Comments on Inorganic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455155

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To cite this Article Ladipo, Folami T.(2006) 'SYNTHESIS AND REACTIVITY OF WELL-CHARACTERIZED LOW-VALENT TITANIUM SPECIES', Comments on Inorganic Chemistry, 27: 3, 73 — 102
To link to this Article: DOI: 10.1080/02603590600767138
URL: http://dx.doi.org/10.1080/02603590600767138

Comments on Inorganic Chemistry, 27: 73–102, 2006

ISSN: 0260-3594 print
DOI: 10.1080/02603590600767138

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SYNTHESIS AND REACTIVITY OF WELL-CHARACTERIZED LOW-VALENT TITANIUM SPECIES

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This account mainly describes results from studies in our laboratory of the reactivity of well-characterized titanium(II) species, supported by chelating bis(aryloxide) ligation, with unsaturated organic compounds, including alkynes, aldehydes, and ketones. Taken together with reported chemistry of related low-valent titanium complexes, our results serve to advance current understanding of the nature of the active species and mechanism(s) of alkyne cyclotrimerization, pinacol coupling, and McMurry reactions.

INTRODUCTION

Low-valent titanium species are often employed to promote reductive coupling reactions of unsaturated organic substrates, such as aldehydes, ketones, alkynes, alkenes, acylsilanes, and imines.[1–30] A molecular level interpretation of the results of low-valent titanium-mediated reductive coupling reactions is frequently difficult because titanium reductants are usually generated in situ and present in heterogeneous phase, hence their oxidation state(s), structure(s), and reactivity are often only vaguely characterized. Development of soluble, well-characterized, and reactive low-valent titanium complexes or synthetic equivalents that have diverse ligand environments would facilitate significant improvement in

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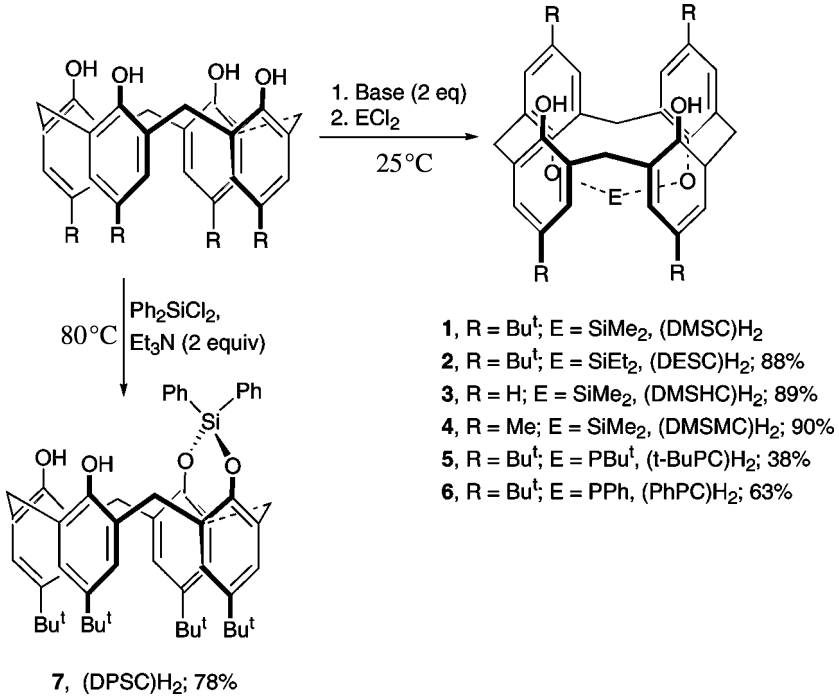
mechanistic understanding and selectivity of titanium-mediated reductive coupling reactions since chemical reactivity of transition metals can be greatly influenced by modification of steric and electronic properties of ancillary ligands. However, with the exception of low-valent metallocenes and related organometallics of the group 4 metals,[31–51] well-characterized monomeric low-valent titanium complexes incorporating non-cyclopentadienyl ligand arrays are rare.[52–80] Consequently, ancillary ligand effects on chemical reactivity of low-valent titanium remain poorly understood.

Over the last several years, we have been investigating the synthesis and reactivity of well-characterized Ti(II) complexes and/or synthetic equivalents supported by chelating bis(aryloxide) ligation. Ti(II) is of interest because it is a strong π-donor and Ti(II) species can be stabilized and sometimes isolated by use of π-acceptor ligands, such as CO, $P(OEt)_3$, alkene, alkyne, or arene.[14–18,77–80] Aryloxide (or alkoxide) ligands are attractive since they can be viewed as isolobal to Cp^-; they are theoretically capable of $\sigma + 2\pi$ (6-electron) donation. However, aryloxide (ArO^-) ligands are more flexible π-donors than Cp^- since donation of six electrons from the oxygen donor is difficult. Thus, aryloxide-based metal centers provide more opportunity for ligand binding and are capable of forming higher coordination number complexes than corresponding Cp-based systems. Hence important differences exist between the chemistry of $(ArO)_2Ti$ and Cp_2Ti fragments.[81,82] Calix[4]arene-derived chelating bis(aryloxide) ligands, such as DMSC (dianion of 1,2-alternate dimethylsilyl-bridged *p-tert*-butylcalix[4]arene (**1**), Scheme 1), offer the possibility to sterically define reaction sites at the metal center. When 1,2-alternate conformation of the calix[4]arene is secured by bridging proximal phenolic oxygen atoms, a pair of phenyl rings and the attached pair of substituent groups essentially project over one of the two remaining "unbridged" phenolic oxygen atoms. As a result, unique *endo*- and *exo* stereochemical environments (inside and outside the calixarene cavity, respectively) are established at the titanium center upon coordination of the ligand (Scheme 2).

This review mainly describes progress made in our laboratory in developing storable and well-defined sources of Ti(II) for use as catalysts and/or stoichiometric reductants in organic synthesis, and for mechanistic modeling of important carbon–carbon bond forming transformations, including alkyne cyclotrimerization, pinacol-, and McMurry coupling reactions. A discussion of the chemistry of well-characterized Ti(II)

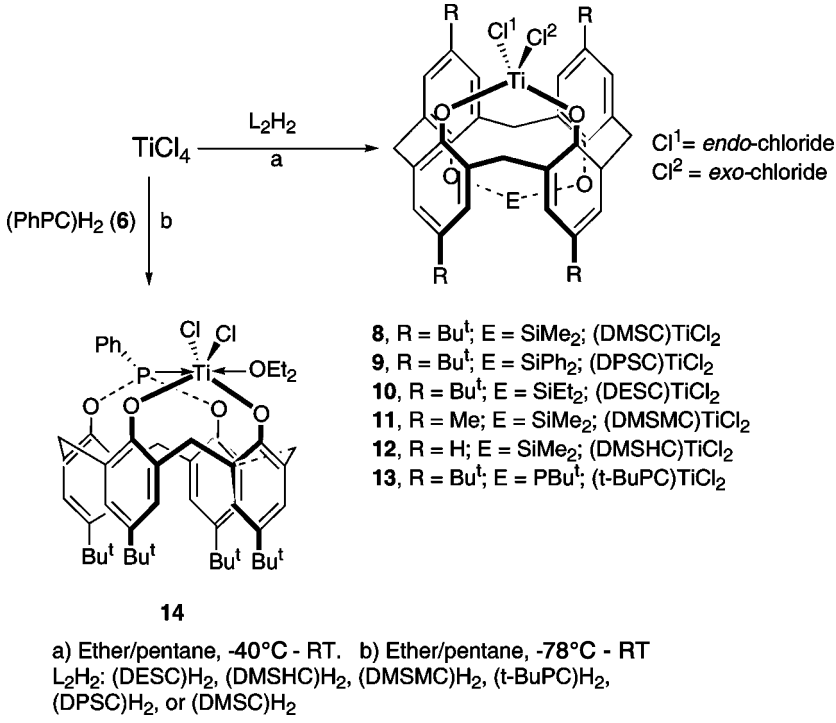


Scheme 1.

species is presented, which serves to inform current understanding of the mechanisms of low-valent titanium-mediated reductive coupling reactions.

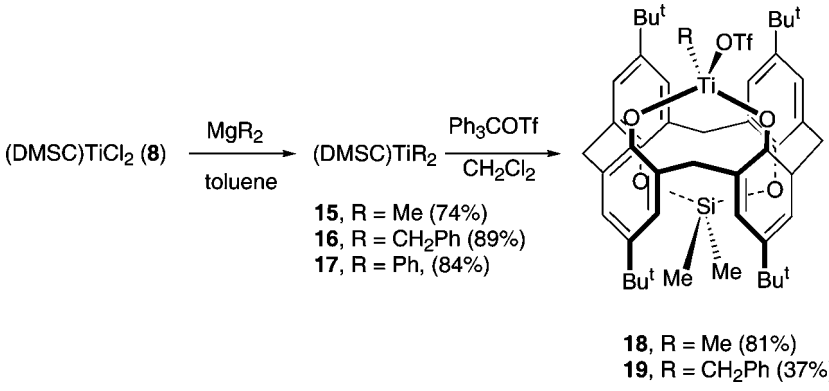
CALIXARENE LIGAND-DIRECTED REACTIVITY

As previously mentioned, 1,2-alternate calix[4]arene-derived chelating bis(aryloxide) ligands afford the opportunity to sterically differentiate reaction sites at the metal center. We have prepared silyl- or phosphinyl-bridged calix[4]arene compounds **2**–**7**[83,84] (Scheme 1) by modification of the method reported by Lattman et al. for synthesis of $(DMSC)H_2$ (**1**);[85] **2**–**6** adopt 1,2-alternate conformation in solution while **7** exists in cone conformation. C_s-symmetric titanium(IV) dichlorides **8**–**14**, supported by calix[4]arene-derived chelating bis(aryloxide) ligands, were readily obtained in high yield from reaction of $TiCl_4$ with **1**–**7** at low to ambient temperatures (Scheme 2).[30,83,84] In solution, **8**–**13** exist in 1,2-alternate conformation while $[(PhPC)TiCl_2]$ (**14**) adopts the cone



Scheme 2.

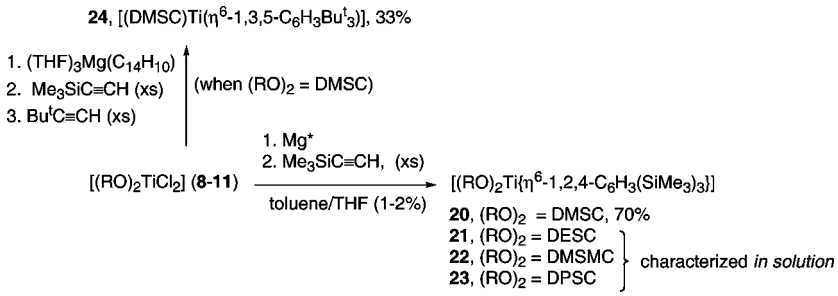
conformation; the compounds are conformationally stable up to at least 348 K (by variable temperature ^{1}H NMR). X-ray crystallographic characterization of the molecular structure of [(DPSC)$TiCl_2$] (**9**) confirmed *endo*- and *exo*-coordination environments (inside and outside the calixarene cavity, respectively) for the titanium-bound chlorides, and that the steric environment around the *endo* chloride is more crowded than that around the *exo* chloride.[84] Steric differentiation of the *endo* and *exo* coordination sites was further apparent from the reactivity of Ti(IV) dialkyls [(DMSC)TiR_2] (**15**, R = Me; **16**, R = CH_2Ph; and **17**, R = Ph), obtained via reaction of [DMSC)$TiCl_2$] (**8**) with appropriate dialkylmagnesium reagents (Scheme 3). Treatment of **15** and **16** with Ph_3COTf (OTf = $CF_3SO_3^-$) in 1:1 molar ratio furnished corresponding alkyltriflato complexes [(DMSC)Ti(OTf)Me] (**18**) and [(DMSC)Ti(OTf)(CH_2Ph)] (**19**), formed by exclusive abstraction of the less hindered *exo*-alkyl group (Scheme 3).[83]



Scheme 3.

