Titanacyclobutane Synthesis by Radical Alkylation of Substituted Allyl Complexes. The Use of Electron-Rich Bis(2-piperidinoindenyl)titanocene(III) Complexes to Control Allyl Ligand Reactivity

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Summary: In contrast to reactions of the bis(pentamethylcyclopentadienyl)titanium system, substituted allyl complexes of the electron-rich bis(2-piperidinoindenyl)-titanium(III) template are converted to 2,3-disubstituted titanacyclobutane complexes by free radical alkylation at the allyl central carbon.

The addition of organic radicals to the d^1-permethyltitanocene(III) η^3-allyl and η^3-propargyl complexes produces titanacyclobutane and titanacyclobutene complexes by regioselective central carbon alkylation.[1] Together with subsequent transformation of the titanacycles (e.g., by carbonylation[2]), this reactivity pattern has considerable potential for applications to organic synthesis.

Radical alkylation of the bis(pentamethylcyclopentadienyl)titanium template, however, does not tolerate substitution on the allyl ligand,[3,4] an obvious impediment to the development of new organic reactions. The origin of this limitation is uncertain: little definitive information is available concerning the solution structure and dynamics of d^1-transition metal allyl complexes.[5] Despite this, it is reasonable to propose that allyl substituents will influence the equilibration between η^3- and η^1-coordination modes.[6] In the η^1-coordination mode, overlap of the singly occupied metal $1a_1$ orbital and the allyl π^* orbital is precluded, disrupting the one-electron back-bond that we believe is responsible for controlling the regioselectivity of η^3-allyl alkylation.[1,7] On the basis of this hypothesis, we initiated an investigation into structure/reactivity relationships for radical alkylation of substituted allyl ligands as a function of the metallocene ancillary ligands.

The radical alkylation of titanocene allyl complexes is sensitive to both steric and electronic effects.[8] The sterically open bis(cyclopentadienyl)titanium template performs poorly at best.[8a] Increasing the electron density at the titanium center activates the system toward central carbon radical alkylation: unsubstituted allyl complexes of 1,1′-bis(*tert*-butylcyclopentadienyl)titanium and (cyclopentadienyl)(pentamethylcyclopentadienyl)-titanium both react efficiently with organic radicals to produce the corresponding titanacyclobutane complexes.[3,8a] Despite the minimal steric demands of these ligand systems, however, neither will mediate the radical alkylation of substituted allyl ligands. The corresponding 1,1′-bis(trimethylsilylcyclopentadienyl)titanium template is equally ineffective.[8b]

Given this background, our investigation turned to the evaluation of very strongly electron-donating dialkylamino-substituted titanocene templates.[9] Here we report the first regioselective central carbon alkylations of *substituted* allyl complexes using the bis(2-piperidinoindenyl)titanium(III) template, providing 2,3-disubstituted titanacyclobutane complexes.[10] Also reported is the solid-state structure of bis(2-piperidinoindenyl)-titanium−(η^3-1-phenylallyl) (**2**), which reveals some unexpected structural features.

Bis(2-piperidinoindenyl)titanium(III) chloride (**1**) is prepared by lithiation of 2-piperidinoindene[11] (n-BuLi, Et_2O, −78 °C → RT, 4 h) followed by treatment with

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(10) Complete experimental, spectroscopic, and analytical data are provided as Supporting Information.

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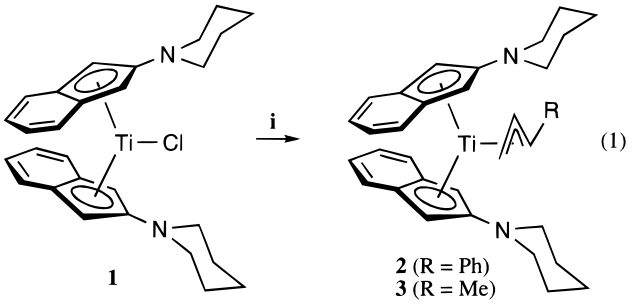
$TiCl_3$•THF in tetrahydrofuran at low temperature.[10] The pale yellow-green complex **1** is isolated in 70% yield as an amorphous solid after precipitation from THF/hexanes. The corresponding cinnamyl (1-phenylallyl) and crotyl (1-methylallyl) complexes **2** and **3** are obtained upon treatment of chloride complex **1** with cinnamyllithium and crotylmagnesium bromide, respectively (eq 1).[10] The dark green cinnamyl complex **2** is



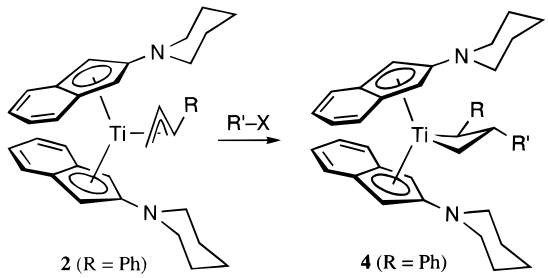
(1)

