. Chem. Soc.* **1957**, *79*, 2975–2976. [CrossRef]
3. Coates, G.W. Precise Control of Polyolefin Stereochemistry Using Single-Site Metal Catalysts. *Chem. Rev.* **2000**, *100*, 1223–1252. [CrossRef] [PubMed]
4. Rosenthal, U.; Burlakov, V.V.; Bach, M.A.; Beweries, T. Five-membered metallacycles of titanium and zirconium—Attractive compounds for organometallic chemistry and catalysis. *Chem. Soc. Rev.* **2007**, *36*, 719–728. [CrossRef] [PubMed]
5. Janiak, C. Metallocene and related catalysts for olefin, alkyne and silane dimerization and oligomerization. *Coord. Chem. Rev.* **2006**, *250*, 66–94. [CrossRef]

6. Vassylyev, O.; Panarello, A.; Khinast, J.G. Enantioselective Hydrogenations with Chiral Titanocenes. *Molecules* **2005**, *10*, 587–619. [CrossRef] [PubMed]
7. Kaminsky, W. Polymerization catalysis. *Catal. Today* **2000**, *62*, 23–34. [CrossRef]
8. Morcillo, S.P.; Miguel, D.; Campana, A.G.; Alvarez de Cienfuegos, L.; Justicia, J.; Cuerva, J.M. Recent applications of Cp2TiCl in natural product synthesis. *Org. Chem. Front.* **2014**, *1*, 15–33. [CrossRef]
9. Richrath, R.B.; Olyschläger, T.; Hildebrandt, S.; Enny, D.G.; Fianu, G.D.; Flowers, R.A., II; Gansäuer, A. Cp_2TiX Complexes for Sustainable Catalysis in Single-Electron Steps. *Chem. Eur. J.* **2018**, *24*, 6371–6379. [CrossRef] [PubMed]
10. Rodriguez, M.C.; Garcia, I.R.; Maecker, R.N.R.; Morales, L.P.; Oltra, J.E.; Martinez, A.R. Cp_2TiCl: An Ideal Reagent for Green Chemistry? *Org. Process Res. Dev.* **2017**, *21*, 911–923. [CrossRef]
11. Machat, M.R.; Jandl, C.; Rieger, B. Titanocenes in Olefin Polymerization: Sustainable Catalyst System or an Extinct Species? *Organometallics* **2017**, *36*, 1408–1418. [CrossRef]
12. Martinez, A.R.; Rodriguez, M.C.; Rodriguez-Garcia, I.; Morales, L.P.; Rodriguez Maecker, R.N. Titanocene dichloride: A new green reagent in organic chemistry. *Chin. J. Catal.* **2017**, *38*, 1659–1663. [CrossRef]
13. Köpf, H.; Köpf-Mayer, P. Titanocen-dichlorid-das erste Metallocen mit cancerostatischer Wirksamkeit. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 477–478.
14. Gomez-Ruis, S.; Maksimovic-Ivanic, D.; Mijatovic, S.; Kaluderovic, G.N. On the Discovery, Biological Effects and Use of Cisplatin and Metallocenes in Anticancer Chemotherapy. *Bioinorg. Chem. Appl.* **2012**, 1–14. [CrossRef] [PubMed]
15. Hogan, M.; Tacke, M. Titanocenes: Cytotoxic and Anti-angiogenic Chemotherapy Against Advanced Renal-Cell Cancer. In *Medicinal Organometallic Chemistry*; Jaouen, G., Metzler-Nolte, N., Eds.; Springer: Berlin/Heidelberg, Germany, 2010; Volume 32, pp. 119–140.
