Carbon–carbon bond formation via oxidative-addition processes of titanium(II) reagents with π-bonded organic substrates. Reactivity modifications by Lewis acids and Lewis bases[☆]
Part 22. Organic chemistry of subvalent transition metal complexes

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Dedicated to Professor Jean F. Normant on the occasion of his 65th birthday

Abstract

A series of titanium(II) derivatives, TiE_2, was prepared by alkylative reduction of TiE_4 by two equivalents of *n*-butyllithium in THF at -78 to 25°C (E = Cl, F, OBu^n, OPr^i and 0.5 $NPh–CH_2–CH_2–NPh$). The LiE by-product could usually be removed by THF evaporation and dissolution of the TiE_2 into toluene. All such TiE_2 derivatives were shown to effect the epimetallation and oligomerization of olefins, acetylenes and carbonyl derivatives in varying degrees. Particularly pertinent were the isolation and chemical reactions of titanium(II) isoproxide, the postulated intermediate in the Kulinkovich synthesis of cyclopropanols from ethyl Grignard reagents and organic esters, as well as an intermediate in many allied reactions developed by the Sato group. The findings of the present study corroborate completely the foregoing hypothesis that titanium(II) isopropoxide is the key intermediate in such novel reactions in organic synthesis. Furthermore, $Ti(OPr^i)_2$ can be prepared readily in a relatively pure state and has been found to react with 1-alkenes, alkynes and ketones by epimetallation at 25°C to form three-membered titanacycles, which can be utilized in organic synthesis. Finally, the ease with which such TiE_2 derivatives epimetallate unsaturated organic substrates has been shown to be decreased by the steric demands of E and by the coordination of Lewis bases or donor solvent to the titanium(II) center. Lewis acids, on the other hand, greatly increase the rate of epimetallation by TiE_2. A dramatic illustration of this effect is in the action of $TiCl_2·Me_2AlCl$ on unsaturated hydrocarbons, wherein the polymerization of ethylene and of 1-alkene and the cyclotrimerization of alkynes are found to occur at room temperature. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Titanium(II) derivatives; Alkylative reduction; Oxidative-addition processes; Lewis acids and bases

1. Introduction

The interaction of subvalent transition metal centers with π-bonded organic substrates has become a hallmark of both structure and reactivity among organotransition metal compounds [1]. The orbital description of the metal-π-bonded substrate interaction in the Dewar–Chatt–Duncanson model involves σ-bonding by a filled π-orbital of the substrate with an unfilled metal d-orbital of proper symmetry, supplemented by $d_π–p_π$ back-bonding from a filled d-orbital to a substrate empty π*-orbital, again with net positive overlap. Depending upon the bonding contributions of the σ- and π-components, the resulting structure can vary from that of a weak π-complex with a slightly perturbed π-bond (**1a**) to a metallacyclopropane (**1b**) wherein the π-bond, based upon the C–C separation, has largely been weakened [2,3], and the M_t valence has increased formally by 2. Judging whether **1a** or **1b** is the more important resonance contribution must be decided upon on the basis of spectroscopic and single-crystal X-ray data for the individual complex. Such

structural assessments have been carried out both for the early transition metal complex, $[(CH_3)_5Cp]_2Ti \cdot H_2C=CH_2$ [4] and the late transition metal complex, $BpyNi \cdot Ph-C \equiv C-Ph$ [5].
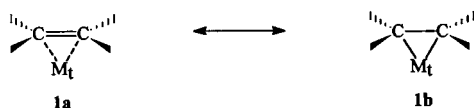

In the last two decades Group 4 metal complexes, especially those formally with titanocene(II) and zirconocene(II) character, have been shown to form diverse π-complexes with benzynes, cycloalkynes and alkynes but with relatively few alkenes. Carbon–carbon couplings, cyclizations and oligomerizations of great importance in organic synthesis have issued rewardingly from such investigations [6,7].

However, the most noteworthy discovery of the last ten years has been the observation that even ordinary subvalent derivatives of Group 4 metals, not involving any cyclopentadienyl ligands, can readily form a wide variety of complexes with simple alkenes or alkynes [8]. This seminal observation was made by Kulinkovich and coworkers in 1989, who reported that ethylmagnesium bromide reacted with carbocyclic acid esters in the presence of catalytic amounts of titanium(IV) isopropoxide to provide high yields of cyclopropanols (Eq. (1)). It was proposed that the intermediate $Ti(OPr^i)_2$ generated then complexed with the ethylene from the Grignard reagent to form reactive intermediate **2** [9].

