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Research Article
doi.org/10.1002/cctc.202401337

Chemistry Europe
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Exploring Dinuclear Titanium Complexes in Titanium(III) Catalysis

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The synthesis of one achiral and two chiral propylene-bridged dititanocenes and their evaluation as catalysts in titanium(III) catalyzed ketone-nitrile coupling reactions are reported. A reaction progress kinetics analysis of the cross-coupling between acetophenone and benzyl cyanide reveals that, using a dinuclear titanocene catalyst, the order in catalyst is reduced from two to one in comparison to a mononuclear catalyst. Although the obtained coupling yields and enantioselectivities did not reach the results obtained with the latter, these examples constitute a proof of concept for the templated C—C coupling through coordination of ketone and nitrile to the two tethered titanium centers of a dinuclear catalyst.

1. Introduction

Titanium(III) catalysis is a growing field in organic chemistry that has enabled a broad range of methods for bond formation and disconnection via unconventional radical chemistry.[1] Usually, titanocene catalysts such as Cp_2TiCl_2 in combination with a metallic reducing agent are used to form the titanium(III) catalyst in situ, although approaches using other catalyst designs (e.g., titanium-salen catalysts) and alternative reducing agents including silanes, electro- and photoreduction have been explored as well.[2] One of the most striking features is the ability of the catalyst to remain coordinated by the substrate during the reaction, often enabling radical reactions with high catalyst-controlled selectivity.

In this context, our group has developed a number of titanium(III)-catalyzed reductive couplings and defunctionalization reactions, specifically, a ketone-nitrile cyclization that proceeded with high enantioselectivity and yield in presence of (*R*,*R*)-(ebthi)$TiCl_2$ [ebthi = ethylenebis(η^5–4,5,6,7-tetrahydroindenyl)] as catalyst (Scheme 1a).[1a,3,4] The corresponding intermolecular coupling, however, gave only up to 30% *ee*. Through in-depth mechanistic investigations it was discovered that the reactions proceeded higher order in catalyst and two catalyst equivalents participated in the rate-limiting C—C coupling step.[5] We hypothesized that, in the case of the cyclization reaction, the tether between ketone and nitrile forced both titanium centers into a "*syn*" conformation that led to a tighter chiral pocket whereas the intermolecular reaction permitted a more open "*anti*" conformation with both Ti centers oriented toward opposite sites of the newly formed C—C bond. We therefore aimed at linking both Ti centers in form of a dinuclear complex and to explore the reactivity of such complexes in the titanium(III) catalyzed ketone-nitrile coupling (Scheme 1b). A change toward a first order in catalyst would confirm a successful coupling using the template effect of the dinuclear catalyst. Preparing corresponding chiral dinuclear catalysts would be difficult since the synthesis of chiral mononuclear titanocene catalysts has already proven to be a formidable challenge.[6]

In the past, dinuclear titanocenes and other dinuclear metallocenes have almost exclusively been evaluated as catalysts for polymerization reactions and not in small organic molecule synthesis. Starting with the infamous "titanocene",[7] fulvalene, and bridged Cp or indene ligands with varied tether length have been employed in the synthesis of dinuclear titanium(IV) complexes (Figure 1).[8] The synthesis is usually carried out by complexation of an α,ω-biscyclopentadienyl ligand (or a silylated derivative) to $CpTiCl_3$ or by coupling two titanocene units together. For the latter, Erker and coworkers could show on the example of **1** that olefin metathesis is mild enough to connect two allyl titanocene dichloride units.[9] Moreover, dinuclear bis(cyclopentadienyl)titanium(IV) complexes with bridging X-type ligands have been prepared,[10] and tartrate-bridged dititanocene **2** resembles, to our knowledge, the only example of a chiral enantioenriched dinuclear titanocene to date.[11]

Regarding the design of a chiral dinuclear titanocene, stereogenic elements could be introduced either into the bridge ligand or the second Cp ligand. Complexes with chiral X-type ligands such as **2**, on the other hand, would undergo ligand exchange under the catalysis conditions in presence of chlorotrimethylsilane and, thus, not be feasible. In continuation of our previous efforts in metallocene catalyst synthesis,[12] we envisioned instead the synthesis of simple alkylidene-bridged dinuclear complexes that would provide enough flexibility and yet keep the two titanium centers at close distance. To our

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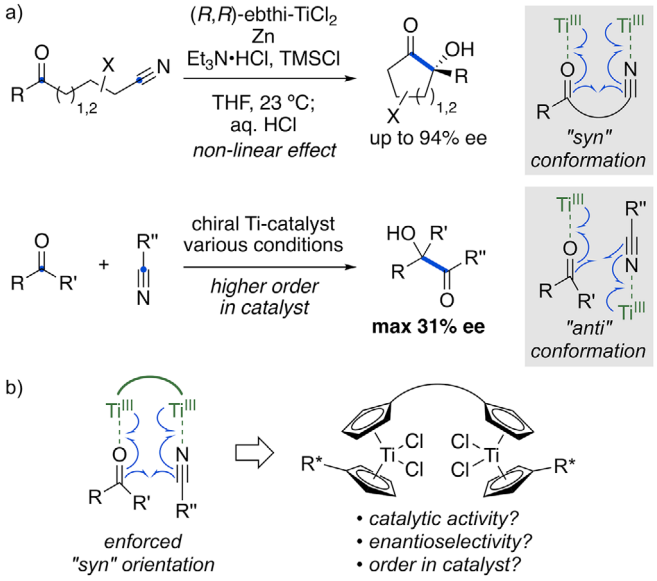
Supporting information for this article is available on the WWW under https://doi.org/10.1002/cctc.202401337



Scheme 1. a) Intra- and intermolecular titanium(III)-catalyzed ketone-nitrile couplings. b) Rationale for the use of dinuclear titanocene catalysts.

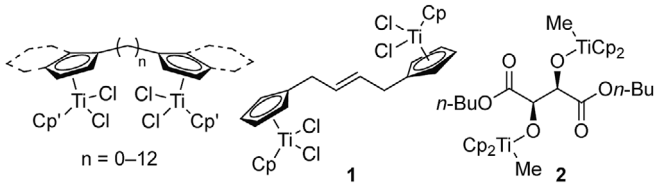
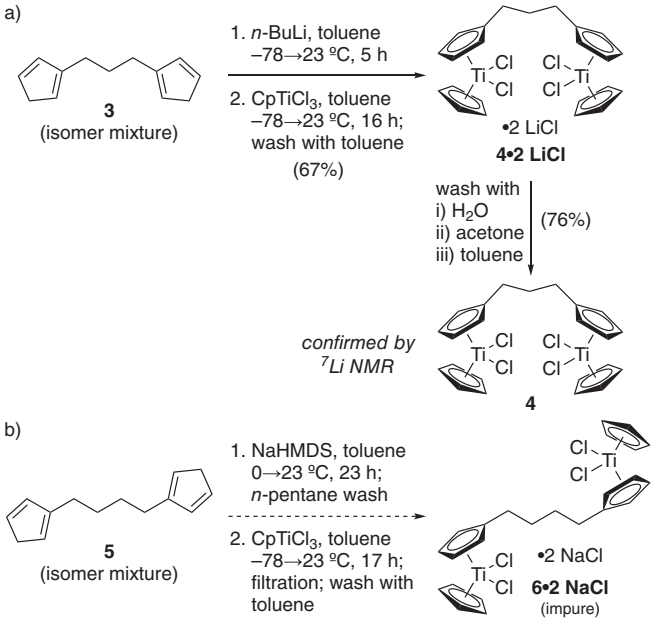


Figure 1. Examples of literature-known dinuclear titanocenes.

surprise, the synthesis and purification of the corresponding basic achiral dimetallocenes proved to be significantly more challenging than expected. Therefore, we herein report in form of a proof of principle study the synthesis and evaluation of three achiral and chiral propylene-linked dititanocenes in titanium(III) catalysis.