16. Skoupilova, H.; Hrstka, R.; Bartosik, M. Titanocenes as Anticancer Agents: Recent Insights. *Med. Chem.* **2017**, *13*, 334–344. [CrossRef]
17. Ellahioui, Y.; Prashar, S.; Gomez-Ruiz, S. Anticancer Applications and Recent Investigations of Metallodrugs Based on Gallium, Tin and Titanium. *Inorganics* **2017**, *5*, 4. [CrossRef]
18. Immel, T.A.; Martin, J.T.; Dürr, C.J.; Groth, U.; Huhn, T. Dimethyl titanocene Y: A valuable precursor for libraries of cytotoxic titanocene derivatives. *J. Inorg. Biochem.* **2010**, *104*, 863–867. [CrossRef] [PubMed]
19. Chirik, P.J. Group 4 Transition Metal Sandwich Complexes: Still Fresh after Almost 60 Years. *Organometallics* **2010**, *29*, 1500–1517. [CrossRef]
20. Alcock, N.W.; Clase, H.J.; Duncalf, D.J.; Hart, S.L.; McCamley, A.; McCormack, P.J.; Taylor, P.C. Synthesis of racemic chiral-at-metal complexes of the Group 4 metals. *J. Organomet. Chem.* **2000**, *605*, 45–54. [CrossRef]
21. Sünkel, K. Coordination Chemistry of Pentahalocyclopentadienyls. *Chem. Berichte* **1997**, *130*, 1721–1730. [CrossRef]
22. Chang, B.H.; Tung, H.S.; Brubaker, C.H., Jr. The Thermal Decomposition of Dibutylbis(η^5-cyclopentadienyl) titanium, other Dialkyl Metallocenes, and Di(η^5-pentamethylcyclopentadienyl) itanium. *Inorg. Chim. Acta* **1981**, *51*, 143–148. [CrossRef]
23. Vyshinskaya, L.I.; Korneva, S.P.; Kulikova, G.P. Reactions of ansa-Titanocenes with Organolithium Compounds. Russ. *J. Gen. Chem.* **2002**, *72*, 68–70. [CrossRef]
24. Morillo, A.; Chirinos, J.; Rajmankina, T.; Ibarra, D.; Arevalo, J.; Parada, A. Ethene polymerization with titanium half-sandwich amido-complexes. *J. Chem. Res.* **2003**, 238–239. [CrossRef]
25. Boyde, N.C.; Rightmire, N.R.; Bierschenk, E.J.; Steelman, G.W.; Hanusa, T.P.; Brennessel, W.W. Reaction environment and ligand lability in group 4 Cp_2MXY (X,Y = Cl, O*t*Bu) complexes. *Dalton Trans.* **2016**, *45*, 18635–18642. [CrossRef] [PubMed]
26. Köpf, H.; Schmidt, H. Bis-π-cyclopentadienyl-titan-mercaptide. *Z. Anorg. Allg. Chem.* **1965**, *340*, 139–145. [CrossRef]
27. Giddings, S.A. Bis(cyclopentadienyl)titanium(IV) Compounds with Sulfur-Containing Groups. *Inorg. Chem.* **1967**, *6*, 849–851. [CrossRef]
28. Horacek, M. Titanocene sulfide chemistry. *Coord. Chem. Rev.* **2016**, *314*, 83–102. [CrossRef]
29. Song, L.C.; Liu, P.C.; Han, C.; Hu, Q.M. Synthesis and characterization of Cp_2Ti-containing organometallics via in situ oxidative-addition of 'Cp_2Ti' intermediate. Crystal Structures of $(1\text{-}C_{10}H_7S)_2TiCp_2$, $[(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4CH_2S)]_2TiCp_2$ and $[\eta^2\text{-}OC(Ph)=C(Ph)O]TiCp_2$. *J. Organomet. Chem.* **2002**, *648*, 119–125. [CrossRef]

30. Meyer, R.; Brink, S.; vanRensburg, C.E.J.; Joone, G.K.; Görls, H.; Lotz, S. Synthesis, characterization and antitumor properties of titanocene derivatives with thiophene containing ligands. *J. Organomet. Chem.* **2005**, *690*, 117–125. [CrossRef]
31. Gomez-Ruiz, S.; Stanojkovic, T.P.; Kaluderovic, G.N. Synthesis, characterization, biological studies and in vitro cytotoxicity on human cancer cell lines of titanium(IV) and tin(IV) derivatives with the α,α′-dimercapto-o-xylene ligand. *Appl. Organomet. Chem.* **2012**, *26*, 383–389. [CrossRef]
32. Pinkas, J.; Lamac, M. Transformation of functional groups attached to cyclopentadienyl or related ligands in group 4 metal complexes. *Coord. Chem. Rev.* **2015**, *296*, 45–90. [CrossRef]
33. Conway, B.G.; Rausch, M.D. Formation and Reactivity of Halogen Derivatives of (η^5-Cyclopentadienyl) thallium. *Organometallics* **1985**, *4*, 688–693. [CrossRef]
34. Anslyn, E.A.; Grubbs, R.H.; Felten, C.; Rehder, D. Dichlorobis(η^5-Chlorocyclopentadienyl)-Titanium, $(ClC_5H_4)_2TiCl_2$. *Inorg. Synth.* **1992**, *29*, 198–201.