SYNTHESIS AND CHARACTERIZATION OF TITANANORBORNADIENES

Both arene and aryloxide ligands can behave as variable electron donors and thereby allow different molecular geometries to be stabilized. An arene can stabilize an electron-rich metal center by accepting metal dπ-electron density into its π^* orbitals while an electrophilic metal can be stabilized via donation of arene π-electron density to the metal. In addition, open coordination site(s) can be generated at the metal center and reactivity achieved through a change in hapticity ($\eta^6 \rightarrow \eta^4 \rightarrow \eta^2$) of the arene ligand.[77–80,86–92] The majority of arene complexes of low-valent titanium that have been described are of the types Ti(η^6-arene)$_2$[93–95] and Ti(II)-η^6-arene.[96–102] The typical synthetic routes involve reduction of tervalent or tetravalent titanium: arene anion reduction of $LTiCl_3$ ($L = C_5Me_5$, $Bu^tSi(CH_2PMe_2)_3$, Cl, etc.) in THF produces corresponding arene complexes in low oxidation states (0 to –2)[103–112] while the Fischer-Hafner method, which involves reduction of TiX_4 by Al metal in the presence of AlX_3 and arene, usually yields Ti(II) complexes of the type $[(\eta^6\text{–arene})Ti\{(\mu\text{–}X)_2AlX_2\}_2]$.[97–101] We found that $[(RO)_2TiCl_2]$ complexes **(8–11)** react with activated magnesium (Mg*) in the presence of ≥ 3 equivalents of $Me_3SiC{\equiv}CH$ to furnish titananorbornadienes $[(RO)_2Ti\{\eta^6\text{-}1,2,4\text{–}C_6H_3(SiMe_3)_3\}]$ **(20–23, Scheme 4)**.[80,84] The reduction of **8–11** was investigated for a range of reducing agents (such as Na, $LiAlH_4$, activated Zn, activated Ca, Mg*, and C_8K) in the presence of an excess of alkyne (including $Me_3SiC{\equiv}CH$, *p*-$MeC_6H_4C{\equiv}CH$,



Scheme 4.

$Bu^tC{\equiv}CH$, MeC≡CMe, and PhC≡CMe) at different temperatures in a variety of solvents, such as toluene, benzene, THF, and 1,4-dioxane. When the reductant was Mg*, the alkyne was $Me_3SiC{\equiv}CH$, and the reaction was conducted at room temperature in toluene or benzene containing 1–2% by volume of THF, black mixtures containing **20–23** were produced in amounts observable by ^1H NMR.[84] Whereas $[(DMSC)Ti\{\eta^6\text{-}1,2,4\text{-}C_6H_3(SiMe_3)_3\}]$ **(20)** is routinely isolated as a diamagnetic yellow solid in greater than 70% yield from the black reaction mixture, **21–23** were characterized only in solution by ^1H NMR. Isolation of **21–23** has so far been hampered by low conversion, and comparable solubility of paramagnetic calix[4]arene-containing side-products, which are most likely Ti−Mg Mg species (*vide infra*).

Fast reduction of $[(RO)_2TiCl_2]$ compounds to give "$(RO)_2Ti(\eta^2$-alkyne)" species is vital to achieving moderate to high conversion of **8–11** into corresponding titananorbornadienes since cyclotrimerization of MeSiC≡CH is catalytic. Bogdanovic et al.[113,114] showed that reduction of $TiCl_3$ or $TiCl_4$ with excess Mg in THF at ambient temperature produced black solutions containing soluble paramagnetic Ti−Mg species, $TiMgCl_2(THF)_x$ **(25)** and $[Ti(MgCl)_2(THF)_x]_y$ **(26)**, with formal oxidation states of 0 and –2, respectively. Apparently, formation of paramagnetic calixarene-containing Ti−Mg species similar to **25** and **26** is competitive with production of titananorbornadiene during reaction of **8–11** with Mg* and excess $Me_3SiC{\equiv}CH$ in toluene or C_6D_6 containing 1–2% by volume of THF; after recrystallization, black solids obtained from reactions of **9–11** showed only trace amounts of **21–23** in their respective ^1H NMR spectrum yet intense resonances characteristic of $(DESC)H_2$, $(DMSMC)H_2$, or $(DPSC)H_2$ were observed upon

exposure of C_6D_6 solutions of the black solids to moist air. This result suggests that the black solutions contained paramagnetic species ligated by calixarene-derived bis(aryloxide) ligand.

Single-crystal X-ray crystallographic characterization of the molecular structure of **20** (Figure 1) revealed substantial folding of the η^6-arene with a dihedral angle of 29.7°, supporting strong contribution to the structure by the highly reduced cyclohexadiene dianion resonance form and loss of aromatic character; two of the $Ti-C_{arene}$ bond distances of **20** are significantly shorter (~2.15 Å) than the other four (2.32–2.42 Å) and the η^6-arene moiety has two short (1.36–1.38 Å) and four long (1.45–1.49 Å) C–C bond distances.[80] A related Ti(II)-η^6-toluene

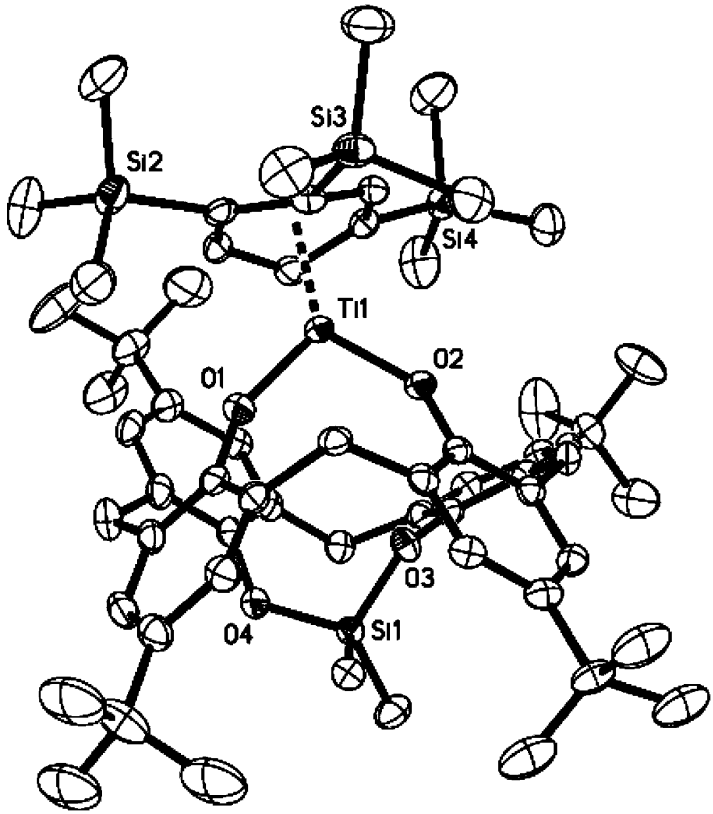


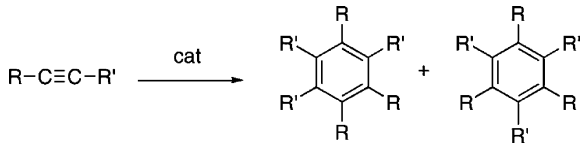
Figure 1. Molecular structure of [(DMSC)Ti{η^6-1,2,4-$C_6H_3(SiMe_3)_3$}] (**20**), (50% probability ellipsoids).

complex [(L^{Me})Ti(η^6-PhCH$_3$)] (**27**, L^{Me} = a cyclohexane-linked bis-(amidinate) ligand) similarly contained a puckered arene moiety with a dihedral angle of 20.0°.[115] In comparison, Ti(II) complexes of the type [(η^6-arene)Ti$\{(\mu - X)_2AlX_2\}_2$] generally show nearly planar arene rings with Ti–C bond distances of $\sim$2.50 Å.[96–101] The stereochemical environment about titanium in **20** is best described as pseudo-tetrahedral and one of the tetrahedral faces is sterically protected by the highly distorted 1,2-alternate DMSC ligand. Reaction of [(DMSC)Ti $\{\eta^6$-1,2,4–$C_6H_3(SiMe_3)_3\}$] (**20**) with $Bu^tC{\equiv}CH$ ($\geq$3 equiv) furnished [(DMSC)Ti$\{\eta^6$-1,3,5 – $C_6H_3Bu^t_3\}$] (**24**) as a diamagnetic orange solid. In contrast to C_1-symmetrical **20**–**23**, ^{1}H and ^{13}C NMR studies established that **24** is C_s-symmetric in solution with a symmetrically substituted η^6-arene and a 1,2-alternate calix[4]arene ligand. The formation of η^6-1,2,4–$C_6H_3Bu^t_3$ is probably disfavored as a result of result of the greater steric repulsion between Bu^t groups.

ALKYNE CYCLOTRIMERIZATION CATALYSIS

The synthesis of arenes in a highly regiocontrolled manner is very attractive because arenes are important building blocks in organic synthesis. Several of the more effective methods for assembling complex organic molecules involve transition metal-catalyzed cycloaddition[16–20] but cyclotrimerization ([2 + 2 + 2] cycloaddition) of alkynes to yield substituted arenes rarely proceeds with high regioselectivity[19,80,116,117] although many transition metals catalyze the reaction.[118–133] Both [(DMSC)Ti$\{\eta^6$-1,2,4–$C_6H_3(SiMe_3)_3\}$] (**20**) and [(DMSC)Ti$\{\eta^6$-1,3,5–$C_6H_3Bu^t_3\}$] (**24**) are active catalysts for cyclotrimerization of terminal alkynes under mild conditions and produce 1,2,4-substituted arenes with high regioselectivity (usually $\geq$95%, Table 1, entries 1–3);[80] aliphatic and aromatic terminal alkynes are usually cyclotrimerized in rapid and exothermic fashion, and terminal diynes undergo cyclotrimerization faster than monoynes. Since **20** catalyzed cyclotrimerization of $Me_3SiC{\equiv}CH$ at a convenient rate over a broad temperature range to furnish 1,2,–$C_6H_3(SiMe_3)_3$ and 1,3,5–$C_6H_3(SiMe_3)_3$ in 99:1 ratio, the reaction was monitored by ^{1}H NMR spectroscopy, which revealed no decrease in intensity of the signals for [(DMSC)Ti$\{\eta^6$-1,2,4–C_6H_3-$(SiMe_3)_3\}$] (**20**) over the course of the reaction and established **20** as the resting state of the catalyst.[80] Kinetic analysis of the reaction under pseudo-first order conditions revealed first-order dependence on both