2. Results and Discussion

We initially aimed at preparing **1** from allylcyclopentadiene (allylCp), but due to the difficulties handling allylCp, the formation of Cp_2TiCl_2 or $[CpTi(Cl)(\mu\text{-}O)]_4$ as byproducts, and unsuccessful purification attempts, we switched to the preparation of simple propylene- and butylene-bridged dititanocenes **4** and **6** (Scheme 2).[8e] We contemplated that these bridge lengths would keep the two titanium centers in close proximity while still offering sufficient freedom to adopt the desired transition state conformation. Both complexes had been reported previously but only with sparse details on preparation, purification, and characterization.[8e] The required known biscyclopentadienes **3** and **5** were prepared through substitution reactions with NaCp from 1,3-dibromopropane and 1,4-dibromobutane, respectively.[13,14] Although **3** could be purified by chromatography at −18 °C and was received as a mixture of double bond isomers, **5** was formed together with spiro[4.4]nona-1,3-diene

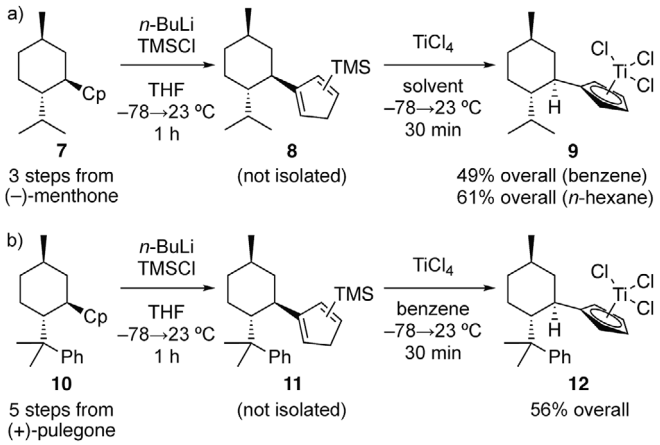


Scheme 2. Synthesis of a) C_3- and b) C_4-bridged dititanocenes **4** and **6**.

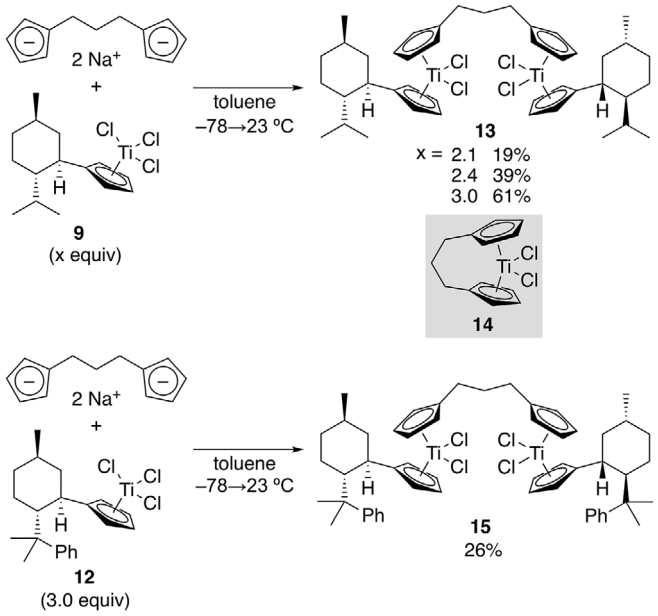
and best used without purification attempts. The formation of the C_3-bridged dititanocene **4** according to literature protocols from the disodium salt of **3** in THF at 0 °C, however, was unsuccessful.[8g] Only after extensive experimentation, it was found in fact that deprotonation with the better soluble *n*-BuLi to form the dilithium salt of **3** needed to be undertaken at −78 °C followed by reaction with $CpTiCl_3$ at −30→23 °C (Scheme 2a).[8e,15] Instead of filtration, evaporation of the solvent and washing with toluene was found to give the desired complex as the dilithium chloride adduct in 67%.[16] In contrast to mononuclear titanocene dichloride, this dinuclear complex was found to be only poorly soluble in toluene and most other solvents. It further decomposed in chlorinated solvents as had been reported for C_1- and C_2-bridged dititanocenes.[8c] This was in contrast to earlier reports on using CH_2Cl_2 for extraction of such complexes.[8e,g–j,17] Moreover, in agreement with the earlier synthesis, THF was an inferior solvent for complexation than toluene but did not lead to decomposition of **4**.[8e] NMR analysis was carried out in DMSO-d_6, in which **4** was soluble and stable over several hours. The remaining lithium chloride could be removed by washing the complex with water, followed by acetone and toluene as indicated by ^{7}Li-NMR analysis (76% yield). However, the following application in titanium(III) catalysis was not affected by residual LiCl (vide infra).

The butylene-bridged complex **6** could not be prepared in the same fashion, since deprotonation of **5** with *n*-BuLi followed by reaction with $CpTiCl_3$ gave only traces of the desired complex. Instead, using NaHMDS and isolation of the disodium salt followed by complexation with $CpTiCl_3$ gave the desired product as adduct with two equivalents of NaCl (Scheme 2b). Purification attempts, however, were unsuccessful and, thus, the propylene bridge was chosen as motif for exploring chiral ligands.

For the ensuing synthesis of chiral C_3-bridged dititanocenes, (−)-menthol- and the corresponding 8-phenylmenthol-derived



Scheme 3. Synthesis of the chiral cyclopentadienyltitanium trichloride precursors.



Scheme 4. Synthesis of chiral dititanocenes **13** and **15**.

cyclopentadiene ligands **7** and **10** were chosen due to their established synthesis and the previous application of the corresponding mononuclear chiral titanocenes in titanium(III) catalysis (Scheme 3).[18,19] **7** and **10** were readily available from menthone and pulegone, respectively.[18b,c] The corresponding half-sandwich complexes **9** and **12** were then synthesized via the silylated derivatives **8** and **11** that could be used without purification.[20] The subsequent reaction of **8** with $TiCl_4$ then gave **9** in 49% overall yield.[21] The yield could be improved to 61% by carrying out the reaction in *n*-hexane instead of benzene. **12** was then prepared in a similar fashion, using benzene as reaction medium, in 56% overall yield. It should be noted that half-titanocenes **9** and **12** proved to be unstable in $CDCl_3$ over prolonged time.

The desired chiral dititanocenes **13** and **15** were then synthesized through reaction with NaHMDS double deprotonated bis-1,3-cyclopentadienyl-propane and the corresponding half-titanocene (Scheme 4). First attempts using stoichiometric amounts of **9** showed the formation of dititanocene **13**, but significant amounts of byproducts were observed in the crude mixture, in particular the prominent *ansa*-metallocene **14**,[22] the ^{1}H-NMR of which showed characteristic pseudo-triplets at δ = 5.90 and 6.50 ppm in C_6D_6. Gratifyingly, an adjustment of the stoichiometry to a 3:1 ratio led to the suppression of the byproduct formation. A sequence of filtration (to remove the formed sodium salts), concentration of the filtrate, and washing of the residue with *n*-pentane gave the analytically pure dititanocene **13** in 61% yield on a 4 mmol scale. The synthesis of **15** was carried out analogously. However, this complex was found to be more sensitive toward air and moisture and a lower yield of 26% was obtained.

