Regio- and stereo-selective coupling reactions of cyclo-1,3-dienes catalysed by titanium aryloxide compounds

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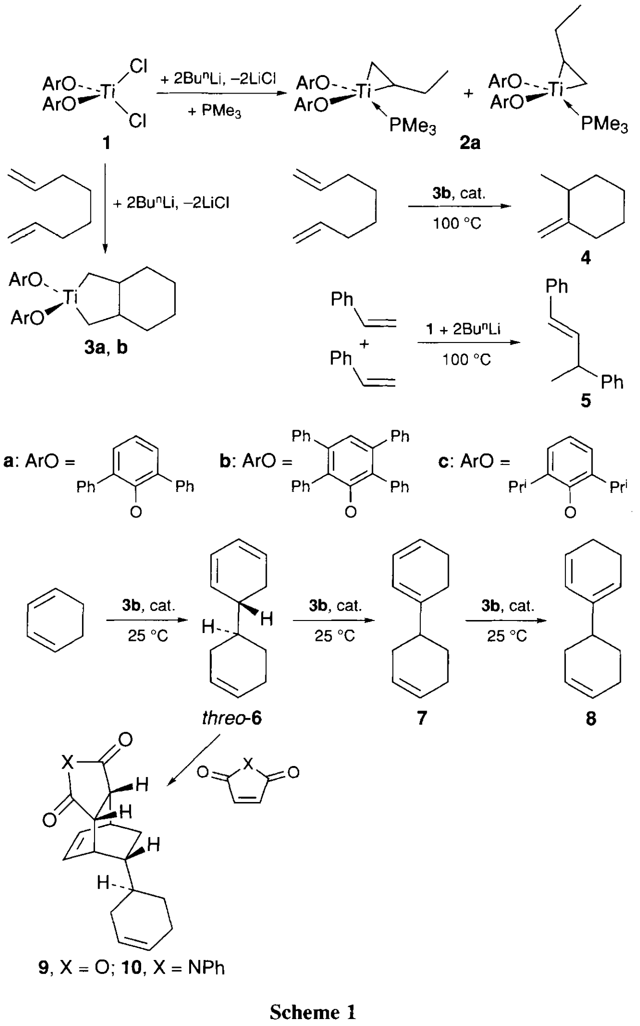
Highly selective non-Diels–Alder dimerization of cyclohexa-1,3-diene and cross-coupling of either cyclohexa-1,3-diene or cycloocta-1,3-diene with α-alkenes is catalysed by titanium aryloxide compounds.

The ubiquitous β-hydrogen abstraction process is typically considered a nuisance in transition-metal organometallic chemistry.[1] In the case of metallacyclopentane rings formed by reductive coupling of alkenes, β-hydrogen abstraction/elimination pathways (although sometimes slow) offer the potential for achieving the overall catalytic dimerization of the substrates.[2] We report here our observations concerning a new series of titanium aryloxide catalysed coupling reactions that utilize cyclo-1,3-dienes as an important component. The high regio- and stereo-selectivity of these reactions is controlled by facile isomerization and β-hydrogen abstraction within α-vinyl titanacyclopentane intermediates.

The bis(aryloxide) substrates $[(ArO)_2TiCl_2]$ **1** (Scheme 1)[3] can be 'activated' with 2 equiv. of Bu^{n}Li (the Negishi method typically applied to the Group 4 metallocene dichlorides)[4] giving access to the organometallic chemistry of these titanium reagents. Addition of Bu^{n}Li to **1a** in the presence of PMe$_3$ produces the previously reported butene complex **2** (Scheme 1).[5] The addition of Bu^{n}Li (2 equiv.) to a benzene solution of the titanium dichlorides **1a** or **1b** mixed with octa-1,7-diene produces the metallacyclic compounds **3a** and **3b** in good yield (Scheme 1). The crystal structure of **3b** obtained from toluene solution shows a *trans* fusion of the titanacyclopentane and cyclohexane rings.[†] Hydrolysis of these compounds leads exclusively (GC analysis) to *trans*-1,2-dimethylcyclohexane. Compound **3b** is thermally stable up to 80 °C in benzene solution. In the presence of an excess of octa-1,7-diene at 100 °C **3b** will catalyse the formation of 2-methylmethylenecyclohexane **4** at a rate of 1 equiv. (Ti h)$^{-1}$ (Scheme 1).[6] Similarly in the presence of excess styrene, either activation of **1** or addition of **3b** followed by heating at 100 °C results in a slow catalytic dimerization reaction to produce *trans*-1,3-diphenylbut-1-ene **5** as the predominant product.