Conditions: **i**. $PhCH{=}CHCH_2Li$ or $CH_3CH{=}CHCH_2MgBr$, THF, -35 °C→ room temperature, 3h. Yields = 51% (**2**), 45% (**3**).

isolated in analytically pure form in 51% yield by crystallization from cold diethyl ether.[12] The crotyl complex **3** is obtained as a dark brown powder in comparable yield, but the complex resists purification by crystallization. The use of infrared spectroscopy as a probe of allyl hapticity[5,6] in these complexes is precluded by overlapping indenyl and, for complex **2**, phenyl absorptions in the characteristic 1450−1600 cm^{-1} region of the spectrum.

Structural ambiguities aside, both the crotyl and cinnamyl complexes undergo alkylation with unstabilized organic radicals generated by using samarium diiodide.[1,13] Thus, addition of 2-iodopropane, iodocyclohexane, or *tert*-butyl chloride to a solution of cinnamyl complex **2** and SmI_2 in tetrahydrofuran leads to the formation of 3-alkyl-2-phenyltitancyclobutane complexes **4a**−**c** cleanly and in high yield (Table 1).[10,14] The thermally stable red-brown titanacyclobutane complexes were isolated and purified by evaporation of the solvent, trituration with benzene, and crystallization from cold diethyl ether layered with hexanes. NMR spectroscopy revealed that the products are fluxional at room temperature, requiring the data to be acquired at 70 °C, above the fast exchange limit. Titanacyclobutane complexes **4a**−**c** show completely consistent ^1H and ^{13}C NMR spectra at this temperature, with characteristic upfield resonances for the β-hydrogen atom and one of the two α-methylene hydrogen atoms. Selected decoupling experiments, difference NOE measurements, and

Table 1 [a]



Entry	Starting complex	R'	X	Product	Yield[b]
1	**2**	^{i}Pr	I	**4a**	72%
2	**2**	Cy	I	**4b**	80%
3	**2**	^{t}Bu	Cl	**4c**	88%
4	**3**	^{i}Pr	I	**5a**	69%
5	**3**	Cy	I	**5b**	70%
6	**3**	^{t}Bu	Cl	**5c**	36%

[a]Conditions: SmI_2•THF (0.1 M in THF), THF, -35 °C → room temperature, 0.5–3h. [b]Isolated yield.

$^{13}C-^1H$ heteronuclear correlated spectroscopy confirm the titanacyclobutane structure and support a tentative assignment of the trans stereochemistry.[10,15] At the low-temperature limit (−40 °C), complex **4c** exists as a 2:1 mixture of conformational isomers, presumably reflecting restricted rotation of the ancillary ligands.

Central carbon alkylation is also observed upon treatment of crotyl complex **3** with unstabilized organic radicals (Table 1).[10] Titanacyclobutane complexes **5a**−**c**, however, are thermally sensitive in solution, decomposing slowly at room temperature to yield intractable material, 2-piperidinoindene, and a terminal olefin.[16] Nonetheless, the initial reaction products are formed very cleanly, giving ^1H NMR spectroscopic data com-

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(12) Experimental procedure: complex **2**. To a cold (−35 °C) solution of bis(2′-piperidinoindenyl)titanium chloride **1** (1.73 g, 3.61 mmol) in THF (10 mL) under nitrogen was added cinnamyllithium (0.44 g in 2 mL of THF, cooled to −35 °C). After 0.75 h, the reaction mixture was allowed to warm to room temperature and stir 2 h. The solvent was removed in vacuo, and the dark green residue was triturated with benzene. The resulting solution was filtered through Celite. Removal of the benzene gave a green residue, which was crystallized from diethyl ether to give dark green cubes (1.03 g, 51%). Anal. Calcd for $C_{37}H_{41}TiN_2$: C, 79.13; H, 7.36; N, 4.99. Found: C, 78.79; H, 7.51; N, 4.94.

(13) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.