Table 1. Catalytic [2 + 2 + 2] cycloaddition of alkynes



#	Alkyne	Catalyst	% Isomer[b] 1,2,4-	1,3,5-
1	$Me_3SiC{\equiv}CH$	**20** or **24**	99	1
2	$CH_3(CH_2)_2C{\equiv}CH$	**20** or **24**	96	4
3	$PhC{\equiv}CH$	**20** or **24**	99	1
4	*p*-$MeC_6H_4C{\equiv}CH$	**20**	99	1
5	1,6-Heptadiyne	**20**	100	
6	$(HC{\equiv}CCH_2)_2O$	**20**	100	
7	$(HC{\equiv}CCH_2)_2S$	**20**	100	
8	$HC{\equiv}CCH_2NMe_2$	**20**	90	10
9	$HC{\equiv}CCH_2OSiMe_3$	**20**	>95	<5
11	$Me_3SiC{\equiv}CH$[c]	**20**	95	5
12	*p*-$MeC_6H_4C{\equiv}CH$[a]	**9**/Mg*	92	8
13	$PhC{\equiv}CH$[d]	**9**/Mg*	>92	<8[d]
14	$PhC{\equiv}CMe$[d]	**11**/Mg*	72	28
15	$PhC{\equiv}CMe$[e]	**9**/Mg*	90	10
16	$PhC{\equiv}CEt$[d]	**11**/Mg*	69	31
17	$PhC{\equiv}CEt$[d]	**9**/Mg*	68	32
18	$MeC{\equiv}CEt$[e]	**9**/Mg*	~75	~25
19	$MeC{\equiv}CEt$[d]	**11**/Mg*	75	25

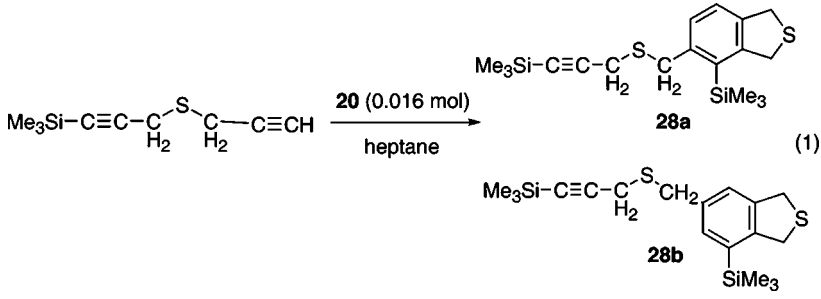
[a]In C_6D_6 or toluene at 25°C; [b]ratios determined from GC-MS and ^1H NMR data; [c]in C_6D_6 in the presence of THF at 25°C; [d]in C_6D_6 containing 1–2% THF at 70–75°C; [e]$C_{14}H_{10}Mg(THF)_3$ was first decomposed in C_6D_6 at 80°C to Mg* and anthracene. All other reactants were added after cooling to ambient temperature.

the concentrations of **20** and $Me_3SiC{\equiv}CH$, confirming that the rate-limiting step is the displacement of 1,2,4−$C_6H_3(SiMe_3)_3$ from **20**. Analysis of the kinetic data gave activation parameters, $\Delta H^{\ddagger} = 14$ kcal/mol, and $\Delta S^{\ddagger} = -11$ cal/mol K, consistent with an associative mechanism.[80]

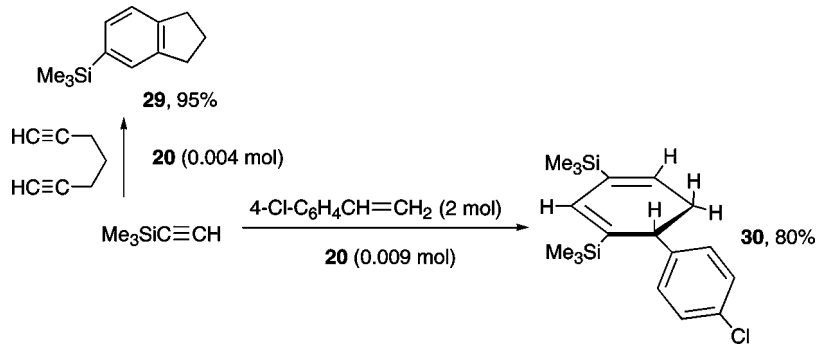
The rate and regioselectivity of alkyne cyclotrimerization is influenced by steric requirements of both the alkyne and the titananorbornadiene. While modest variation in substituent size of terminal alkynes did not adversely affect regioselectivity (Table 1, entries 1–11), bulky terminal alkynes displayed sluggish or no reaction with **20** or **24**. Thus,

reaction of **20** with excess of $Bu^tC{\equiv}CH$ furnished **24** in moderate yield (*vide supra*) but no evidence of catalytic cyclotrimerization of $Bu^tC{\equiv}CH$ was observed even after 14 days at 25°C. Moreover, no reaction occurred between **20** and $Pr^i_3SiC{\equiv}CH$ over several hours at 80°C. That **20** did not react with bulky terminal alkynes such as $Pr^i_3SiC{\equiv}CH$ may be explained by the inability of the substrates to displace the η^6-arene moiety. In agreement with the preceding explanation, [2 + 2 + 2] cycloaddition of $Bu^tC{\equiv}CH$ is not catalyzed by $[(DMSC)Ti\{\eta^6\text{-}1,3,5\text{-}C_6H_3Bu^t_3\}]$ **(24)** but less bulky terminal alkynes, such as phenylacetylene and 1-pentyne, are catalytically cyclotrimerized with identical regioselectivities as **20** (Table 1, entries 2 and 3);[80] **24** apparently reacts with these substrates to generate the corresponding η^6-arene complex, which carries out the catalysis.

Internal alkynes are rarely cyclotrimerized by **20**, even at elevated temperatures. Neither $EtC{\equiv}CEt$ nor $Me_3SiC{\equiv}CMe$ reacted with **20** at 80°C in benzene while 94% conversion of 65 equivalents of 2-butyne into C_6Me_6 required 93 h at 25°C and only 79% of **20** was consumed. In the latter transformation, $MeC{\equiv}CMe$ evidently reacts much slower with **20** than with the presumed titananorbornadiene intermediate "$(DMSC)Ti(\eta^6\text{-}1,2,4\text{-}C_6Me_6)$." $[(DMSC)Ti\{\eta^6\text{-}1,2,4\text{-}C_6H_3(SiMe_3)_3\}]$ **(20)** displayed modest functional group tolerance, allowing catalytic cyclotrimerization of propargylic compounds bearing heteroatoms $HC{\equiv}CCH_2R$ ($R = NMe_2$, $OSiMe_3$, $SCH_2C{\equiv}CH$, $OCH_2C{\equiv}CH$, or $SCH_2C{\equiv}CSiMe_3$) to be accomplished with high regioselectivity (Table 3); reaction of **20** with $Me_3SiC{\equiv}CCH_2SCH_2C{\equiv}CH$ in heptane afforded 1,3-dihydrobenzo[c]thiophene derivative **28** as 1,2,3,4- and 1,2,3,5-substitutional isomers (**28a** and **28b**, respectively; equation 1) in 91:9 ratio and in 91% yield.[80] Cross coupling reaction of



1,6-heptadiyne with $Me_3SiC{\equiv}CH$ was also catalyzed by **20** at 25°C in benzene to yield 5-trimethylsilylindane **29** in near quantitative yield



Scheme 5.

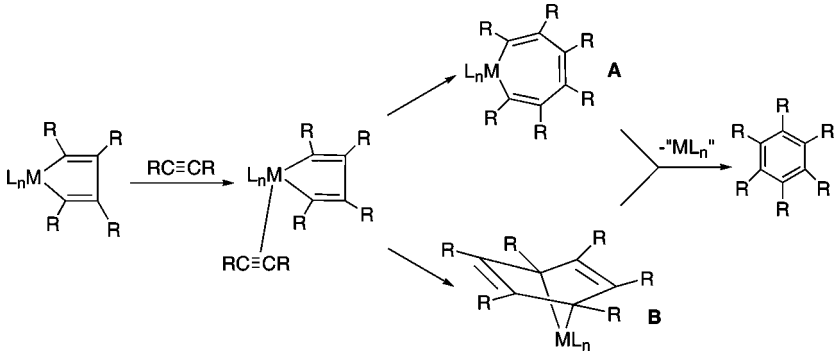
(Scheme 5). However, cross coupling cycloaddition of $Me_3SiC{\equiv}CH$ with a variety of terminal alkynes generally produced a mixture of products; similar reaction of $Me_3SiC{\equiv}CH$ with alkenes catalyzed by **20** either produced a mixture of products (for example, when the alkene was ethylene) or resulted only in cyclotrimerization of $Me_3SiC{\equiv}CH$ (in the case of bulky terminal or disubstituted olefins, such as $Me_3SiCH{=}CH_2$, $Ph_2C{=}CH_2$, $Cl_2C{=}CCl_2$, and $H_2C{=}Cme{-}CMe{=}CH_2$). Nonetheless, **20** catalyzed [2 + 2 + 2] cycloaddition of 4-chlorostyrene with $Me_3SiC{\equiv}CH$ to afford 1-[2,4-bis(trimethylsilyl)-cyclohexa-2,4-dienyl]-4-chlorobenzene 30 as the major product (80%, GC-MS, Scheme 5); minor isomeric cyclohexadienyl products (~8%, GC-MS) and $1,2,4{-}C_6H_3(SiMe_3)_3$(~12%) were also formed.[80]

Calix[4]arene-derived bis(aryloxide) ligands can be modified to enhance the efficiency of catalytic cyclotrimerization of internal alkynes. Reactions of $[(DPSC)TiCl_2]$ (**9**) or $[(DMSMC)TiCl_2]$ (11) with Mg^* in the presence of 10 equivalents of PhC≡CMe, PhC≡CEt, MeC≡CMe, EtC≡CEt, or EtC≡CMe at 70–75°C in C_6D_6 usually proceed to completion in <24 h (Table 1, entries 12–19).[84] Cyclotrimerization of PhC≡CMe was more facile and selective when the calixarene ligand was DPSC versus DMSMC; 10 equivalents of PhC≡CMe was cyclotrimerized at 70°C in ~1 h using $9/Mg^*$ versus ~24 h when $11/Mg^*$ was used under identical conditions). This suggests that DPSC provides a less crowded Ti center and thereby reduces steric inhibition of rate-limiting alkyne coordination while exerting greater kinetic control over the course of the cyclotrimerization, due presumably to smaller distortion of the stereochemical environment about Ti during the reaction (*vide infra*).

For unsymmetrically substituted internal alkynes, preference for formation of 1,2,4-substituted arene decreased as the difference between sizes of the alkyne substituents decreased (Table 1, entries 14–19).