Scheme 1

In dramatic contrast to these slow coupling reactions, addition of cyclohexa-1,3-diene to a hydrocarbon solution of **3b** results, following a short induction period of a few minutes, in an extremely rapid [> 500 equiv. (Ti h)$^{-1}$ at 25 °C] and high-yield dimerization reaction to produce a single isomer (GC, ^{13}C NMR) of 5-(cyclohexen-3-yl)cyclohexa-1,3-diene **6** (Scheme 1). This non-Diels–Alder product has not previously been obtained by thermal or photochemical dimerization of cyclohexa-1,3-diene.[7] This catalytic transformation can also be achieved by adding cyclohexa-1,3-diene to mixtures of **1** + 2Bu^{n}Li. Following complete dimerization of cyclohexa-1,3-diene into **6**, the titanium catalyst then isomerizes (1,5-shift) **6** into 1-(cyclohexen-3-yl)cyclohexa-1,3-diene **7** and eventually into a 70:30 mixture (GC analysis) of **7** and 2-(cyclohexen-3-yl)cyclohexa-1,3-diene **8** (Scheme 1).

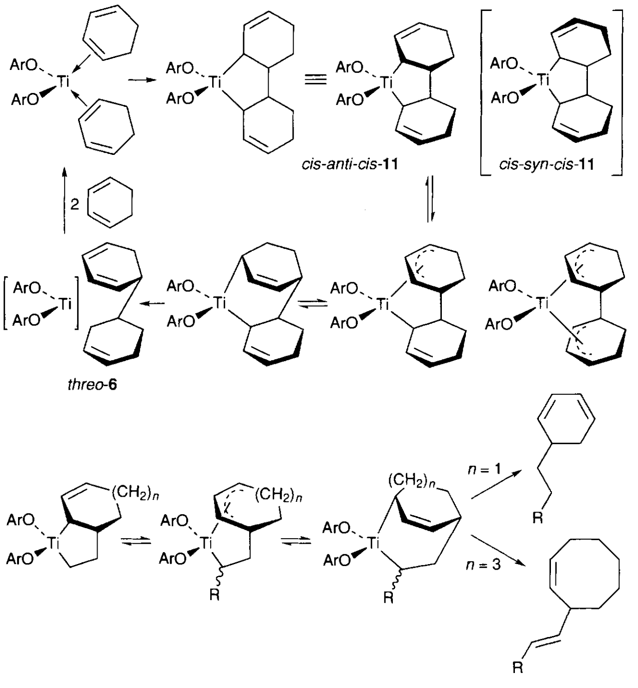
The stereochemistry of **6** was determined by crystal structure analysis of the maleic anhydride adduct **9**.[†] The *threo* configuration for **6** and the regiochemistry of this dimer are consistent with its formation *via* the sequence outlined in Scheme 2. Coupling of 2 equiv. of cyclohexa-1,3-diene at a titanium metal centre can be envisaged to produce six isomeric 9-titanaoctahydrofluorene complexes. The *cis-anti-cis*- and *cis-syn-cis*-3,4,5,6,1a,4a,5a,8a-octahydro derivatives **11** (Scheme 2) have the potential for stabilization *via* formation of π-allyllic interactions. Direct elimination of **7** from either of these intermediates is disallowed as both central β-hydrogens are *trans* to the metal centre. The observed product **6** can be generated by abstraction of a hydrogen atom from the 4-position of one of the rings. This hydrogen can be made accessible to the metal centre *via* a 1,3-shift. The *threo* geometry observed in product **6** indicates that the catalytic coupling reaction proceeds exclusively *via* the *cis-anti-cis* form of **11** (Scheme 2).

The above results strongly indicate that elimination from titanacyclopentane rings is accelerated by the presence of α-vinyl groups. Consistent with this notion is the observation that when a combination of cyclohexa-1,3-diene and vinyltrimethylsilane are heated at 100 °C with **1** + 2Bu^{n}Li mixtures, cross-coupling is observed (along with the formation of **6**) to initially produce 5-(β-trimethylsilylethyl)cyclohexa-1,3-diene