We therefore carried on with complexes **4•2 LiCl** and **13** and characterized both by cyclic voltammetry using a Pt working electrode at a scan rate of 0.1 V s^{-1}. Interestingly, the achiral complex showed only one single reduction wave, even at higher scan rates (Figure 2).[16] The observed reduction wave appeared at E_p = −1.38 V and a value of $E_{p/2}$ = −1.28 V was determined, which was close to the value determined for Cp_2TiCl_2 ($E_{p/2}$ = −1.33 V) but slightly less negative.[23] For chiral dinuclear complex **13**, a second reduction wave became clearly visible with the first reduction occurring at surprisingly mild E_p = −1.29 V ($E_{p/2}$ = −1.15 V, Figure 3). The second reduction occurred then at E_p = −1.47 V with $E_{p/2}$ = −1.30 V, which was closer to the mononuclear complex **16** ($E_{p/2}$ = −1.41 V). Overall, the reduction of the dinuclear complexes occurred at less negative potentials than of the mononuclear counterparts. The electrochemical reduction of the chiral complexes **13** and **16** was almost completely irreversible as was indicated by the barely visible corresponding oxidation waves. This absence of an oxidation wave may originate from Ti—Cp cleavage or other decomposition pathways under the electrochemical reduction conditions. Under catalytic conditions, however, the zinc chloride that is formed in the reduction of the titanium center is known to facilitate instead

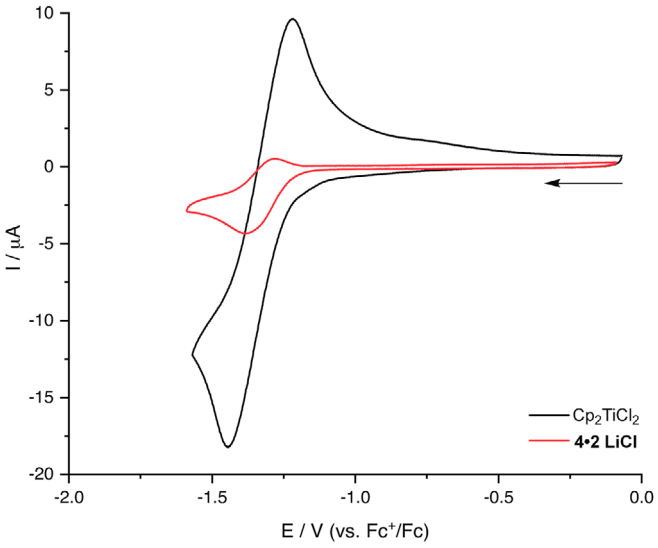


Figure 2. Cyclic voltammogram of **4•2 LiCl** (c = 2 mM; v = 0.1 V/s; versus Fc^+/Fc) in comparison to Cp_2TiCl_2.

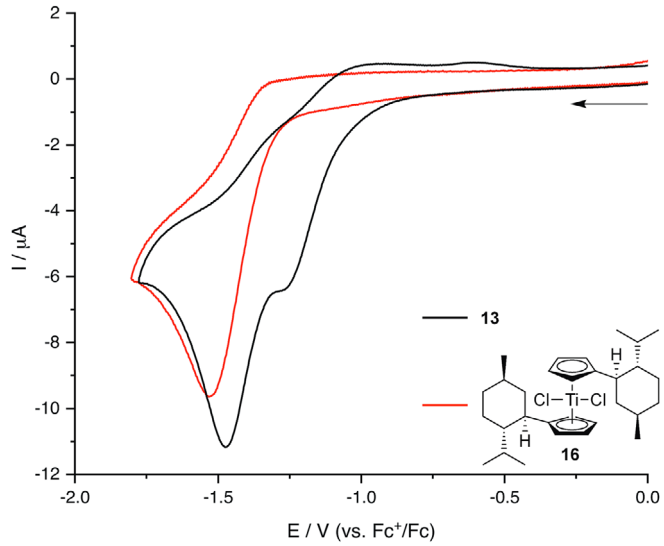
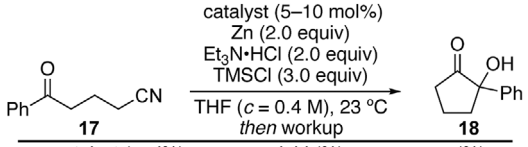


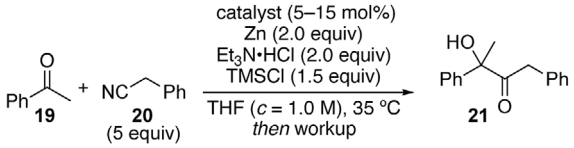
Figure 3. Cyclic voltammogram of **13** (c = 2 mM; v = 0.1 V/s; versus Fc^+/Fc) in comparison to the corresponding mononuclear **16**.

a)



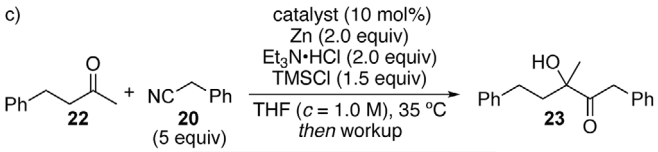
catalyst (mol%)	yield (%)	*ee* (%)
4•2 LiCl (10)	85	-
13 (5)	75	9
15 (5)	78	5
Cp_2TiCl_2 (10)	84	-

b)



catalyst (mol%)	yield (%)	*ee* (%)
4•2 LiCl (10)	59	-
13 (5)	25	5
15 (5)	25	3
$(EtCp)_2TiCl_2$ (10)	81	-

c)



catalyst (mol%)	yield (%)
4•2 LiCl (10)	28
$(ECp)_2TiCl_2$ (10)	18

Scheme 5. Performance of the dinuclear catalysts in selected ketone-nitrile coupling reactions.

a Ti—Cl cleavage after the electron transfer and the presence of Et_3N•HCl further stabilizes the titanium(III) species, preventing decomposition.[24,25]

The catalytic activity of the dititanocenes **4•2 LiCl**, **13**, and **15** was then evaluated in ketone-nitrile coupling reactions using three exemplary substrates (Scheme 5). All three dinuclear catalysts performed well in the cyclization of 5-oxo-

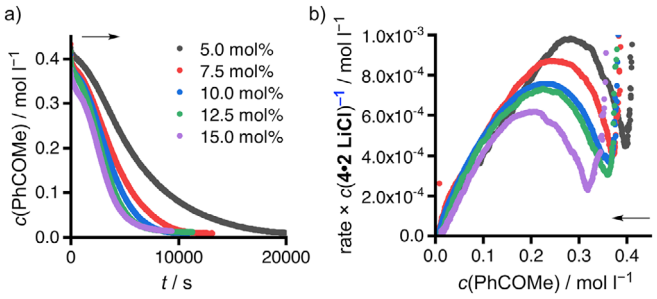
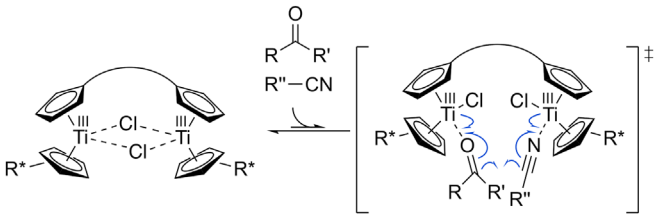


Figure 4. a). Monitoring of the reaction in Scheme 5b with varying amounts of **4•2 LiCl** as catalyst. b) Plot to determine the order in catalyst. Arrows indicate the direction of reaction progress.