MECHANISM OF ALKYNE CYCLOTRIMERIZATION

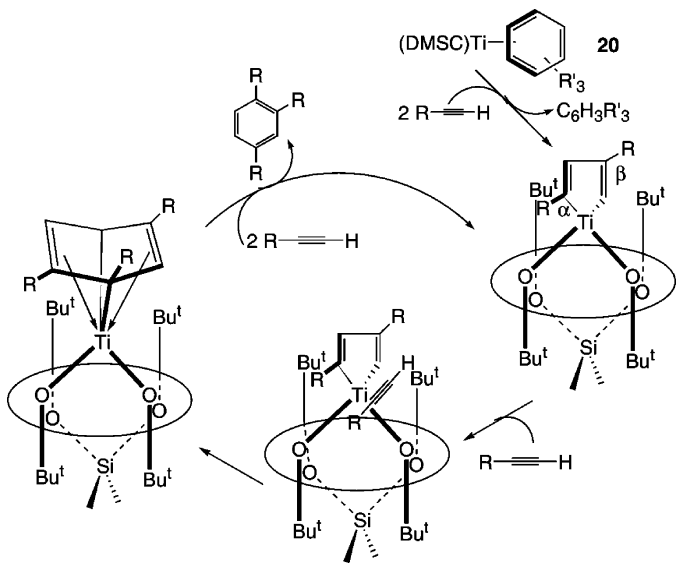
Both metallacyclopentadiene and metallanorbornadiene intermediates[118–139] have been implicated in alkyne cyclotrimerization. Reaction of a metallacyclopentadiene with one equivalent of alkyne to produce the free arene is usually proposed to proceed by stepwise formation of two new C−C bonds via a metallacycloheptatriene intermediate (**A**), or by concerted formation of two new C−C bonds (as in Diels-Alder reaction) via a metallanorbornadiene intermediate (**B**, Scheme 6). In general, both experimental and theoretical studies support a concerted pathway. For example, reactions of alkynes with aryloxide-based titanacyclopentadiene,[23,127–131] tantalacyclopentadiene,[124,125] and tantalanorbornadiene[124–126] complexes, and cylotrimerization of acetylene at iridium centers[137] are best interpreted in terms of a concerted pathway. DFT calculations of the mechanism for [$CpCoL_2$]-catalyzed (L=CO, PR_3, olefin) acetylene cyclotrimerization also concluded that intermediacy of a cobaltocycloheptatriene is energetically prohibitive and favored a concerted addition pathway.[138] As mentioned above, [(DMSC)Ti-{η^6-1,2,4−$C_6H_3(SiMe_3)_3$}] (**20**) is the resting state of the catalyst in $Me_3SiC{\equiv}CH$ cyclotrimerization hence we favor a concerted addition pathway for [2 + 2 + 2] cycloaddition catalyzed by titananorbornadienes by **20** and **24**. Consistent with this suggestion, whereas products that can



Scheme 6.

be attributed to β−H migration from a titanacyclohepta-2,4-diene intermediate were not observed in cross-coupling reaction of 4-chlorostyrene with $Me_3SiC{\equiv}CH$ catalyzed by **20**, the related complex $[(2,6{-}Ph_2C_6H_3O)_2Ti(CH_2CMe{=}CMeCH_2)]$ catalyzed cross coupling of 2,3-dimethyl-1,3-butadiene and ethylene via β−H elimination from an isolable titanacyclohept-3-ene.[139]

A mechanism in which DMSC-directed reactivity plays a key role best accounts for highly regioselective production of 1,2,4-substituted arene in alkyne cyclotrimerization catalyzed by titananorbornadienes **20** and **24**. Apparently, the stereochemical environment imposed at titanium by DMSC facilitates predominant (or possibly exclusive) formation of an α,β′ -substituted titanacyclopentadiene intermediate (Scheme 7) even though α,α′-, α′,β-, α,β′-, and/or β,β′-substituted titanacyclopentadienes are all possible intermediates. Accordingly, **30** with its 2,4-substituted cyclohexadienyl moiety constituted ∼91% of all cyclohexadienyl-containing products formed in [2 + 2 + 2] cycloaddition of 4-chlorostyrene with $Me_3SiC{\equiv}CH$ using **20** as catalyst (Scheme 5). Highly regioselective formation of 1,2,4-substituted arene is consistent with the DMSC ligand also exerting steric control over the approach



Scheme 7.

of an alkyne molecule to the titanacyclopentadiene intermediate since an α,β′-substituted titanacyclopentadiene can furnish either 1,2,4- or 1,3,5-substituted arene.[127,131] For example, [(2,6−$Ph_2C_6H_3O)_2$-Ti($C_4H_2Bu^t_2$)] was shown to catalyze cyclotrimerization of $Me_3SiC{\equiv}CH$ to yield 1,3,5- and 1,2,4-$C_6H_3(SiMe_3)_3$ in ∼95:5 ratio while aliphatic alkynes, such as 1-pentyne and 1-hexyne, were cyclotrimerized to furnish 1,3,5- and 1,2,4-substituted arenes in ∼1:3 ratio.[127] In [2 + 2 + 2] cycloaddition of terminal alkynes catalyzed by **20**, the DMSC ligand enforces orientation of the more bulky alkyne substituent outside the calixarene cavity (*exo*-orientation) as it reacts with the α,β′-substituted titanacyclopentadiene intermediate (Scheme 7); formation of **28a** and **28b** in 91:9 ratio and in excellent yield via catalytic cyclotrimerization of $Me_3SiC{\equiv}CCH_2SCH_2C{\equiv}CH$ by **20** clearly demonstrates that reaction of $Me_3SiC{\equiv}CCH_2SCH_2C{\equiv}CH$ with the putative titanacyclopentadiene intermediate occurs selectively via the less hindered terminal end of the alkyne (Scheme 5). However, the regiochemistry of the arene product is also influenced by at least one competing factor, steric interaction between ortho-positioned substituents in the transition state leading to arene formation. When the alkyne substituents are Bu^t groups, the latter factor apparently overwhelms the directing influence of the DMSC ligand, resulting in formation of 1,3,5-susbstituted arene as observed for **24**.

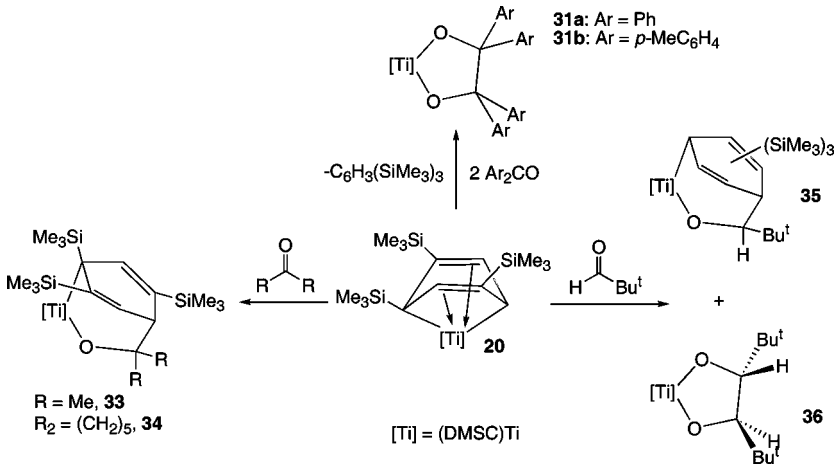
A loss of regioselectivity was noted when alkyne cyclotrimerization reactions were catalyzed by **20** in the presence of a donor, such as THF or TMEDA (Table 1, entry 11). This is presumably due to attenuation of the stereochemical influence of the DMSC ligand on the reactivity of coordinatively unsaturated intermediates generated from **20**, as coordination of THF (or other donor molecule) distorts the environment about titanium from pseudo-tetrahedral. As noted before, the preference for 1,2,4-susbtitution decreased as the difference between the sizes of substituent groups of unsymmetrically substituted internal alkynes decreased. Clearly, steric differentiation of the reaction sites at the Ti center, imposed by the calixarene ligand, becomes less important as the substituent groups become more similar in size. These results represent a sharp departure from those previously observed for related titanium-aryloxide systems, where titanacyclopentadienes are usually formed as stable species and high regioselectivity is rare. In 1,2-alternate conformation, the DMSC ligand sterically defines the reaction sites at Ti and exerts steric control over approach of a substrate to the metal center

by directing the less bulky end of a substrate into the calixarene cavity. Thus, the DMSC ligand results in a dramatic change in the reaction mechanism and regioselectivity in comparison with that previously observed for Ti-aryloxide systems.

REDUCTIVE COUPLING OF ALDEHYDES AND KETONES

Recent reviews of the scope, mechanism, and applications of low-valent titanium reagents in pinacol and McMurry coupling reactions have shown that intra- or intermolecular coupling of a wide variety of carbonyl compounds, such as aldehydes, ketones, acylsilanes, ketoesters, and oxoamides, can be applied to provide a remarkably diverse array of synthetic and natural products.[1–10] However, low-valent titanium reagents are usually prepared by reaction of $TiCl_3$ or $TiCl_4$ in an ethereal solvent with a reductant, hence the active titanium reductant is present in heterogeneous phase and the reactivity often depends markedly upon the choice of reductant and the experimental conditions. Well-defined and conveniently handled sources of Ti(II), such as [(DMSC)Ti(1,2,4-$(Me_3Si)_3C_6H_3$)] (**20**), offer the potential for mechanistic modeling of pinacol and McMurry reactions. Analogous to reactions of titanocene derivatives, $Cp_2Ti(CO)_2$ and $CpTiX_2(THF)_2$ (X = Cl, Br) with carbonyl compounds,[140] we found that **20** reacts with aromatic ketones Ph_2CO or (p-$C_6H_5Me)_2CO$ to give good yields of corresponding titanapinacolate complexes [(DMSC)Ti($OCAr_2CAr_2O$)] (**31a**, Ar = Ph and **31b**, Ar = p-C_6H_5Me, Scheme 8);[77,79] less bulky PhCOMe or PhCHO react with **20** to generate multiple DMSC-containing products. Recently, Woo et al. have shown that reactions of [(TTP)Ti(η^2-PhC≡CPh)] (**32**, TTP = tetratolylporphyrin) with various aromatic aldehydes and ketones also furnish titanapinacolate products.[141] X-ray crystallographic characterization of the molecular structure of **31a** revealed that the unit cell contained two independent molecules, and that each molecule possessed a long pinacolic C–C distance (ca. 1.62 Å); the related compound [$L_2Ti(OCPh_2CMe_2O)$] (L = N,N′-dimethylaminotroponiminate) has been shown to have a similarly long pinacolic C–C distance of 1.610(2) Å.[142]

Interestingly, reactions of aliphatic ketones, acetone or cyclohexanone, with **20** proceeded via formal insertion into the *endo*-Ti–C bond to initially give 2-oxatitanacycloheptene derivatives [(DMSC)Ti{C_6H_3-$(SiMe_3)_3$-Me_2CO}] (**33**) and [(DMSC)Ti{$C_6H_3(SiMe_3)_3$-$C_6H_{10}O$}] (**34**),



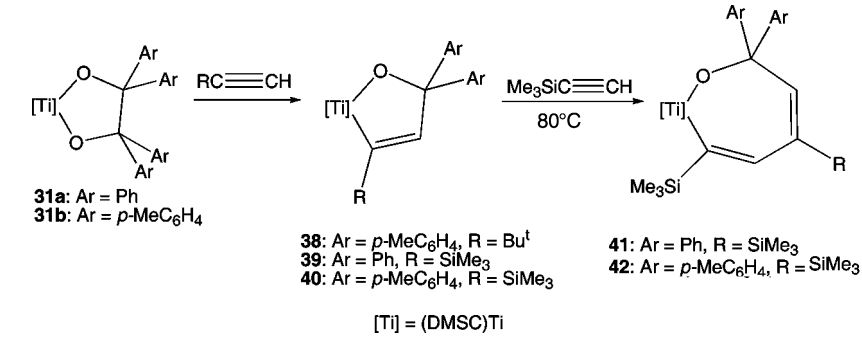
Scheme 8.

respectively (Scheme 8).[79] X-ray crystallographic characterization of the molecular structure of **34** established selective insertion at the less-substituted *endo*-CH carbon of the η^6-arene, and revealed η^2-coordination of the cyclohexadienyl fragment to titanium; a related tungstanorbornadiene was shown to undergo similar insertion of aliphatic ketones and aldehydes.[143] In solution, pure samples of **33** and **34** undergo gradual decomposition with release of 1,2,4-$(Me_3Si)_3C_6H_3$. However, both **33** and **34** react with added ketone ($\geq$1 equiv of acetone or cyclohexanone, respectively) to generate the corresponding titanapinacolate species. The reaction between bulky Bu^tCHO and **20** furnished both [(DMSC)Ti{$C_6H_3(SiMe_3)_3$-Bu^tCHO}] (**35**) and [(DMSC)Ti{OCH-(Bu^t)CH(Bu^t)O}] (**36**) in 30:70 ratio (Scheme 8); both **35** and **36** were present in solution throughout the course of the reaction and the product ratio did not change over 7 days at ambient temperature (after complete consumption of **20**) in the presence of excess Bu^tCHO. Thus, **35** does not convert into **36** and is stable at ambient temperature, unlike **33** and **34**. Since two diastereomers of [(DMSC)Ti{$C_6H_3(SiMe_3)_3$-Bu^tCHO}] can result if Bu^tCHO insertion into the Ti–C bond of **20** occurs exclusively at the less-substituted *endo*-CH, the other isomer of **35** presumably reacts preferentially with Bu^tCHO to yield **36**.