35. Bernhartzeder, S.; Sünkel, K. Coordination Chemistry of Perhalogenated Cyclopentadienes and Alkynes. Part 30. New High-Yield Syntheses of Monochloroferrocene and 1,2,3,4,5-Pentachloroferrocene. Molecular Structures of 1,2-Dichloroferrocene and 1,2,3-Trichloroferrocene. *J. Organomet. Chem.* **2012**, *716*, 146–149. [CrossRef]
36. Sünkel, K.; Bernhartzeder, S. Coordination Chemistry of Perhalogenated Cyclopentadienes and Alkynes. XXVIII New High-yield Synthesis of Monobromoferrocene and Simplified Procedure for the Synthesis of Pentabromoferrocene. Molecular structures of 1,2,3-tribromoferrocene and 1,2,3,4,5-pentabromoferrocene. *J. Organomet. Chem.* **2011**, *696*, 1536–1540.
37. Sünkel, K.; Weigand, S.; Hoffmann, A.; Blomeyer, S.; Reuter, C.G.; Vishnevskiy, Y.V.; Mitzel, N.W. Synthesis and Characterization of 1,2,3,4,5-Pentafluoroferrocene. *J. Amer. Chem. Soc.* **2015**, *137*, 126–129. [CrossRef] [PubMed]
38. Hedberg, F.L.; Rosenberg, H. Preparation and reactions of decachloroferrocene ad decachlororuthenocene. *J. Am. Chem. Soc.* **1973**, *95*, 870–875. [CrossRef]
39. Butler, I.R. 1,2,3,4,5-Pentabromoferrocene and related compounds: A simple synthesis of useful precursors. *Inorg. Chem. Commun.* **2008**, *11*, 484–486. [CrossRef]
40. Klein-Heßling, C.; Stramm, C.; Sünkel, K. Metalation Studies on Carbonyl-Halocyclopentadienyl Manganese Complexes. Manuscript in preparation. 2018.
41. Gansäuer, A.; Kube, C.; Daasbjerg, K.; Sure, R.; Grimme, S.; Fianu, G.D.; Sadasivam, D.V.; Flowers, R.A., II. Substituent Effects and Supramolecular Interactions of Titanocene(II) Chloride: Implications for Catalysis in Single Electron Steps. *J. Am. Chem. Soc.* **2014**, *136*, 1663–1671. [CrossRef] [PubMed]
42. Johnston, R.F.; Borjas, R.E.; Furilla, J.L. Investigation of the electrochemical properties of substituted titanocene dichlorides. *Electrochim. Acta* **1995**, *40*, 473–477. [CrossRef]
43. Rosales, A.; Rodriguez-Garcia, I.; Munoz-Bascon, J.; Roldan-Molina, E.; Padial, N.M.; Morales, L.P.; Garcia-Ocana, M.; Oltra, J.E. The Nugent Reagent: A Formidable Tool in Contemporary Radical and Organometallic Chemistry. *Eur. J. Org. Chem.* **2015**, 4567–4591.
44. Wielstra, Y.; Gambarotta, S.; Spek, A.L.; Smeets, W.J.J. Binuclear Zirconium(III) and Zirconium(IV) Complexes: Mild Oxidation of Low-Valent Zirconium as a Synthetic Pathway to a Class of Tri- and Tetravalent Zirconium Fulvalene Complexes. Molecular Structures of $[\eta^5{:}\eta^5\text{-}C_{10}H_8][CpZrSPh]_2$, $[\eta^5{:}\eta^5\text{-}C_{10}H_8][CpZr(CH_3)_2]_2$ and $[\eta^5{:}\eta^5\text{-}C_{10}H_8][CpZr]_2[\mu\text{-}S]_2$. *Organometallics* **1990**, *9*, 2142–2148.
45. Cuenca, T.; Herrmann, W.A.; Ashworth, T.V. Chemistry of Oxophilic Transition Metals. 2. Novel Derivatives of Titanocene and Zirconocene. *Organometallics* **1986**, *5*, 2514–2516. [CrossRef]
46. Pinkas, J.; Gyepes, R.; Cisarova, I.; Kubista, J.; Horacek, M.; Zilkova, N.; Mach, K. Hydrogenation of titanocene and zirconocene bis(trimethylsilyl)acetylene complexes. *Dalton Trans.* **2018**, *47*, 8921–8932. [CrossRef] [PubMed]
47. Fenwick, A.E.; Fanwick, P.E.; Rothwell, I.P. Synthesis, Characterization, and Reduction Chemistry of Mixed Cyclopentadienyl/Arylsulfide Titanium Dichlorides. *Organometallics* **2003**, *22*, 535–540. [CrossRef]