5-phenylpentanenitrile (**17**), giving yields comparable to the reaction with Cp_2TiCl_2 as catalyst. However, the observed enantioselectivity with **13**, and **15** was surprisingly low (<10% *ee*), considering that Kagan's mononuclear catalyst **16** earlier gave 25% *ee* (Scheme 5a).[4] The achiral dititanocene **4•2 LiCl** then was a competent catalyst for the cross-coupling of acetophenone with benzyl cyanide at a 10 mol% catalyst loading with 59% yield, which corresponded to a lower reactivity than the respective reaction with $(EtCp)_2TiCl_2$ (Scheme 5b).[3d] In comparison, the chiral catalysts **13**, and **15** (5 mol%) were inferior and gave essentially racemic product. The challenging coupling between the aliphatic ketone benzyl acetone and benzyl cyanide was then tested and **4•2 LiCl** gave a low 28% yield, which, however, was an improvement over 18% yield with $(EtCp)_2TiCl_2$ as catalyst carried out at the same catalyst loading (Scheme 5c).[26] An application in the diastereoselective pinacol coupling of acetophenone was briefly investigated as well using **13**, but Cp_2TiCl_2 gave better a yield and *rac/meso* ratio.[16] Hence, the dinuclear catalysts performed well in the cyclization but were less efficient in the cross couplings. The chiral catalysts did unfortunately not show the desired asymmetric induction.

We therefore wondered whether the dinuclear catalysts acted as templates for the reaction or whether still two catalyst equivalents (with four Ti centers in total) would participate in the C—C coupling step. In order to investigate this, the order in catalyst was determined for the reaction of acetophenone and benzyl cyanide with **4•2 LiCl** at varied catalyst loadings (5–15 mol%) by monitoring via in situ IR spectroscopy. As with mononuclear catalysts such as $(EtCp)_2TiCl_2$, the kinetic profile for the consumption of acetophenone showed a characteristic S-shape (Figure 4a).[5] Plotting the rate corrected by the catalyst concentration to its presumed order versus the concentration of acetophenone gave a good overlay of the curves for an order of 1 in catalyst (Figure 4b).[16,27] From this, it could be concluded that the envisioned "dual activation" of the coupling partners by one titanium center each was in fact taking place. A hypothesis for the observed lower reactivity could be the formation of the μ-Cl-bridged titanium(III)-dimer, which could also be favored by the tether, thus hampering the reaction (Scheme 6). This is consistent with previous works that demonstrated the presence of monomer-dimer equilibria in solutions of titanocene(III) complexes and their effect on the catalysis efficiency.[3j,24]



Scheme 6. Proposed competition between a chloride-bridged dititanium(III) catalyst state and a possible product-forming transition state.

3. Conclusion

Reliable synthetic protocols for one achiral and two chiral dinuclear titanocene catalysts having C_3 tethers were established. In comparison with mononuclear catalysts, the dinuclear titanocenes performed well in the cyclization but did not lead to an enhanced performance in cross-coupling reactions. Moreover, the chiral catalysts did not lead to significant asymmetric induction, which indicates that addressing the low enantioselectivity in titanium(III) catalyzed cross couplings will require a different approach. Nevertheless, this study provides a proof of concept for the application of such dinuclear titanocenes in titanium(III) catalyzed reactions. The observed first-order catalyst dependence observed in the ketone-nitrile coupling confirms the participation of both titanium centers of a single catalyst entity in the C—C bond forming step and, hence, the envisioned templating effect of the dinuclear catalyst.

Looking to the future, a detailed computational study, in analogy to an earlier investigation of the cobalt-catalyzed hydrolytic kinetic resolution of epoxides,[28] could potentially give more insight into potential cooperative effects of the titanocene entities and their spatial orientation. Furthermore, the use of X-ligands other than chloride could lead to an improved reactivity and enantioselectivity.[29]

4. Experimental Section

All reactions were carried out in flame-dried Schlenk tubes under argon atmosphere (argon 5.0) and using absolute solvents unless noticed otherwise. Absolute THF and absolute toluene were dried over potassium under argon atmosphere and freshly distilled prior to use. Dichloromethane and diethyl ether were purchased in p.a. quality from SigmaAldrich. Zinc powder was purchased from Merck and used without further activation. Chlorotrimethylsilane was purchased from Acros and used as received. Titanocene dichloride was purchased from AlfaAesar and used as received. All other chemicals were purchased from SigmaAldrich and used without further purification. *n*-Butyllithium was titrated using diphenylacetic acid as indicator before use.[30] An IKAmag temperature modulator in combination with an oil bath or stainless steel heating block was used to control the reaction temperatures. Thin layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching or staining ($KMnO_4$ or anisaldehyde). In general, Macherey-Nagel silica gel 60 (particle size 0.04–0.063 mm) was used for flash chromatography. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker DRX 500, a Bruker Avance II 400, a Bruker Avance III 300, and a Bruker DRX 250 spectrometer and reported to be $CDCl_3$ [$\delta(^1H)$ = 7.26 ppm and $\delta(^{13}C)$ = 77.16 ppm] and C_6D_6 [$\delta(^1H)$ = 7.16 ppm and $\delta(^{13}C)$ = 128.06 ppm]. The following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, oct = octet, ps = pseudo, br = broad signal. NMR spectra were recorded at room temperature (298–300 K) unless noted otherwise. IR spectra for characterization purposes were recorded on a thermo scientific Nicolet iS10 FT-IR spectrometer equipped with a diamond ATR unit and are reported in frequency of absorption. Mass spectrometry analyses were performed by the service department at the Institute for Organic Chemistry, University of Freiburg. Low resolution fragmentation MS analyses were carried out on a Thermo Finnigan TSQ 700 for electron impact ionization (EI) at 70 eV, 200 °C. High resolution mass analyses (HRMS) were carried out on a Thermo Exactive with Orbitrap analyzer using atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI).

Compounds **3**,[13] **5**,[14] **7**,[18c] **10**,[18b] **16**,[18c] and **17**[4] were synthesized following the reported procedures.

4.1. μ_2-(1,3-(Di-η5-cyclcopentadienyl)propanediyl)-di(dichloro-(η5-cyclopentadienyl)titanium(IV)) lithium chloride adduct (4•2 LiCl)

A flame-dried argon-backfilled 250 mL Schlenk flask equipped with a magnetic stir bar was filled with toluene (125 mL) and a solution of 1,3-di(cyclopentadienyl)propane (**3**) (480 mg, 2.79 mmol) in toluene (15 mL) was added. While stirring, the solution was cooled to −70 °C and *n*-BuLi (2.52 M in hexanes, 2.45 mL, 6.17 mmol, 2.2 equiv) was added dropwise. The mixture was warmed to 4 °C over a time of 1 h 25 min, which resulted in a colorless suspension. The cooling bath was removed and the suspension was stirred for another 4 h at 23 °C. A separate flame-dried argon-backfilled 250 mL Schlenk flask equipped with a magnetic stir bar was filled with $CpTiCl_3$ (1.104 g, 5.034 mmol, 2.0 equiv) and toluene (30 mL) was added. While stirring, the resulting yellow suspension was cooled to −30 °C. Next, the suspension of the double-deprotonated ligand (0.02 M in toluene, 125 mL, 2.5 mmol) was added over a time of 45 min, which resulted in a brown solution. The cooling bath was removed and the mixture was stirred for 16 h at 23 °C, which led to conversion into a red suspension. The solvent was removed at 40 °C at the Schlenk (using a liquid N_2 cooling trap) and the residue was dried under high vacuum. The residue was washed with toluene (3 × 30 mL) and dried again under high vacuum. In order to facilitate the removal of residual toluene, the solid can be washed with *n*-pentane (2 × 15 mL). The desired dinuclear complex was received as a red-brown solid in 67% yield (1.04 g, 1.68 mmol) and analysis by ^{7}Li-NMR revealed that it still contained LiCl. The compound was stable for a short time under air and was stored under argon at room temperature. The compound was found to be poorly soluble in toluene and was unstable in THF or chlorinated solvents. Crystallization attempts were unsuccessful. mp: >210 °C. ^{1}H-NMR (500.1 MHz, DMSO-d_6): δ = 1.79 (psquint, J = 7.8 Hz, 2H), 2.61 (pst, J = 7.7 Hz, 4H), 6.39 (pst, J = 2.6 Hz, 4H), 6.63 (s, 10H), 6.68 (pst, J = 2.6 Hz, 4H). ^{13}C-NMR (125.8 MHz, DMSO-d_6): δ = 29.61, 30.07, 116.62, 119.97, 122.90, 137.82. ^{7}Li-NMR (194.4 MHz, DMSO-d_6): δ = −1.03. HRMS (ESI, pos): calcd for $C_{23}H_{24}Cl_3Ti_2$ $[M-Li_2Cl_3]^+$: 500.9897, found: 500.9904. IR (ATR): ν [cm^{-1}] = 3388, 3115, 2941, 1656, 1631, 1492, 1442, 1420, 1370, 1048, 1014, 855, 823, 726.