Remarkably facile fragmentation of the pinacolic C–C bond occurred in reactions of titanapinacolates **31a** and **31b** with unsaturated

substrates, such as terminal alkynes, ketones, and aromatic diimines, to yield a variety of well-defined organometallic products. ^{13}C NMR monitoring of the reaction between [(DMSC)Ti($OCPh_2CPh_2O$)] (**31a**) and Ph_2 ^{13}CO (1.1 equiv) in C_6D_6 at 25°C revealed that statistical and reversible incorporation of $Ph_2{}^{13}CO$ into *endo*- and *exo*-positions of the titanapinacolate ring occurred within 30 minutes.[77] Woo et al. have similarly reported that treatment of [(TTP)Ti($OCPh_2CPh_2O$)] (**37**) with PhCHO, PhCOMe, or Me_2CO resulted in selective formation of unsymmetrical titanapinacolate complexes.[141] Also, reaction of [(TTP)Ti(η^2-PhC≡CPh)] (**32**) with a mixture of unreactive aliphatic aldehydes or ketones and aromatic ketone selectively produced unsymmetrical titanapinacolates. In contrast to the case with aldehydes and ketones, terminal alkynes reacted sluggishly with **31a** or **31b** at 25°C. However, 2-oxatitanacyclopent-4-enes (**38**–**40**, Scheme 9) are formed in <3 h at 80°C, via alkyne displacement of one of the Ar_2CO units of the titanapinacolate; reduced steric hindrance of the *exo*-Ti−C bond of **39** and **40** allow further reaction with alkyne to yield oxatitanacycloheptadienes **41** and **42**, respectively (Scheme 9).[77]

Kinetic analysis of the reaction of **31b** with $Bu^tC{\equiv}CH$ at 50°C under pseudo-first-order conditions (at concentrations of $Bu^tC{\equiv}CH$: **31b** = 50:1) established first-order dependence each on the concentration of **31b** and $Bu^tC{\equiv}CH$. The observed rate constant (k_{obs}) for the reaction was $7.50 \times 10^{-4} \pm 4.84 \times 10^{-5}\ s^{-1}$ in the absence of added $(p\text{-}MeC_6H_4)_2CO$ while $k_{obs} = 2.34 \times 10^{-4} \pm 8.31 \times 10^{-6}\ s^{-1}$ and $9.95 \times 10^{-5} \pm 1.08 \times 10^{-6}\ s^{-1}$ in the presence of one or three equivalents of added $(p\text{-}MeC_6H_4)_2CO$, respectively.[77] Taken together with facile



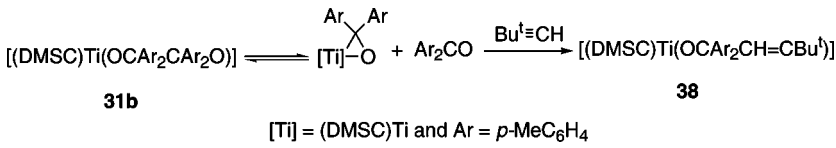
31a: Ar = Ph
31b: Ar = *p*-MeC_6H_4

38: Ar = *p*-MeC_6H_4, R = Bu^t
39: Ar = Ph, R = $SiMe_3$
40: Ar = *p*-MeC_6H_4, R = $SiMe_3$

41: Ar = Ph, R = $SiMe_3$
42: Ar = *p*-MeC_6H_4, R = $SiMe_3$

[Ti] = (DMSC)Ti

Scheme 9.

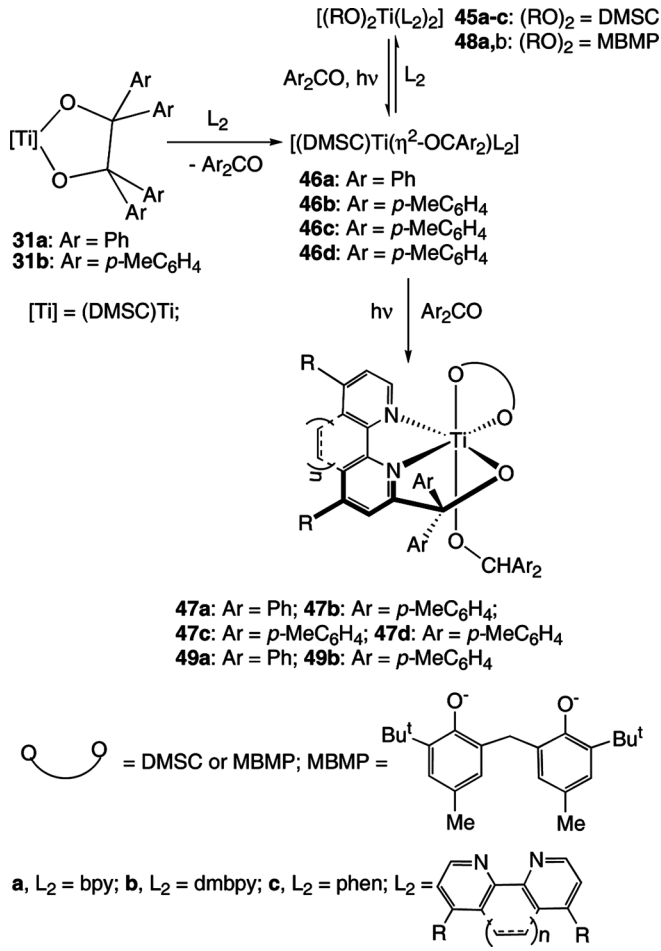


Scheme 10.

reversible exchange of Ph_2 ^{13}CO into *endo*- and *exo* positions of the pinacolate ring of **31a** (*vide supra*), these data strongly support a pre-equilibrium mechanism for titanapinacolate carbon–carbon bond rupture that involves reversible formation of (DMSC)Ti(η^2-$OCAr_2$) species prior to rate-limiting reaction with an alkyne or ketone molecule (Scheme 10); rapid formation of cross-coupled products from [(TTP)Ti($OCPh_2$ CPh_2O)] (**37**) and carbonyl compounds is similarly consistent with an equilibrium between **37** and an η^2-ketone species (TTP)Ti (η^2-$OCPh_2$).[141] It seems reasonable that the presumed (DMSC)Ti (η^2-$OCAr_2$) species reacts rapidly with ketone to regenerate the titanapinacolate and hence does not accumulate to an appreciable level. In fact, stable ligand-free $(RO)_2$Ti(η^2-ketone) (R = alkyl or aryl) complexes are unknown and well-characterized mononuclear group 4 metal-ketone complexes bearing alkyl or aryl substituents, such as [(TC-3,5)Hf(η^2-$OC(CH_2Ph)_2$)] (**43**, TC-3,5 = tropocorand ligand)[144] and [Ti(OC_6H_3 Ph_2-2,6)$_2$(η^2-$OCPh_2$)(PMe_3)] (**44**)[145,146] are rare. We have found that reactions of **31a** or **31b** with aromatic diimines (L_2), such as 2,2′-bipyridine (bpy), 4,4′-dimethyl-2,2′-dipyridyl (dmbpy), or 1,10-phenanthroline (phen) occur in pentane in essentially the time of mixing to give isolable [(DMSC)Ti(η^2-$OCAr_2$)L_2] complexes (**46a–d**) (Scheme 11).[76]

REDUCTIVE COUPLING OF KETONES WITH AROMATIC DIIMINES

Titanium-promoted reductive coupling of ketones with 2,2′-bipyridines or 1,10-phenanthrolines to form 6-(1-hydroxyalkyl)-2,2′-bipyridines and 2-(1-hydroxyalkyl)-1,10-phenanthrolines is attractive because these types of compounds, especially chiral derivatives, are of interest as ligands for catalyst exploration[147–155] and only a small number of methods have been reported for their synthesis.[147–158] We have found that light-assisted reactions of [(DMSC)Ti(η^2-$OCAr_2$)L_2] complexes (**46a–d**) with corresponding ketones ($\geq$1 equiv) yield 2-aza-5-oxa-titanacyclopentenes



Scheme 11.

47a–d (Scheme 11);[76] aqueous work-up of the reaction mixtures afforded 6-(1-hydroxyalkyl)-2,2′-bipyridine and 2-(1-hydroxyalkyl)-1, 10-phenanthroline compounds. Similarly, titanium bis(diimine) complexes $[(DMSC)Ti(L_2)_2]$ (**45a–c**; a, L_2 = bpy; b, L_2 = dmbpy; c, L_2 = phen)* and $[(MBMP)Ti(bpy)_2]$ (**48a**, MBMP = 2,2′-methylenebis(6-*tert*-butyl-4-methyl-phenol) dianion) undergo light-assisted reaction with $\geq$2 equivalents of aromatic ketone to yield corresponding 2-aza-5-oxa-titanacyclopentenes (Scheme 11).[75] The efficiency of 2-aza-5-oxa-titanacyclopentene production from reductive coupling reactions of