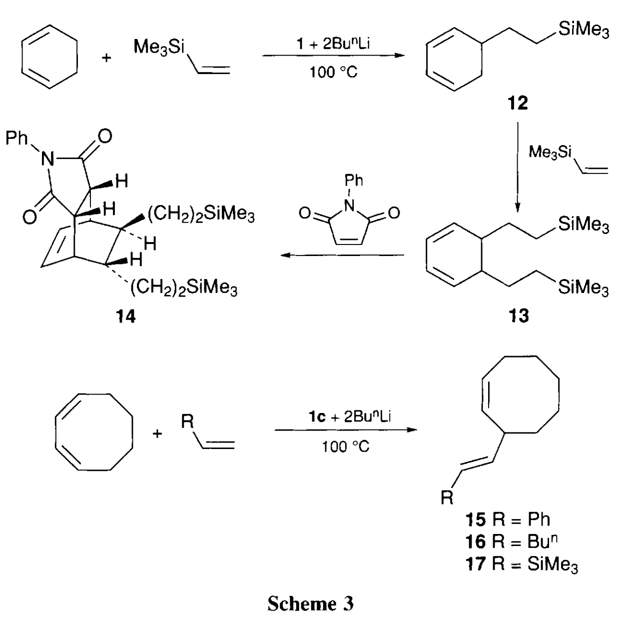
12. In the presence of an excess of vinyltrimethylsilane, **12** is converted to *trans*-5,6-bis(β-trimethylsilylethyl)cyclohexa-1,3-diene **13**. The *trans*-stereochemistry of **13** was confirmed by synthesis of the Diels–Alder adduct **14** (Scheme 3).

In contrast, neither **1a** nor **1b** (activated with 2Bu^{n}Li) will catalyse the cross-coupling of α-alkenes RCH=CH$_2$ (R=Ph, SiMe$_3$, Bu^n) with cycloocta-1,3-diene at 100 °C. The sterically less demanding precursor **1c** will, however, slowly produce products identified as *trans*-3-(β-substituted vinyl)cyclooctenes, **15**–**17** (Scheme 3) along with **5** when styrene is the substrate. The regio- and stereo-chemistry of **15**–**17** are based upon the NMR spectra of samples purified by preparative TLC.

We propose that these cross-coupling reactions initially proceed *via* coupling of the α-alkene with one of the cyclodiene double bonds to produce titanacyclopentane intermediates (Scheme 2). By analogy with the cyclohexa-1,3-diene dimerization above we propose a 1,3-shift of the metal leading to seven-membered metallacycles (Scheme 2). In the case of cyclohexa-1,3-diene, abstraction of a β-hydrogen from the ring leads to conjugated diene **12**, while the non-conjugated products **15**–**17** are generated by abstraction from the alkyl tether originating from the initial α-alkene (Scheme 2). Support for this pathway is provided by carrying out the cross-coupling of [^{2}H$_8$]styrene with cycloocta-1,3-diene. The product, [^{2}H$_8$]**15**, was found to contain almost exclusive deuterium incorporation into the pseudo-equatorial position on C^8. Molecular mechanics calculations on **15** confirm that the vinyl group occupies a pseudo-equatorial site, so that the overall reaction can be described as a *cis*-1,4-hydrovinylation of cycloocta-1,3-diene.[8]



Scheme 2



Scheme 3

The lack of formation of conjugated cycloocta-1,3-diene products may be a consequence of the greater conformational flexibility of the eight-membered carbon ring, making abstraction of the ring hydrogen more difficult.

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Footnote

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† *Crystal data* for **3**·2C$_7$H$_8$; C$_{82}$H$_{72}$O$_2$Ti, at 203 K using Mo-Kα radiation, M = 1137.39, space group $C2/c$, a = 1617.7(6), b = 1677.2(6), c = 2423.8(5) pm, β = 106.56(3)°, U = 6303(7) × 10^6 pm^3, Z = 4, D_c = 1.097 g cm^{-3}; 4196 independent reflections, 4185 with $F_o^2 > 2\sigma(F_o^2)$ used in refinement, R = 0.055, R_w = 0.128. The crystals were found to contain two molecules of toluene per Ti in the unit cell.

For **9**; C$_{16}$H$_{18}$O$_3$, at 223 K using Cu-Kα radiation, M = 258.32, space group $P2_1/c$, a = 2557.9(2), b = 654.7(1), c = 1627.6(3) pm, β = 104.96(1)°, U = 2633(1) × 10^6 pm^3, Z = 8, D_c = 1.303 g cm^{-3}; 5243 independent reflections, 3044 with $I > 3\sigma(I)$ used in refinement, R = 0.045, R_w = 0.053. The unit cell contains both enantiomers of **9**.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/247.

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