4.2. Procedure for the removal of LiCl from 4•2 LiCl

On a Büchner funnel, complex **4•2 LiCl** (340 mg, 0.546 mmol) was washed with H_2O (4 × 5 mL), acetone (4 × 5 mL), and toluene (3 ×

5 mL). The solid was dried under high vacuum and **4** was received as an orange-red amorphous solid in 76% yield (224 mg, 0.416 mmol). An ^{7}Li-NMR in DMSO-d_6 showed only a trace signal of LiCl. The ^{1}H-NMR shifts were identical to **4•2 LiCl**.

4.3. μ_2-(1,4-(Di-η5-cyclcopentadienyl)butanediyl)-di(dichloro-(η5-cyclopentadienyl)titanium(IV)) sodium chloride adduct (6•2 NaCl)

A flame-dried argon-backfilled 25 mL Schlenk flask equipped with a magnetic stir bar was charged with a solution of 1,4-di(cyclopentadienyl)butane (**5**) (189 mg, 1.01 mmol) in toluene (3 mL). The solution was stirred and cooled to 0 °C. A solution of NaHMDS (403 mg, 2.20 mmol, 2.2 equiv) in toluene (3.7 mL) that was freshly prepared under argon was added dropwise, which led to the formation of a yellow suspension. The reaction vessel was tightly sealed and allowed to warm to room temperature (23 °C) in the cooling bath over 16 h. The reaction was inertly filtered and the filter cake was rinsed with *n*-pentane (2 × 3 mL). Drying under high vacuum gave the disodium salt of the dicyclopentadienyl butane ligand (281 mg), which was used in this form in the complexation step. A flame-dried argon-backfilled 50 mL Schlenk flask equipped with a magnetic stir bar was charged with the disodium salt from the previous step (114 mg, 0.41 mmol) and toluene (20 mL) was added. The resulting suspension was stirred and cooled to −78 °C. An inertly prepared solution of $CpTiCl_3$ (179 mg, 0.816 mmol) in toluene (5 mL) was added slowly. The reaction mixture was allowed to warm to room temperature (23 °C) over 17 h in the cooling bath, which resulted in a red color. Toluene (20 mL) was added and the reaction solution was removed with the help of a syringe filter. The residue was dried under high vacuum. The title compound was received as brown-red solid, but was of insufficient purity for complete characterization or usage in catalysis experiments. Further attempts to purify the material were unsuccessful. ^{1}H-NMR (300.1 MHz, DMSO-d_6): δ = 1.48–1.56 (m, 4H), 2.56–2.65 (m, 4H), 6.38 (pst, J = 2.6 Hz, 4H), 6.62 (s, 10H), 6.68 (pt, J = 2.6 Hz, 4H).

4.4. Trichloro-η5-((−)-menthyl)cyclopentadienyl)titanium(IV) (9)[21]

To a flame-dried argon-backfilled Schlenk flask containing a magnetic stir bar was added a solution of **7** (6.00 g, 29.4 mmol, 1.0 equiv) in THF (120 mL) at −78 °C. While stirred, a solution of *n*-butyllithium in *n*-hexane (2.28 M, 13.5 mL, 30.8 mmol, 1.05 equiv) was added dropwise. The reaction mixture was then warmed to 23 °C, stirred for 1 h, and then cooled down again to −78 °C. Chlorotrimethylsilane was added dropwise and the reaction mixture was again warmed to 23 °C followed by stirring for 1 h. The mixture was poured on ice water (180 g). The organic layer was separated and the aqueous layer extracted with petroleum spirit (3 × 75 mL). The combined organic layers were washed with water (2 × 50 mL), dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The silylated cyclopentadiene **8** was received as an orange oil in 99% yield (8.45 g, 30 mmol) and directly used in the next step. The NMR data showed the presence of two sets of signals for the silyl group and the remaining allylic hydrogen in a 1.1:1 ratio (either rotamers or regioisomers). ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = −0.04 (s, 4.7H), −0.03 (s, 4.3H), 0.69 (d, J = 6.8 Hz, 3H), 0.82 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 6.5 Hz, 3H), 0.90–1.13 (m, 3H), 1.22–1.49 (m, 3H), 1.61–1.79 (m, 3H), 2.37 (dt, J = 3.5, 11.5 Hz, 1H), 3.18 (s, 0.5H), 0.38 (s, 0.5H), 6.05 (s, 1H), 6.42 (s, 1H), 6.48 (s, 1H). A flame-dried argon-backfilled Schlenk flask containing a magnetic stir bar was charged with a solution of **8** (2.3 g, 5.0 mmol, 1.0 equiv) in benzene (3 mL). While stirring, $TiCl_4$ (0.55 mL, 5.0 mmol, 1.0 equiv) was added dropwise over a time of 10 min. Afterwards, stirring of the mixture was continued for 30 min at room temperature (23 °C). The solvent was removed under reduced pressure and the residue was washed with *n*–pentane (1 × 15 mL, 2 × 10 mL) and dried in vacuo. Complex **9** was received as a red solid in 49% yield (1.06 g, 2.45 mmol) and stored under inert gas atmosphere. A reaction carried out in *n*-hexane (50 mL) as solvent on a 14.7 mmol scale followed by the same workup gave the product in 61% overall yield (3.2 g, 9.0 mmol). The NMR data matched the literature values.[21] ^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.82 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.5 Hz, 3H), 0.93–1.02 (m, 1H), 1.07–1.52 (m, 5H), 1.74–1.85 (m, 2H), 1.95 (ddd, J = 3.3, 5.4, 12.6, Hz, 1H), 2.84 (ddd, J = 3.2, 10.4, 12.0, Hz, 1H), 6.72 (ddt, J = 0.5, 2.3, 3.1 Hz, 1H), 6.78 (td, J = 2.2, 3.2 Hz, 1H), 7.02–6.99 (m, 1H), 7.08 (dt, J = 2.1, 3.2, Hz, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 15.67, 21.63, 22.59, 24.78, 27.89, 32.68, 35.02, 41.40, 43.34, 51.01, 120.91, 122.97, 123.45, 123.97, 150.25. HRMS (APCI, MeOH, neg) calcd for $C_{15}H_{23}Cl_3Ti^{+}$ $[M+MeO]^{-}$: 387.0529, found: 387.0537.