(14) Experimental procedure: complex **4a**. To a cold (−35 °C) solution of bis(2′-piperidinoindenyl)titanium(cinnamyl) **2** (31.0 mg, 0.0552 mmol) and SmI_2 (552 μL, 0.1 M in THF) in THF (10 mL) under nitrogen was added 2-iodopropane (1 equiv) and the reaction mixture was allowed to warm to room temperature. After stirring for 0.75 h, the solvent was removed in vacuo, and the resulting red-brown residue was triturated with benzene. The solution was filtered through Celite and, after removal of the solvent, crystallized from diethyl ether layered with hexane at −35 °C, yielding dark red-brown needles (24.0 mg, 72%). The analytical sample proved to be an etherate. Selected spectroscopic and analytical data:[10] ^1H NMR (400 MHz, C_6D_6, 70 °C, nonaromatic resonances only, pip = piperidine): δ 2.91 (m, 3H, pip) 2.74 (m, 2H, pip), 2.61 (t, J = 10.0 Hz, 1H, α-CH_2), 2.49 (m, 1H, pip), 2.48 (d, J = 11.6 Hz, 1H, α-CHPh), 1.54 (m, 1H, CHMe$_2$), 1.35 (m, 14H, pip), 1.04 (d, J = 6.6 Hz, 3H, CHMe_2), 0.95 (d, J = 6.6 Hz, 3H, CHMe_2), 0.84 (m, 1H, β-CH), 0.04 (t, J = 10.0 Hz, 1H, α-CH_2). Anal. Calcd for $C_{40}H_{48}TiN_2$•$(C_2H_5)_2O$: C, 77.85; H, 8.61; N, 4.13. Found: C, 77.74; H, 8.24; N, 4.57.

(15) The trans stereochemistry is that expected from exo radical alkylation of the syn-substituted allyl complex, the latter determined for cinnamyl complex **2** by X-ray crystallography. For titanacyclobutane complex **4a**, the stereochemical assignment is supported by difference NOE spectroscopy: irradiation of the β-hydrogen resonance leads to strong enhancement (7%) of the ortho-phenyl hydrogen resonance,[10] a result most consistent with placing the phenyl substituent cis to the β-hydrogen and trans to the isopropyl group).

(16) The decomposition of complex **5a** gives 3,4-dimethyl-1-pentene, as identified by ^1H NMR spectroscopy and GC−MS. The organic decomposition products presumably arise from β-hydride elimination at the α-methyl substituent, followed by reductive elimination. In contrast, cinnamyl-derived complex **4c** decomposes by [2 + 2] cycloreversion at elevated temperatures (<80 °C), giving 3,3-dimethylbutene as the exclusive organic product.

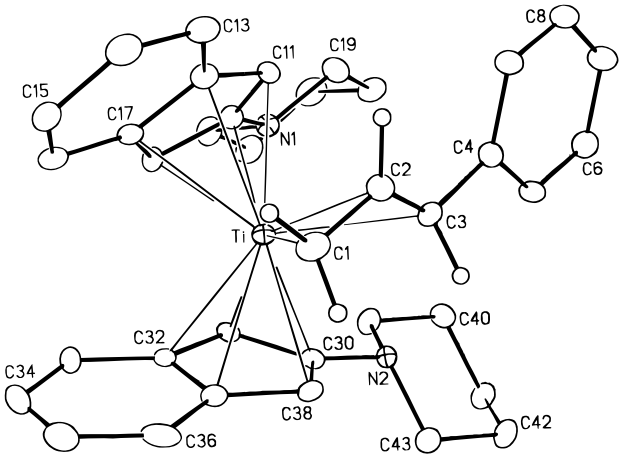

Figure 1. ORTEP diagram of complex **2**. Selected bond distances (Å): Ti−C1 = 2.318(6), Ti−C2 = 2.351(6), Ti−C3 = 2.448(6), C1−C2 = 1.387(8), C2−C3 = 1.381(8), C3−C4 = 1.480(8), N1−C10 = 1.416(7), N1−C19 = 1.453(7), N1−C23 = 1.463(7), N2−C30 = 1.409(7), N2−C39 = 1.462(7), N2−C43 = 1.469(7).

pletely consistent with the assignment as 2,3-disubstituted titanacyclobutane complexes.[17] For both the cinnamyl and crotyl complexes, attempted alkylation using SmI_2 and stabilized radical precursors (benzyl chloride, allyl bromide) provides only organic radical-derived products and paramagnetic material(s).

The short reaction times and low temperatures observed for alkylation of both cinnamyl and crotyl complexes **2** and **3** stand in stark contrast to the elevated temperatures required for alkylation of $(C_5Me_5)_2Ti(\eta^3\text{-allyl})$ with unstabilized radical precursors.[1a] This suggests that the initial radical generation is mediated by the reaction of the haloalkane with the electron-rich titanium(III) complex rather than with SmI_2, leading to a 1:1 mixture of the observed titanacyclobutane and an allyltitanium(IV) halide intermediate. The SmI_2 reagent then functions more slowly to abstract halogen radical from this latter intermediate, regenerating the reactive allyltitanium(III).[1b]

To gain insight into the function of the ancillary ligands, the structure of cinnamyl complex **2** was determined by X-ray crystallography (Figure 1).[10,18] In the crystal, the cinnamyl ligand adopts the anticipated η^3-coordination, syn stereochemistry, pyramidalized allyl terminal carbons, and unsymmetrical coordination to the metal.[19] Along with the expected longer bond to the substituted carbon, the complex has the shortest reported Ti−C1 and Ti−C2 bonds, which *may* reflect greater d → π* back-donation from the d[1]-metal center. The shortened C3−C4 bond and the coplanarity of the phenyl π-system and allyl backbone suggest the presence of substantial conjugative stabilization. Presumably in response to the steric demands of the phenyl substituent, the ancillary ligands adopt a unique[9] syn spatial orientation, placing the piperidine rings on the same side of the titanocene wedge. One of the indenyl rings is positioned *over* the unsubstituted end of the cinnamyl ligand, rotating the piperidine substituent back to provide an unencumbered space for the phenyl substituent.