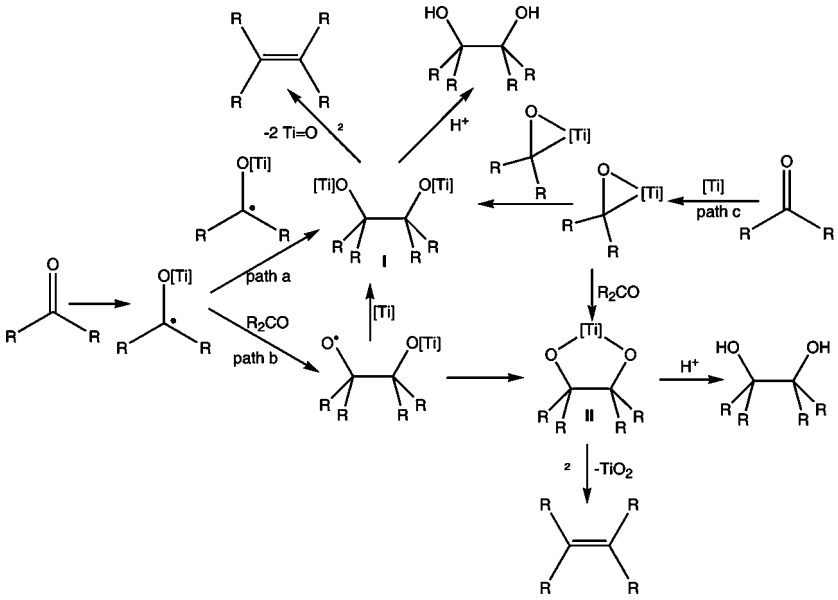
titanium bis(diimine) complexes **45a–c** or **48a** with ketones depended on the relative abilities of the ketone and the diimine to accept π-electron density; although the oxidation state of titanium in **45a–c** and **48a** is formally +2, structural data obtained from X-ray crystallographic characterization of the molecular structures of **45a** and **48a** along with the UV-visible and magnetic susceptibility data for the compounds are consistent with some electron transfer into the LUMO (π^* orbitals) of the diimine ligands.[75]

^{1}H NMR studies of reactions between [(DMSC)Ti(L_2)$_2$] (**45a–c**) and (p-MeC_6H_4)$_2$CO revealed that [(DMSC)Ti{η^2-OC(p-MeC_6H_4)$_2$}(L_2)] (**46a–c**) are reversibly formed and that the position of the equilibrium between **45a–c** and **46a–c** shifted increasingly toward **46a–c** as diimine π-acidity decreased. These studies also revealed that **46a–c** react faster with aromatic diimines than (p-MeC_6H_4)$_2$CO. Hence the rate of formation of 2-aza-5-oxa-titanacyclopentenes **47a–c** from **45a–c** increased with increasing ketone concentration. Qualitatively, the rate of formation of **47a–c** from [(DMSC)Ti(L_2)$_2$] (**45a–c**) followed the order: L_2 = bpy < dmbpy < phen while the rate of reaction between [(DMSC)Ti{η^2-OC(p-MeC_6H_4)$_2$}(L_2)] (**46a–c**) and (p-MeC_6H_4)$_2$CO (1 equiv) in C_6D_6 increased in the order: L_2 = dmbpy < bpy << phen. Consequently, the efficacy of the formation of 2-aza-5-oxa-titanacyclopentenes **47a–c** from **45a–c** depends on relative concentrations of **45a–c** and **46a–c** in solution, as well as on the rate of reaction of **46a–c** with (p-MeC_6H_4)$_2$CO. These results strongly support a mechanism involving reversible formation of [(DMSC)Ti{η^2-ketone}(L_2)] (**46a–c**) intermediates followed by reversible coordination of ketone to **46a–c** prior to the rate-limiting step. For [(MBMP)Ti(bpy)$_2$] (**48a**), we found that the yield of 2-aza-5-oxa-titanacyclopentene product decreased with decreasing ketone π-acidity in the order: Ph_2CO > PhCOR ≫ R_2CO (R = alkyl) ~ (p-$Me_2NC_6H_4$)$_2$CO.[75] Presumably, aliphatic ketones and (p-$Me_2NC_6H_4$)$_2$CO react sluggishly with **48a** because formation of [(MBMP)Ti(η^2-ketone)(bpy)] species is thermodynamically unfavorable since aliphatic ketones and (p-Me_2N-C_6H_4)$_2$CO are weaker π-acids than bipyridine.

RELEVANCE TO MECHANISMS OF PINACOL AND McMURRY COUPLING

The development of a molecular level understanding of the mechanism(s) of low-valent titanium-mediated reductive coupling of carbonyl

compounds is complicated by heterogeneity of the reaction conditions, which makes characterization of detailed structure(s) and the exact oxidation state(s) of the active titanium reductant(s) difficult. However, recent studies of the $TiCl_3$-Mg-THF,[113,114] $TiCl_3$-$LiAlH_4$,[159] and $TiCl_3(DME)_{1.5}$-Zn(Cu)[160] reagent systems have ruled out metallic Ti particles as the active species. Typical mechanisms proposed for stoichiometric McMurry and pinacol coupling reactions involve either single electron or double electron transfer steps (Scheme 12).[5–10] Single electron reduction of carbonyl substrate produces a ketyl radical, which can dimerize to form the titanapinacolate intermediate **I** (path a) or add to a second carbonyl group (path b) by formation of a C–C bond. In path b, a second single electron reduction must occur to generate titanapinacolate intermediate **II**. Alternatively, double electron reduction of a carbonyl group generates a Ti-η^2-carbonyl species (path c), which can dimerize to give **I** or insert a carbonyl group into the titanium–carbon bond to form **II**. Hydrolysis of **I** or **II** provides the pinacol while deoxygenation of the same titanapinacolate intermediates at elevated temperature yields the olefin.



Scheme 12.

Mononuclear titanium-ketyl complexes $[(Bu^t_3SiO)_3Ti(OCR^{\cdot}_2)]$ (**51**, R = aryl or alkyl) have been prepared by reaction of sterically crowded $Ti\{OSiBu^t_3\}_3$ (**50**)[68,69] with carbonyl compounds, and characterized by EPR spectroscopy; these titanium-bound ketyl radicals did not couple to produce titanapinacolates for steric reasons, but instead underwent disproportionation or intermolecular carbonyl C_α to phenyl C_{para} coupling.[69] As this review clearly demonstrates, althouth neither Ti-η^2-carbonyl nor titanapinacolate intermediates have been characterized in reductive coupling reactions of carbonyl compounds mediated by heterogeneous low-valent titanium reagent, soluble reductant systems that possess the titanium in a single well-defined oxidation state have allowed such species to be characterized. Reversible fragmentation of titanapinacolates $[(DMSC)Ti(OCAr_2CAr_2O)]$ (**31a**, Ar = Ph and **31b**, Ar = *p*-C_6H_5Me) by ketones, alkynes, or aromatic diimines, and isolation of $[(DMSC)Ti(\eta^2\text{-}OCAr_2)L_2]$ complexes (**46a–d**) support a carbonyl insertion pathway for formation of titanapinacolate complexes. As does observation of putative η^2-carbonyl complexes in reactions of $[(TTP)Ti(\eta^2\text{-}PhC{\equiv}CPh)]$ (**32**) with benzaldehyde and *p*-chlorobenzaldehyde.[141] Also, formation of unsymmetrically substituted titanapinacolates from reaction of L_2TiR_2 complexes (R = Me or Ph; L = N,N′-dimethylaminotroponiminate) with CO and aldehydes or ketones was proposed to proceed via a reactive titanium-η^2-carbonyl intermediate, formed by double alkyl migration to CO.[142]

Alkene formation from an isolated titanapinacolate has not yet been reported although titanapinacolates are undoubtedly intermediates in pinacol and McMurry reactions, since for many substrates, pinacols and alkenes can be obtained using the same low-valent titanium reagent system, depending on reactions conditions.[7] Besides, deoxygenation of metallapinacolate intermediates to give alkenes has been demonstrated in uranium-mediated reductive coupling of aliphatic and aromatic ketones[161–163]. Reaction of ketones with the UCl_4-M(Hg) systems (M = Li or Na) has allowed isolation and characterization of several metallapinacolate complexes, such as $[UCl_3(THF)_2\}_2(\mu\text{-}OCMe_2C\text{-}Me_2O)]$ (**52**), $[UCl_2(OCPh_2CPh_2O)]$ (**53**), $[UCl_2(OCPh_2CPh_2O)_2(THF)_2]$ (**54**), and $[UCl_2(OCMe_2CMe_2O)(THF)_2]$ (**55**). Regardless of the amalgam used, UCl_4 reacted with acetone to first produce **52** as the intermediate;[163] dimerization of the ketyl species $Cl_3U(OCMe^{\cdot}_2)$, which was trapped with Ph_3SnH, afforded **52**. Hydrolysis of the metallapinacolates gave pinacols while deoxygenation of the metallapinacolates

into alkenes was observed at high temperatures. The mechanism of the rate-limiting deoxygenation step, however, remains unclear and the nature of the amalgam greatly affected this transformation; only Li(Hg) in refluxing THF proved effective in the process.[162,163]

CONCLUSION

Our studies of well-characterized titananorbornadienes revealed that the DMSC ligand enforces *exo*-orientation of the alkyne substituent (outside the calixarene cavity), and that the directing influence of the DMSC ligand is key to the formation of 1,2,4-substituted arene with high regioselectivity in catalytic cyclotrimerization of terminal alkynes. To the best of our knowledge, these studies represent the first unambiguous demonstration of the involvement of a titananorbornadiene in the rate-determining step of [2 + 2 + 2] cycloaddition of alkynes. Reactions of well-characterized titanium reductants with carbonyl compounds described in this review have led to improved mechanistic understanding of pinacol and McMurry reactions. Titanium-η^2-carbonyl and titanapinacolate complexes have been established as viable intermediates in pinacol and McMurry reactions, although knowledge of the mechanism of the metallapinacolate deoxygenation step remains vague. We reasonably anticipate that development of soluble reductant systems that possess titanium in a single well-defined oxidation state and in diverse ligand environments would greatly aid elucidation of the reaction mechanisms, as well as enhance control of selectivity in pinacol and McMurry coupling reactions.

ACKNOWLEDGMENTS

Thanks are expressed to the US National Science Foundation (grant numbers CHE-9984776 and CHE-0416098) for financial support of our research program in low-valent titanium chemistry.

REFERENCES

1. Wirth, T. 1996. *Angew. Chem. Int. Ed. Engl.*, **35**, 61–63.
2. Fürstner, A. and B. Bogdanovic, 1996. *Angew. Chem. Int. Ed. Engl.*, **35**, 2442–2469.
3. Gansauer, A. and H. Bluhm, 2000. *Chem. Rev.*, **100**, 2771–2788.