4.5. Trichloro-η5-(((1*R*,2*R*,5*R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl)cyclopentadienyl)titanium(IV) (12)

The silylated Cp ligand **11** was synthesized following the procedure for compound **8** along with **10** as precursor on a 22.4 mmol scale.[31] A crude mixture was received (9.61 g) that contained the desired product as a mixture of isomers (calculated yield: 91%, 20.5 mmol) and was used directly in the next step. Purification of a sample via flash chromatography (*n*-hexane, R_F = 0.25) gave a 1:2:7 mixture of diastereomers. The ^{1}H-NMR spectrum could be assigned in full for the major isomer. For the minor isomers, only the olefinic and TMS signals could be assigned. The ^{13}C-NMR data is given for the isomeric mixture. Major: ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = −0.05 (s, 9H), 0.82 (d, J = 6.4 Hz, 3H), 1.00- 1.45 (m, 8H), 1.09 (s, 3H), 1.24 (s, 3H), 1.86 (dt, J = 11.3, 2.9 Hz, 1H), 2.54 (dq, J = 11.3, 3.4 Hz, 2H), 3.02 (br s, 1H), 5.97–5.98 (m, 1H), 2.18–6.20 (m, 1H), 6.33 (br d, J = 4.0 Hz, 1H), (d,7.02–7.24 (m, 5H). Minor, only TMS and olefinic signals: ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = 0.01 (s, 2.34H), 0.04 (s, 1.37H), 5.76 (dd, J = 1.69 Hz, 0.14H), 5.89 (br, 0.15H), 6.03 (psq, J = 1.5 Hz, 0.21H), 6.38 (psq, J = 1.4 Hz, 0.28H), 6.41 (br, 0.31H), 6.57 (psq, J = 1.6 Hz, 0.31H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = −2.1, −1.8, −1.3, 22.4, 22.5, 22.5, 24.4, 24.4, 25.7, 28.7, 28.7, 29.1, 29.2, 32,8, 32.9, 32.9, 33.8, 35.7, 35.8, 35.8, 35.9, 41.7, 43.2, 46.2, 49.2, 49.2, 50.1, 50.1, 124.8, 124.9, 125.9, 125.9, 126.2, 126.2, 127.4, 127.5, 127.6, 127.6, 127.7, 127.8, 128.8, 129.8, 130.4, 130.5, 132.8, 151.9, 151,9, 152.0, 152.1. MS (EI, 70 eV): m/z (%) = 353.3 (15), 352.5 $[M]^{+}$ (54), 233.2 (20), 159.2 (15), 119.2 (25), 91.1 (20), 73.1 (100). HRMS (ESI, pos) calcd for $C_{24}H_{37}Si^{+}$ $[M+H]^{+}$: 353.2659, found: 353.2659. IR (ATR) ν [cm^{-1}] = 2950, 2912, 1709, 1599, 1495, 1455, 1442, 1385, 1367, 1247, 1089, 1031, 985, 961, 908, 869, 836, 805, 779, 761, 733, 698, 654, 631, 615. A flame-dried, argon-backfilled Schlenk flask equipped with a magnetic stir bar was charged with a solution of **11** (4 mmol, 1 equiv) in benzene (3 mL). While stirring, $TiCl_4$ (0.55 mL, 5 mmol, 1.25 equiv) was added dropwise within 10 min. The reaction mixture was stirred for 30 min at 23 °C (room temperature) after which the solvent was removed under reduced pressure. The residue was washed with *n*-pentane (1 × 15 mL, 2 × 10 mL) and then dried in vacuo. The title product was received as a red solid in 61% yield (1.06 g, 2.45 mmol, 56% overall yield) and stored under inert gas atmosphere. ^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.91 (d, J = 6.4 Hz, 3H), 1.10 (s, 3H), 1.30 (s, 3H), 1.38–1.55 (m, 1H), 1.83–1.90 (m, 2H), 2.03–2.12 (m, 2H), 2.84 (dt, J = 10.3, 3.0 Hz, 1H), 6.07 (td, J = 3.0, 2.7 Hz, 1H), 6.54–6.57 (m, 2H), 6.62 (td,

J = 3.2, 2.2 Hz, 1H) 6.95–7.08 (m, 5H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.95, 22.37, 28.50, 32.25, 32.62, 35.51, 40.72, 43.02, 44.06, 53.91, 121.80, 122.19, 123.01, 124.16, 125.27, 125.96, 128.07, 151.05, 151.20. MS (EI, 70 eV): m/z (%) = 432.2 $[M]^+$ (4), 315.1 (12), 313.1.1 (12), 279.2 (12), 277.1 (14), 141.1 (6), 119.1 (100), 91.1 (25), 40.9 (10). HRMS (APCI, MeOH, neg) calcd for $C_{22}H_{30}Cl_3OTi^-$ $[M + MeO]^-$: 463.0842, found: 463.0850. IR (ATR) ν [cm^{-1}] = 3095, 2953, 2915, 2850, 2161, 1980, 1597, 1493, 1483, 1456, 1442, 1428, 1386, 1364, 1258, 1155, 1102, 1073, 1049, 150, 1029, 1017, 1002, 901, 855, 834, 780, 702, 666, 614.

4.6. μ_2-η5-(1,3-(Dicyclcopentadienyl)propanediyl)-di(dichloro-((−)-menthyl)-η5-cyclopentadienyl)-titanium(IV)) (13)

In a flame-dried argon-backfilled Schlenk flask containing a magnetic stir bar, 1,3-di(cyclopentadienyl)propane (**3**) (689 mg, 4.00 mmol, 1.0 equiv) was dissolved in toluene (100 mL) at 0 °C. While stirring, a solution of NaHMDS (1.47 g, 8.00 mmol, 2.0 equiv) in toluene (150 mL) was slowly added within 10 min. The mixture was stirred at room temperature for 3 h and then cooled to −40 °C. In a separate Schlenk tube containing a stir bar, half-titanocene **9** (4.28 g, 12.00 mmol, 3.0 equiv) was suspended in toluene (100 mL). This stirred suspension was slowly added under inert conditions over a time span of 15 min to the solution of the deprotonated di(cyclopentadienyl)propane at −40 °C. The Schlenk tube was rinsed with toluene (2 × 5 mL). The reaction vessel was closed, and the reaction mixture slowly allowed to warm to room temperature (23 °C). After stirring at room temperature for 40 h, the mixture was filtered and the solvent removed under reduced pressure. The residue was washed with *n*-pentane (4 × 10 mL) and dried in vacuo. The dinuclear complex was received in form of a red solid in 61% yield (1.99 g, 2.44 mmol). ^{1}H-NMR (500.1 MHz, C_6D_6): δ = 0.76 (d, J = 6.9 Hz, 6H), 0.81 (d, J = 6.8 Hz, 6H), 0.88 (dq, J = 3.5, 12.8, Hz, 2H), 0.96 (d, J = 6.5 Hz, 6H), 0.98–1.11 (m, 2H), 1.06 (p, J = 12.2 Hz, 4H), 1.37–1.48 (m, 2H), 1.55 (dtd, J = 2.4, 6.8, 13.7, Hz, 2H), 1.62 (dd, J = 3.0, 12.8, Hz, 2H), 1.71 (tdd, J = 3.3, 5.7, 12.1, Hz, 2H), 1.91 (quint, J = 7.7 Hz, 2H), 2.04 (qd, J = 2.9, 12.3, Hz, 2H), 2.83–2.95 (m, 6H), 5.47 (q, J = 2.8 Hz, 2H), 5.73 (q, J = 3.0 Hz, 2H), 5.82 (q, J = 3.0 Hz, 2H), 6.07–6.11 (m, 8H), 6.28 (q, J = 3.1 Hz, 2H). ^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 0.78 (d, J = 6.9 Hz, 6H), 0.84 (d, J = 6.8 Hz, 6H), 0.89 (d, J = 6.5 Hz, 6H), 0.86–0.91 (m, 2H), 0.98 (tt, J = 2.7, 11.4 Hz, 2H), 1.05 (q, J = 11.9 Hz, 2H), 1.11 (dq, J = 3.5, 12.9, Hz, 2H), 1.36–1.47 (m, 4H), 1.59 (qd, J = 3.2, 12.3, Hz, 2H), 1.69 (qd, J = 3.1, 12.9, Hz, 2H), 1.75–1.80 (m, 2H), 1.94 (quint, J = 7.7 Hz, 2H), 2.71 (dt, J = 3.0, 11.4, Hz, 2H), 2.80 (psoct, J = 7.5 Hz, 4H), 6.18 (q, J = 2.9 Hz, 2H), 6.26–6.29 (m, 6H), 6.35 (q, J = 2.9 Hz, 2H), 6.45 (q, J = 3.0 Hz, 2H), 6.48 (q, J = 2.2 Hz, 2H), 6.66 (dt, J = 2.1, 3.1, Hz, 2H). ^{13}C-NMR (125.8 MHz, C_6D_6): δ = 15.76, 21.80, 23.01, 25.08, 27.69, 30.09, 30.83, 32.89, 35.58, 41.17, 42.47, 51.10, 109.20, 114.03, 114.68, 119.15, 119.94, 122.68, 122.80, 122.92, 138.03, 143.31. ^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 15.69, 21.77, 22.88, 24.78, 27.52, 30.28, 30.62, 32.59, 35.25, 40.98, 42.29, 51.05, 110,59, 114.69, 115.84, 117.55, 120.65, 122.17, 123.03, 125.05, 138.74, 144.15. MS (EI, 70 eV): m/z (%) = 611.2 [M–(menthylCp)]$^+$ (6), 609.2 (5), 492.4 (6), 491.4 (23), 490.4 (21), 489.4 (50), 488.(8), 487.4 (7), 454.4 (5), 453.4 (11), 452.5 (32), 392.1 (5), 391.0 (21), 390.1 (17), 389.0 (55), 388.0 (23), 387.1 (57), 386.0 (10), 385.0 (8), 325.2 (14), 324.2 (14), 323.2 (67), 322.2 (32), 321.2 (100), 320.2 (19), 319.2 (14), 290.1 (16), 288.2 (24), 287.3 (6), 286.2 (22), 285.2 (15), 284.2 (42), 283.2 (18), 282.2 (8), 281.2 (11), 279.1 (6), 255.1 (21), 254.1 (16), 253.1 (53), 251.2 (10), 250.1 (8), 242.1 (6), 241.2 (7), 239.1 (6), 218.2 (31), 217.2 (26), 216.2 (43), 215.2 (9), 214.2 (7), 203.3 (42), 175.3 (7), 174.1 (25), 173.1 (7), 161.2 (13), 148.1 (5), 132.2 (11), 123.2 (7), 117.2 (12), 93.2 (6), 92.2 (13), 91.2 (17), 79.2 (27). HRMS (ESI, pos) calcd for $C_{43}H_{64}NCl_3{}^{37}ClTi_2{}^+$ $[M + NH_4]^+$: 832.2723, found: 832.2717. IR (ATR) ν [cm^{-1}] = 3116, 2955, 2915, 2855, 1486, 1443, 1407, 1386, 1369, 1248, 1040, 1040, 821, 752, 615, 610.