The most compelling report on the state of the 17-electron Ti(III) center is provided by the piperidinoindenyl ligands. The amine functionality is pyramidal rather than planar, and as a consequence of this hybridization, the indene carbon−nitrogen bonds at 1.416(7) and 1.409(7) Å are only minimally contracted from normal C−N single-bond lengths. While this observation must be interpreted cautiously,[20] also observed are significant differences between the structures of the two ancillary ligands: the nitrogen atoms are pyramidalized to different extents[21] and the overlap of each nitrogen lone pair with its respective indene π-system differs markedly, with greater pyramidalization and much less n/π overlap evident in the "bottom" aminoindenyl ligand.[22] Taken together, these data suggest that the titanium center is electronically saturated and draws considerably less electron density from the piperidine reservoirs than is available for donation.

The aminoindenyl ligands, however, clearly provide sufficient electron density to promote radical alkylation and control the reactivity of substituted allyl complexes. It is attractive to attribute this control to a stronger interaction between the half-occupied metal orbital and the π* orbital of the allyl ligand, but this hypothesis requires further substantiation.

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Supporting Information Available: Experimental procedures and spectroscopic data for all new compounds; details of the crystal structure determination, diagrams, and bond lengths and angles for complex **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) Selected spectroscopic data, complex **5a**.[10] ^{1}H NMR (300 MHz, C_6D_6, titanacyclobutane only): δ 2.53 (t, J = 10.0 Hz, 1H, α-CH_2), 1.96 (m, 1H, CHMe$_2$), 1.86 (d, J = 6.4 Hz, 3H, α-CHMe_2, 1.70 (dq, J = 12.0, 6.4 Hz, 1H, α-CHMe, 1.18 (d, J = 6.6 Hz, 3H, CHMe_2), 1.08 (d, J = 6.6 Hz, 3H, CHMe_2), 0.33 (t, J = 10.0 Hz, 1H, α-CH_2), −0.24 (m, 1H, β-CH).

(18) Crystal data for complex **2** ($C_{37}H_{41}N_2Ti$, −60 °C): monoclinic, $P2_1/c$, a = 16.688(2) Å, b = 15.369(2) Å, c = 12.160(2) Å, β = 109.285(10)°, V = 2943.7(7) Å^3, Z = 4, ρ_{calcd} = 1.267 g cm^{-1}, μ = 0.319 mm^{-1}, R1 = 0.0868, wR2 = 0.1382 ($F_o^2 > 2\sigma(F_o^2)$).[10]

(19) Other structurally characterized titanocene allyl complexes: (a) Helmholdt, R. B.; Jellinek, F.; Martin, H. A.; Vos, A. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1263. (b) Chen, J.; Kai, Y.; Kasai, N.; Yasuda, H.; Yamamoto, H.; Nakamura, A. *J. Organomet. Chem.* **1991**, *407*, 191.

(20) Planar nitrogen and shortened nitrogen−carbon bonds (ca. 1.32−1.38 Å) are common to structurally characterized Ti(IV) and Zr(IV) bis(amino)metallocene complexes.[9] Nonetheless, pyramidal nitrogen and longer C−N bond distances are observed in two *ansa*-bridged bis(aminoindenyl) Zr(IV) complexes, in which the hybridization is attributed to specific steric interactions with the ligand bridges.[9c,d]

(21) Torsion angles (deg): C19−N1−C10−C11 = −14.6(9), C19−N1−C10−C18 = 171.8(6), C23−N1−C10−C11 = −150.2(6), C23−N1−C10−C18 = 36.2(9); C39−N2−C30−C31 = 2.8(8), C39−N2−C30−C38 = −177.6(6), C43−N2−C30−C31 = −124.9(6), C43−N2−C30−C38 = 54.7(7).

(22) Maximum overlap occurs when the dihedral angle (θ_d) between the nitrogen lone pair orbital and the indene π-system is 0°. In complex **2**, the less pyramidal "top" indenyl ligand is apparently more strongly donating ($\theta_d \approx 16°$) than is the more pyramidal "bottom" ligand ($\theta_d \approx 29°$).[10] While such distortions can certainly arise from intermolecular crystal packing forces, there is nothing obvious in the extended structure to suggest that this is the case.