4. Armbruster, J., S. Grabowski, T. Ruch, and H. Prinzbach, 1998. *Angew. Chem. Int. Ed. Engl.*, **37**, 2242–2245.
5. McMurry, J. E. 1989. *Chem. Rev.*, **89**, 1513–1524.
6. Kahn, B. E. and R. D. Rieke, 1988. *Chem. Rev.*, **88**, 733–745.
7. Ephritikhine, M. and C. Villiers, 2004. In *Modern Carbonyl Olefination*, Takeda, T. (ed.), pp. 223–284, Wiley-VCH, Weinheim.
8. Fürstner, A. 2004. In *Transition Metals for Organic Synthesis*, 2nd ed., Beller, M. and C. Bolm (eds.), vol. 1, pp. 449–468, Wiley-VCH, Weinheim.
9. Dushin, R. G. 1996. In *Comprehensive Organometallic Chemistry II*, Hegedus, L. S. (ed.), vol. 12, pp. 1071–1085, Pergamon, Oxford.
10. Robertson, G. M. 1991. In *Comprehensive Organic Synthesis I*, Trost, B. M. (ed.), vol. 3, pp. 563–611, Pergamon, New York.
11. Negishi, E. 2005. *Dalton Trans*., **5**, 827–848.
12. Negishi, E.-I. and T. Takahashi, 1998. *Bull. Chem. Soc. Jpn*., **71**, 755–769.
13. Negishi, E. 1991. *Comprehensive Organic Synthesis*, Trost, B. M. (ed.), vol. 5, pp. 1163–1184, Permagon, Oxford.
14. Togni, A. and R. L. Halterman (eds.), 1998. *Metallocenes: Synthesis, Reactivity, Applications*, vol. 1, Wiley-VCH, Weinheim.
15. Togni, A. and R. L. Halterman (eds.), 1998. *Metallocenes: Synthesis, Reactivity, Applications*, vol. 2, Wiley-VCH, Weinheim.
16. Marek, I. (ed.), 2002. *Titanium and Zirconium in Organic Synthesis*, Wiley-VCH, Weinheim.
17. Takeda, T. 2005. *Bull. Chem. Soc.*, **78**, 195–217.
18. Dang, Y. and H. J. Geise, 1991. *J. Organomet. Chem*., **405**, 1–39.
19. Schore, N. E. 1988. *Chem. Rev.*, **88**, 1081–1119.
20. Ojima, I., M. Tzamarioudaki, L. Zhaoyang, and R. J. Donovan, 1996. *Chem. Rev.*, **96**, 635–662.
21. Hanazawa, T., K. Sasaki, Y. Takayama, and F. Sato, 2003. *J. Org. Chem*., **68**, 4980–4983.
22. Balaich, G. J., J. E. Hill, S. A. Waratuke, P. E. Fanwick, and I. P. Rothwell, 1995. *Organometallics*, **14**, 656–665.
23. Johnson, E. S., G. J. Balaich, and I. P. Rothwell, 1997. *J. Am. Chem. Soc.*, **119**, 7685–7693.
24. Van Tamelen, E. E. 1970. *Acc. Chem. Res*., **3**, 361–367.
25. Eisch, J. J., X. Shi, and J. Lasota, 1995. *Z. Naturforsch*., **B50**, 342–350.
26. Eisch, J. J., X. Shi, J. R. Alila, and S. Thiele, 1997. *Chem. Ber.*, **130**, 1175–1187.
27. Eisch, J. J., A. A. Adeosun, and J. N. Gitua, 2003. *Eur. J. Org. Chem*., 4721–4727.
28. Eisch, J. J. and J. N. Gitua, 2003. *Organometallics*, **22**, 24–26.
29. Eisch, J. J., J. N. Gitua, P. O. Otieno, and X. Shi, 2001. *J. Organomet. Chem*., **624**, 229–238.

30. Ozerov, O. V., F. T. Ladipo, and B. O. Patrick, 1999. *J. Am. Chem. Soc.*, **121**, 7941–7942.
31. Williams, G. M., K. I. Gell, and J. Schwartz, 1980. *J. Am. Chem. Soc.*, **102**, 3660–3662.
32. Hollis, T. K., T. J. Ahn, and F. S. Tham, 2003. *Organometallics*, **22**, 1432–1436.
33. Takahashi, T., M. Kotora, R. Fischer, Y. Nishihara, and K. Nakajima, 1995. *J. Am. Chem. Soc.*, **117**, 11039–11040.
34. Williams, G. M. and J. Schwartz, 1982. *J. Am. Chem. Soc.*, **104**, 1122–1124.
35. Kiplinger, J. L. and T. G. Richmond, 1996. *J. Am. Chem. Soc.*, **118**, 1805–1805.
36. Jones, W. D. 2003. *Dalton Trans.*, 3991–3995.
37. Edelbach, B. L., A. K. F. Rahman, R. J. Lachiotte, and W. D. Jones, 1999. *Organometallics*, **18**, 3170–3177.
38. Kraft, B. M., R. J. Lachiotte, and W. D. Jones, 2001. *J. Am. Chem. Soc.*, **123**, 10973–10979.
39. Manriquez, J. M., D. R. McAlister, R. D. Sanner, and J. E. Bercaw, 1978. *J. Am. Chem. Soc.*, **100**, 2716–2724.
40. Pez, G. P. and J. N. Armor, 1981. *Adv. Organomet. Chem.*, **19**, 1–50.
41. Van Wagenen, B. C. and T. Livingstone, 1989. *Tetrahedron Lett.*, **30**, 3495–3498.
42. Bishop, L. A., M. A. Turner, and L. B. Kool, 1998. *J. Organomet. Chem.*, **553**, 53–57.
43. Hiller, J., U. Thewalt, M. Polasek, L. Petrusova, V. Varga, P. Sedmera, and K. Mach, 1996. *Organometallics*, **15**, 3752–3759.
44. Trost, B. M. (ed.), 1991. *Comprehensive Organic Synthesis*, vols. 1 and 2, Pergamon Press, Oxford.
45. Pool, J. A., W. H. Bernskoetter, and P. J. Chirik, 2004. *J. Am. Chem. Soc.*, **126**, 14326–14327.
46. Kreutzer, K. A., R. A. Fisher, W. M. Davis, E. Spaltenstein, and S. L. Buchwald, 1991. *Organometallics*, **10**, 4031–4035.
47. Takahashi, T., M. Hasegawa, N. Suzuki, M. Saburi, C. J. Rousset, P. E. Fanwick, and E. Negishi, 1991. *J. Am. Chem. Soc.*, **113**, 8564–8566.
48. Bradley, C. A., E. Lobkovsky, and P. J. Chirik, 2003. *J. Am. Chem. Soc.*, **125**, 8110–8111.
49. Bradley, C. A., I. Keresztes, E. Lobkovsky, V. G. Young, and P. J. Chirik, 2004. *J. Am. Chem. Soc.*, **126**, 16937–16950.
50. Veiros, L. F. 2005. *Chem.-Eur. J.*, **11**, 2505–2518.
51. Bradley, C. A., E. Lobkovsky, I. Keresztes, and P. J. Chirik, 2005. *J. Am. Chem. Soc.*, **127**, 10291–10304.
52. Du, G. and L. K. Woo, 2003. *Organometallics*, **22**, 450–455.
53. Thorman, J. L. and L. K. Woo, 2000. *Inorg. Chem.*, **39**, 1301–1304.

54. Kim, H.-J., S. Jung, Y.-M. Jeon, D. Whang, and K. Kim, 1999. *Chem. Commun*., 1033–1034.
55. Gray, S. D., J. L. Thorman, V. A. Adamian, K. M. Kadish, and K. L. Woo, 1998. *Inorg. Chem*., **37**, 1–4.
56. Wang, X., S. D. Gray, J. Chen, and K. L. Woo, 1998. *Inorg. Chem*., **37**, 5–9.
57. Woo, K. L. and J. A. Hays, 1993. *Inorg. Chem*., **32**, 2228–2229.
58. Woo, K. L., J. A. Hays, R. A. Jacobson, and C. L. Day, 1991. *Organometallics*, **10**, 2102–2104.
59. Hagadorn, J. R. and J. Arnold, 1998. *Organometallics*, **17**, 1355–1368.
60. Hagadorn, J. R. and J. Arnold, 1997. *Dalton Trans*., 3087–3096.
61. Hagadorn, J. R. and J. Arnold, 1994. *Organometallics*, **13**, 4670–4672.
62. Hagadorn, J. R. and J. Arnold, 1996. *J. Am. Chem. Soc*., **118**, 893.
63. Hao, S., K. Feghali, and S. Gambarotta, 1997. *Inorg. Chem*., **36**, 1745–1748.
64. Flamini, A., D. J. Cole-Hamilton, and G. Wilkinson, 1978. *Dalton Trans*., 454–459.
65. Morris, R. and G. S. Girolami, 1990. *Inorg. Chem*., **29**, 4167–4169.
66. Durfee, L. D., P. E. Fanwick, and I. P. Rothwell, 1987. *J. Am. Chem. Soc*., **109**, 4720–4722.
67. Durfee, L. D., J. E. Hill, J. L. Kerschner, P. E. Fanwick, and I. P. Rothwell, 1989. *Inorg. Chem*., **28**, 3095–3096.
68. Covert, K. J. and P. T. Wolczanski, 1989. *Inorg. Chem*., **28**, 4565–4567.
69. Covert, K. J., P. T. Wolczanski, S. A. Hill, and P. J. Krusic, 1992. *Inorg. Chem*., **31**, 66–78.
70. Cummins, C. C. 1998. In *Progress in Inorganic Chemistry*, Karlin, K. D. (ed.), vol. 47, pp. 685–836, John Wiley & Sons, New York.
71. Minhas, R., R. Duchateau, S. Gambarotta, and C. Bensimon, 1992. *Inorg. Chem*., **31**, 4933–4938.
72. Scoles, L., R. Minhas, J. J. Duchateau, and S. Gambarotta, 1994. *Organometallics*, **13**, 4978–4983.
73. Minhas, R. K., L. Scoles, S. Wong, and S. Gambarotta, 1996. *Organometallics*, **15**, 1113–1121.
74. Latesky, S. L., J. Keddington, A. K. McMullen, I. P. Rothwell, and J. C. Huffman, 1985. *Inorg. Chem*., **24**, 995–1001.
75. Owiny, D., J. V. Kingston, M. Maynor, S. Parkin, J. W. Kampf, and F. T. Ladipo, 2005. *Organometallics*, **24**, 3995–4002.
76. Kingston, J. V., V. Sarveswaran, S. Parkin, and F. T. Ladipo, 2003. *Organometallics*, **22**, 136–144.
77. Kingston, J. V., O. V. Ozerov, S. Parkin, C. P. Brock, and F. T. Ladipo, 2002. *J. Am. Chem. Soc*., **124**, 12217–12224.
78. Ozerov, O. V., C. P. Brock, S. D. Carr, and F. T. Ladipo, 2000. *Organometallics*, **19**, 5016–5025.