4.7. μ_2-η5-(1,3-(Dicyclopentadienyl)propanediyl)-di(dichloro-((−)-(8-phenyl)menthyl-η5-cyclopentadienyl)titanium(IV)) (15)

In a flame-dried argon-backfilled Schlenk flask equipped with a magnetic stir bar, 1,3-di(cyclopentadienyl)propane (**3**) (17 mg, 0.1 mmol, 1.0 equiv) was stirred in toluene (30 mL) at 0 °C. In a separate flame-dried Schlenk tube, NaHMDS (37 mg, 0.5 mmol, 2.0 equiv) was dissolved in toluene (4 mL). This NaHMDS solution was then slowly added to the solution of the ligand at 0 °C over a time of 10 min. The reaction mixture was stirred for 3 h at 0 °C and then cooled to − 78 °C. Next, a solution of the half-sandwich titanium complex **12** (107 mg, 0.25 mmol, 2.5 equiv) in toluene (3 mL) was added over a time of 5 min. The reaction was allowed to slowly warm to room temperature, the vessel was closed, and stirred for another 18 h. Using a Schlenk frit, the mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was washed with *n*–pentane (3 × 4 mL) and then dried under high vacuum. The dinuclear complex **15** was received as a red solid in 26% yield (25 mg, 0.026 mmol). NMR analysis showed minor impurities and residual *n*-pentane. Regardless, **15** prepared this way was found to be suitable for applications in catalysis. NMR assignment was facilitated by an HSQC NMR experiment. ^{1}H-NMR (400.1 MHz,C_6D_6): δ = 0.92–1.10 (m, 4H), 0.94 (d, J = 6.4 Hz, 6H), 1.02 (s, 6H), 1.06 (s, 6H), 1.11–1.19 (m, 2H), 1.36–1.47 (m, 2H), 1.67–1.91 (m, 10H), 2.73–2.88 (m, 6H), 5.07–5.09 (m, 2H), 5.68–5.70 (m, 2H), 5.76–5.77 (m, 2H), 5.79–5.81 (m, 2H), 5.92–5.93 (m, 2H), 5.96–6.01 (m, 6H), 6.89–7.04 (m, 10H). ^{13}C-NMR (100.6 MHz, C_6D_6): δ = 22.80, 23.56, 29.22, 30.34, 30.79, 30.81, 32.94, 36.08, 40.83, 42.26, 44.04, 54.08, 109.16, 114.03, 114.70, 120.14, 121.94, 122.41, 122.58, 124.98, 125.98, 137.80, 143.11, 151.68. HRMS (APCI, pos, NH_4^+) calcd for $C_{55}H_{68}Cl_3Ti_2^+$ $[M–Cl]^+$: 929.3345, found: 929.3335. Repeated HRMS from a second experiment: HRMS (APCI, pos, NH_4^+) calcd for $C_{55}H_{72}Cl_4NTi_2^+$ $[M + NH_4]^+$: 982.3372, found: 982.3374. IR (ATR) ν [cm^{-1}] = 2950, 2917, 2865, 1494, 1454, 1442, 1420, 1385, 1368, 1260, 1089, 1031, 1017, 966, 762, 811, 725, 697, 663, 614, 558, 513, 496, 489, 470, 464, 454.

4.8. Cyclic voltammetry

Cyclic voltammograms were recorded using a Princeton Applied Research VersaSTAT4 Potentiostat Galvanostat under exclusion of air and moisture and using 0.2 M Bu_4NPF_6 in THF as electrolyte. A standard three-electrode setup was used with a Pt milli-electrode (model G0228, AMETEK) as working electrode, Pt wire in electrolyte as counter electrode, and Ag wire in 3 M NaCl/sat AgCl solution as reference electrode.

4.9. Experimental procedure for the CV measurements

Bu_4NPF_6 (387 mg, 1.00 mmol) and 0.01 mmol of the desired titanocene complex were added to an electrochemical cell. The cell was closed and gently flushed with argon for 5–10 min. Next, THF (5.0 mL) was added and argon was bubbled through the resulting solution until the measurement was started. During the measurement, a stream of argon was gently maintained on top of the solution. The cyclic voltammograms were measured using rates of 0.1, 1, and 5 V/s, respectively. After the measurements, a small amount of ferrocene was added and the Fc^+/Fc redox pair was measured as reference.