79. Ozerov, O. V., S. Parkin, C. P. Brock, and F. T. Ladipo, 2000. *Organometallics*, **19**, 4187–4190.
80. Ozerov, O. V., B. O. Patrick, and F. T. Ladipo, 2000. *J. Am. Chem. Soc.*, **122**, 6423–6431.
81. Gibson, V. C. 1994. *Dalton Trans.*, 1607–1618.
82. Wolczanski, P. T. 1995. *Polyhedron*, **14**, 3335–3362.
83. Ozerov, O. V., N. P. Rath, and F. T. Ladipo, 1999. *J. Organomet. Chem.*, **586**, 223–233.
84. Ladipo, F. T., V. Sarveswaran, J. V. Kingston, R. A. Huyck, S. Y. Bylikine, S. D. Carr, R. Watts, and S. Parkin, 2004. *J. Organomet. Chem.*, **689**, 502–514.
85. Fan, M., H. Zhang, and M. Lattman, 1996. *Organometallics*, **15**, 5216–5219.
86. Howell, J. A. S., N. F. Ashford, D. T. Dixon, J. C. Kola, T. A. Albright, and S. K. Kang, 1991. *Organometallics*, **10**, 1852–1864.
87. Brezinski, M. M. and K. J. Klabunde, 1983. *Organometallics*, **2**, 1116–1123.
88. Torres, F., E. Sola, M. Martin, J. A. Lopez, F. J. Lahoz, and L. A. Oro, 1999. *J. Am. Chem. Soc.*, **121**, 10632–10633.
89. Schneider, J. J. and D. Wolf, 1998. *Z. Naturforsh.*, **B53**, 1267–1272.
90. Schneider, J. J., D. Wolf, C. Janiak, O. Heinemann, J. Rust, and C. Kruger, 1998. *Chem. Eur. J.*, **4**, 1982–1991.
91. Seaburg, J. K., P. J. Fischer, V. G. Young, Jr., and J. E. Ellis, 1998. *Angew. Chem. Int. Ed. Engl.*, **37**, 155–158.
92. Muetterties, E. L., H. Schaeffer, R. I. Mink, M. Y. Darensbourg, M. Millar, T. Groshens, and K. J. Klabunde, 1979. *Inorg. Chem.*, **18**, 883–884.
93. Anthony, M. T., M. L. H. Green, and D. Young, 1975. *Dalton Trans.*, 1419–1420.
94. Morand, P. D. and C. G. Francis, 1985. *Inorg. Chem.*, **24**, 56–61.
95. Hawker, P. N., E. P. Kundig, and P. L. Timms, 1978. *Chem. Commun.*, 730–731.
96. Gardner, T. G. and G. S. Girolami, 1988. *Angew. Chem. Int. Ed. Engl.*, **27**, 1693–1695.
97. Thewalt, U. and F. Osterle, 1979. *J. Organomet. Chem.*, **172**, 317–324.
98. Thewalt, U. and F. Stollmaier, 1982. *J. Organomet. Chem.*, **228**, 149–152.
99. Calderazzo, F., I. Ferri, G. Pampaloni, U. Englert, and M. L. H. Green, 1997. *Organometallics*, **16**, 3100–3101.
100. Troyanov, S. 1994. *J. Organomet. Chem.*, **475**, 139–147.
101. Troyanov, S., J. Polacek, H. Antropiusova, and K. Mach, 1992. *J. Organomet. Chem.*, **430**, 317–325.
102. Calderazzo, F. and G. Pampaloni, 1995. *J. Organomet. Chem.*, **500**, 47–60.
103. Brennessel, W. W., J. E. Ellis, M. K. Pomije, V. J. Sussman, E. Urnezius, and V. G. Young, Jr., 2002. *J. Am. Chem. Soc.*, **124**, 10258–10259.

104. Seaburg, J. K., P. J. Fischer, V. G. Young, Jr., and J. E. Ellis, 1998. *Angew. Chem. Int. Ed. Engl.*, **37**, 155–158.
105. Fischer, P. J., K. A. Ahrendt, V. G. Young, Jr., and J. E. Ellis, 1998. *Organometallics*, **17**, 13–15.
106. Jang, M. and J. E. Ellis, 1994. *Angew. Chem. Int. Ed. Engl.*, **33**, 1973–1975.
107. Ellis, J. E., B. K. Stein, and S. R. Frerichs, 1993. *J. Am. Chem. Soc.*, **115**, 4066–4075.
108. Ellis, J. E., S. R. Frerichs, and B. K. Stein, 1993. *Organometallics*, **12**, 1048–1057.
109. Ellis, J. E., D. W. Blackburn, P. Yuen, and M. Jang, 1993. *J. Am. Chem. Soc.*, **115**, 11616–11617.
110. Blackburn, D. W., D. Britton, and J. E. Ellis, 1992. *Angew. Chem. Int. Ed. Engl.*, **31**, 1495–1498.
111. Brennessel, W. W., J. E. Ellis, S. N. Roush, B. R. Strandberg, O. E. Woisetschlaeger, and V. G. Young, 2002. *Chem. Commun.*, 2356–2357.
112. Pomije, M. K., C. J. Kurth, J. E. Ellis, and M. V. Barybin, 1997. *Organometallics*, **16**, 3582–3287.
113. Aleandri, L. E., B. Bogdanovic, A. Gaidies, D. J. Jones, S. Liao, A. Michalowicz, J. Roziere, and A. Schott, 1993. *J. Organomet. Chem.*, **459**, 87–93.
114. Aleandri, L. E., B. Bogdanovic, P. Bons, C. Durr, A. Gaides, T. Hartwig, S. C. Huckett, M. Lagarden, U. Wilczok, and R. A. Brand, 1995. *Chem. Mater.*, **7**, 1153–1170.
115. Hagadorn, J. R. and J. Arnold, 1998. *Angew. Chem. Int. Ed. Engl.*, **37**, 1729–1731.
116. Farnetti, E. and N. Marsich, 2004. *J. Organomet. Chem.*, **689**, 14–17.
117. Rubin, M., A. W. Sromek, and V. Gevorgyan, 2003. *Synlett*, 2265–2291.
118. Tamao, K., K. Kobayashi, and Y. Ito, 1992. *Synlett*, 539–546.
119. Trost, B. M. 1986. *Angew. Chem. Int. Ed. Engl.*, **25**, 1–20.
120. Volhardt, K. P. C. 1984. *Angew. Chem. Int. Ed. Engl.*, **23**, 539–644.
121. McAlister, D. R., J. E. Bercaw, and R. G. Bergman, 1977. *J. Am. Chem. Soc.*, **99**, 1666–1668.
122. Grigg, R., R. Scott, and P. Stevenson, 1988. *J. Chem. Soc. Perkin Trans. I.*, 1357–1364.
123. Sigman, M. S., A. W. Fatland, and B. E. Eaton, 1998. *J. Am. Chem. Soc.*, **120**, 5130–5131.
124. Strickler, J. R., M. A. Bruck, and D. E. Wigley, 1990. *J. Am. Chem. Soc.*, **112**, 2814–2816.
125. Smith, D. P., J. R. Strickler, S. D. Gray, M. A. Bruck, R. S. Holmes, and D. E. Wigley, 1992. *Organometallics*, **11**, 1275–1288.

126. Bruck, M. A., A. S. Copenhaver, and D. E. Wigley, 1987. *J. Am. Chem. Soc.*, **109**, 6525–6527.
127. Hill, J. E., G. Balaich, P. E. Fanwick, and I. P. Rothwell, 1993. *Organometallics*, **12**, 2911–2924.
128. Warantuke, S. A., E. S. Johnson, M. G. Thorn, P. E. Fanwick, and I. P. Rothwell, 1996. *Chem. Commun*., 2617–2618.
129. Balaich, G. J. and I. P. Rothwell, 1993. *J. Am. Chem. Soc.*, **115**, 1581–1583.
130. Warantuke, S. A., M. G. Thorn, P. E. Fanwick, A. P. Rothwell, and I. P. Rothwell, 1999. *J. Am. Chem. Soc.*, **121**, 9111–9119.
131. Wielstra, Y., S. Gambarotta, A. Meetsma, J. L. de Boer, and M. Y. Chiang, 1989. *Organometallics*, **8**, 2696–2702.
132. Buchwald, S. L. and R. B. Nielsen, 1989. *J. Am. Chem. Soc.*, **111**, 2870–2874.
133. Wakatsuki, Y., O. Nomura, K. Kitaura, K. Morkuma, and H. Yamazaki, 1983. *J. Am. Chem. Soc.*, **105**, 1907–1912.
134. Gesing, E. R. F., J. P. Tane, and K. P. C. Vollhardt, 1980. *Angew. Chem. Int. Ed. Engl.*, **19**, 1023–1024.
135. Meijer-Veldman, M. E. E. and H. J. de Liefde Meijer, 1984. *J. Organomet. Chem*., **260**, 199–205.
136. Strickler, J. R., P. A. Wexler, and D. E. Wigley, 1988. *Organometallics*, **7**, 2067–2069.
137. Bianchini, C., K. G. Caulton, C. Chardon, O. Eisenstein, K. Folting, T. J. Johnson, A. Meli, M. Peruzzini, D. J. Rauscher, W. E. Streib, and F. Vizza, 1991. *J. Am. Chem. Soc.*, **113**, 5127–5129.
138. Hardesty, J. H., J. B. Koerner, T. A. Albright, and G.-Y. Lee, 1999. *J. Am. Chem. Soc.*, **121**, 6055–6067.
139. Hill, J. E., P. E. Fanwick, and I. P. Rothwell, 1992. *Organometallics*, **11**, 1775–1777.
140. Coutts, R. S. P., P. C. Wailes, and R. L. Martin, 1973. *J. Organomet. Chem*., **50**, 145–151.
141. Du, G., G. A. Mirafzal, and L. K. Woo, 2004. *Organometallics*, **23**, 4230–4235.
142. Steinhuebel, D. P. and S. J. Lippard, 1999. *J. Am. Chem. Soc.*, **121**, 11762–11772.
143. Lockwood, M. A., P. E. Fanwick, and I. P. Rothwell, 1996. *Chem. Commun*., 2013–2014.
144. Scott, M. J. and S. J. Lippard, 1997. *J. Am. Chem. Soc.*, **119**, 3411–3412.
145. Hill, J. E., P. E. Fanwick, and I. P. Rothwell, 1992. *Organometallics*, **11**, 1771–1773.
146. Thorn, M. G., J. E. Hill, S. A. Warantuke, E. S. Johnson, P. E. Fanwick, and I. P. Rothwell, 1997. *J. Am. Chem. Soc.*, **119**, 8630–8641.
147. Chelucci, G. and R. P. Thummel, 2002. *Chem. Rev.*, **102**, 3129–3170.

148. Schoffers, E. 2003. *Eur. J. Org. Chem*., 1145–1152.
149. Johnson, J. S. and D. A. Evans, 2000. *Acc. Chem. Res*., **33**, 325–335.
150. Wolter, M., A. Klapars, and S. L. Buchwald, 2001. *Org. Lett*., **3**, 3803–3805.
151. Widenhoefer, R. A. 2002. *Acc. Chem. Res*., **35**, 905–913.
152. Milani, B., A. Scarel, G. Mestroni, S. Gladiali, R. Taras, C. Carfagna, and L. Mosca, 2002. *Organometallics*, **21**, 1323–1325.
153. Gladiali, S., L. Pinna, G. Delogu, S. De Martin, G. Zassinovich, and G. Mestroni, 1990. *Tetrahedron: Asymmetry*, **1**, 635–648.
154. Chelucci, G., G. Loriga, G. Murineddu, and G. A. Pinna, 2002. *Tetrahedron Lett*., **43**, 3601–3604.
155. Chelucci, G., S. Gladiali, M. G. Sanna, and H. Brunner, 2000. *Tetrahedron: Asymmetry*, **11**, 3419–3426.
156. Weitgenant, J. A., J. D. Mortison, D. J. O'Neill, B. Mowery, A. Puranen, and P. Helquist, 2004. *J. Org. Chem*., **69**, 2809–2815.
157. O'Neill, D. J. and P. Helquist, 1999. *Org. Lett*., **1**, 1659–1162.
158. Gladiali, S., G. Chelucci, M. S. Mudadu, M.-A. Gastaut, and R. P. Thummel, 2001. *J. Org. Chem*., **66**, 400–405.
159. Aleandri, L. E., S. Becke, B. Bogdanovic, D. J. Jones, and J. Roziere, 1994. *J. Organomet. Chem*., **472**, 97–112.
160. Bogdanovic, B. and A. Bolte, 1995. *J. Organomet. Chem*., **502**, 109–121.
161. Villiers, C., R. Adam, M. Lance, M. Nierlich, and M. Ephritikhine, 1991. *Chem. Commun*., 1144–1145.
162. Maury, O., C. Villiers, and M. Ephritikhine, 1996. *Angew. Chem. Int. Ed*., **35**, 1129–1130.
163. Ephritikhine, M., O. Maury, C. Villiers, M. Lance, and M. Nierlich, 1998. *Dalton Trans*., 3021–3028.