4.10. Evaluation of the Catalysts in Ketone-Nitrile Couplings

The titanium(III)-catalyzed reductive couplings were carried out following published procedures for the ketonitrile cyclization[4] and the cross-coupling between ketones and nitriles.[3d]

4.11. 2-Hydroxy-2-phenylcyclopentanone (18)[4,32]

Prepared via the ketonitrile cyclization of 5-oxo-5-phenylpentanenitrile (**17**) (0.2 mmol) using the desired catalyst as described in Scheme 5. The analytical data matched the literature values. R_F(CH_2Cl_2/EtOAc 10:1) = 0.3. R_F(cyclohexane/EtOAc 4:1) = 0.2. ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = 1.74–1.91 (m, 1H), 1.98–2.13 (m, 1H), 2.16–2.30 (m, 1H), 2.41–2.56 (m, 3H), 3.08 (br s, 1H), 7.16–7.42 (m, 5H). ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ = 17.25, 35.77, 37.82, 80.71, 125.84, 128.26, 128.75, 140.75, 218.75. MS (EI, 70 eV): m/z (%) = 176.1 $[M]^+$ (36), 148.1 (94), 120.1 (100), 105.1 (84), 91.1 (10), 77.2 (26), 51.4 (4). HRMS (APCI, pos, NH_4^+) calcd for $C_{11}H_{16}NO_2$ $[M+NH_4]^+$: 194.11756, found: 194.11760. IR (NaCl): ν [cm^{-1}] = 3088, 3010, 3028, 2967, 2888, 1958, 1888, 1743, 1684, 1600, 1582, 1496, 1466, 1448, 1402, 1368, 1311, 1271, 1237, 1165, 1132, 1072, 1017, 1025, 979, 919, 848, 816, 798, 759, 701. HPLC conditions: AD-3, *n*-heptane/EtOH 90:10, 0.8 mL/min; t_1 = 12.0 min, t_2 = 21.8 min.

4.12. 3-Hydroxy-1,3-diphenylbutan-2-one (21)[3d]

Prepared via the ketone-nitrile cross coupling procedure using acetophenone (58 µL, 60 mg, 0.50 mmol) and benzyl cyanide (0.29 mL, 300 mg, 2.6 mmol, 5.2 equiv) as coupling partners and the desired catalyst as described in Scheme 5. The analytical data matched the literature values. ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = 1.84 (s, 3H), 3.67 (s, 2H), 4.45 (br s, 1H), 6.89–6.96 (m, 2H), 7.17–7.28 (m, 3H), 7.32–7.49 (m, 5H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 24.42, 42.56, 80.52, 126.48, 128.20, 128.50, 128.71, 129.06, 129.62, 134.01, 141.33, 203.39. MS (EI, 70 eV): m/z (%) = 240.2 $[M]^+$ (1), 122.1 (8), 121.1 (100.00), 91.1 (8), 43.2 (23). HRMS (APCI, pos, NH_4^+) calcd for $C_{16}H_{20}NO_2^+$ $[M+NH_4]^+$: 258.14940, found: 258.14930. IR (NaCl): ν [cm^{-1}] = 3087, 3062, 3030, 2980, 2933, 1955, 1885, 1809, 1714, 1601, 1584, 1496, 1447, 1404, 1370, 1329, 1315, 1221, 1161, 1118, 1104, 1069, 1035, 1002, 940, 915, 825, 759, 724, 698. HPLC conditions: AD-3, *n*-heptane/EtOH 95:5, 0.8 mL/min; t_1 = 10.0 min, t_2 = 12.1 min.

4.13. 3-Hydroxy-3-methyl-1,5-diphenylpentan-2-one (23)

Prepared via the ketone-nitrile cross coupling procedure using benzylacetone (75 µL, 74 mg, 0.50 mmol) and benzyl cyanide (0.29 mL, 300 mg, 2.6 mmol, 5.2 equiv) as coupling partners. **4•2 LiCl** (26 mg, 0.048 mmol, 10 mol%) was employed as catalyst. The reaction was run for 41 h at 35 °C. The product was received in form of a colorless oil in 28% yield (37.8 mg, 0.14 mmol). ^{1}H-NMR (300.1 MHz, $CDCl_3$): δ = 1.47 (s, 3H), 2.04–2.15 (m, 2H), 2.33 (ddd, J = 6.7, 10.4, 13.6, Hz, 1H), 2.76 (ddd, J = 6.9, 9.7, 13.6, 1H), 3.78 (d, J = 16.1 Hz, 2H),3.80 (br s, 1H, OH), 3.87 (d, J = 16.1 Hz, 1H), 7.10–7.13 (m, 2H), 7.17–7.23 (m, 3H), 7.25–7.31 (m, 3H), 7.32–7.37 (m, 2H). ^{13}C-NMR (100.61 MHz, $CDCl_3$): δ = 25.76, 29.99, 41.54, 42.72, 79.08, 126.16, 127, 33, 128.48, 128.59, 128.77, 129.63, 133.40, 141.52, 211.54. HRMS (APCI, MeOH) calcd for $C_{18}H_{20}O_2Na^+$ $[M+Na]^+$: 291.13555, found: 291.13571. IR (NaCl): ν [cm^{-1}] = 3088, 3014, 3030, 2981, 2883, 1907, 1716, 1599, 1495, 1454, 1400, 1370, 1329, 1219, 1155, 1094, 1035, 1013, 1003, 936, 837, 769, 734, 721, 700.

4.14. In situ infrared spectroscopy

The in situ IR experiments were carried out on a Mettler Toledo ReactIR 15 instrument equipped with a diamond window fiberoptics probe (DiComp) with a measuring window of 2 mm diameter and a LN2 MCT detector. The measuring window was 3000–650 cm^{-1}. The Mettler Toledo iC IR (V 4.3.35 SP1) software was used for recording and OriginPro 2019 was used for the data analysis. The carbonyl stretch of acetophenone was recorded at 1689 cm^{-1}. A calibration using varying amounts of acetophenone was carried out. A second order polynomial fit was applied to give Equation (1) for the conversion of absorption (x) into concentration of acetophenone:

$$c\,(PhOMe) = 1.14556 \times x + 1.80891 \times x^2 \quad (1)$$

Before each experiment, a background measurement was recorded that was automatically subtracted. Likewise, a spectrum of the solvent (THF) was recorded and subtracted automatically. The measurements were carried out in intervals of 15 s.

4.15. Experimental procedure for in situ IR measurements

A custom-made 10 mL Schlenk tube having two septum-capped joints (NS19/26) containing a magnetic stir bar was flame-dried and argon-backfilled. In a positive argon stream, the titanium catalyst (5–15 mol%), zinc (130 mg, 2.00 mmol, 2.00 equiv), and Et_3N•HCl (137 mg, 2.00 mmol, 2.00 equiv) were added. The tube was evacuated, backfilled with argon, and attached to the diamond probe in such a way that the probe and stir bar were in about 0.5 cm distance from each other. The vessel was again evacuated and backfilled with argon and immersed in a temperature-controlled oil bath (35 °C). While stirring, THF (1.00 mL) was added and a color change of the resulting mixture from red to green occurred. The measurement was started. Next, benzyl cyanide (580 µL, 5.00 mmol, 5.00 equiv), acetophenone (117.5 µL, 1.00 mmol, 1.00 equiv), and TMSCl (190 µL, 1.50 mmol, 1.50 equiv) were added through the remaining septum using Hamilton gas-tight glass syringes. The septum was replaced by a greased glass stopper and the reaction mixture was stirred until no further conversion occurred. The reaction was then stopped by addition of H_2O and discarded.

Supporting Information

The authors have cited additional references within the Supporting Information.[33,34]

Acknowledgements

The German Research Foundation (DFG, projects 333382543 and 408295365) is acknowledged for financial support.

Open access funding enabled and organized by Projekt DEAL.

Conflict of Interests

The authors declare no conflicts of interest.

Data Availability Statement

Reproductions of NMR spectra and HPLC reports are available free of charge in the Supporting Information. The NMR, MS, CV, and kinetic data files are available on Zenodo at https://doi.org/10.5281/zenodo.13145153.

Keywords: Catalysis · Metallocenes · Radicals · Reduction · Titanium

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Manuscript received: July 31, 2024
Revised manuscript received: September 07, 2024
Accepted manuscript online: September 08, 2024
Version of record online: October 01, 2024