(1)
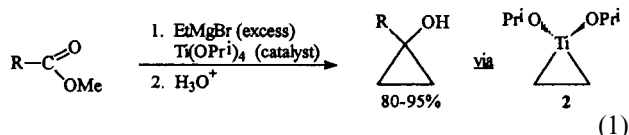
Numerous subsequent reactions involving analogs of the original eponymous Kulinkovich reagent **2** have been studied with substituted alkenes and alkynes both by the Kulinkovich group in Russia [10] and after 1995 by the Sato group in Japan [11], leading to the great enrichment of modern organic synthesis.

In our own research with subvalent Group 4 metal reagents and catalysts, the observed cyclotrimerizations of alkynes and the stereoselective *racemic* bimolecular reduction of methyl phenyl ketone led us to propose in 1995 that metallacyclopropenes **3** and **4** were appealing intermediates in such possible two-electron transfers (TET) or oxidative addition processes [12]. Our subsequent studies on the synthesis of metallocene dihalides by the reductive dimerization of fulvenes by Group 4 dihalides [13] and the reduction and dimerization of either alkynes or ketones by $LiCrH_2$ [14,15] have strengthened our confidence in the presence of such intermediates. Particular support for the presence of **5** in the reduction of $Ph_2C=O$ by $LiCrH_2$ is that workup with D_2O produced almost a 90% yield of Ph_2CD-OD [15].
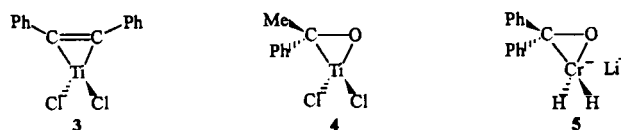

The purpose of the present study, therefore, has been to examine the facility with which divalent titanium salts form such titanacyclopropane intermediates with π-bonds, such as C=C, C≡C and C=O, as a function of the groups primarily bonded on titanium (Cl, OPr^i, F and NR_2) as well as a function of any added Lewis acid or any Lewis basic solvent.

2. Results

2.1. Preparation of titanium(II) derivatives by alkylative reduction

The most general, convenient and reliable method for preparing titanium(II) compounds, TiE_2 (**8**), is the treatment of a solution or suspension of TiE_4 (**6**) in anhydrous tetrahydrofuran (THF) under argon with two equivalents of *n*-butyllithium at $-78°C$ [12]. Slow warming of the reaction mixture to 25°C causes the intermediate **7** to decompose with the formation of invariably black **8** (E = Cl, OPr^i, F and one-half of $NPhCH_2CH_2NPh$). The by-product LiE can usually be separated from the reagent **8** by evaporating all of the THF under reduced pressure with warming. Such treatment also serves to disrupt any complex between TiE_2 and 1-butene (Eq. (2)). The residue is extracted with toluene, which dissolves the TiE_2 and leaves the LiE which can be filtered off (except for $LiOPr^i$, which is soluble). The toluene extract contains TiE_2 either as the bis-tetrahydrofuran complex (E = Cl, F) or as the solvate-free TiE_2 (E = OPr^i or one-half of $NPhCH_2CH_2NPh$). For routine use as a reagent, the TiE_2–2LiE mixture can be used directly.
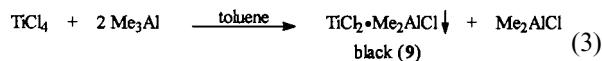

(2)
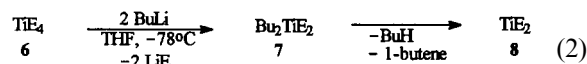
These LiE-free complexes of TiE_2 can be obtained and analyzed for the amount of Ti, E and complexed THF according to the methods described previously [12].

The preparation of TiE_2 (**8**) can alternatively be conducted in THF at $-78°C$ with ethyl-, *n*-propyl- or allylmagnesium chloride in diethyl ether and the reaction mixture brought to 25°C. In this procedure there is evidence that the TiE_2 and MgE_2 form stable complexes with each other [16].

Finally, the preparation of TiE_2 (**8**) can be undertaken in toluene, in order to avoid any complexation with a donor solvent such as THF. In this situation a

cooled solution or suspension of TiE_4 in toluene at $-78°C$ is treated with two equivalents of butyllithium in hexane, one equivalent of butyl(ethyl)magnesium in heptane (Akzo-Nobel) or two equivalents of trimethylaluminum in hexane. In each case the reaction mixture is brought to 25°C and allowed to stir for 20 h to complete the decomposition to black TiE_2. Especially with Bu_2TiF_2, stirring and warming are essential to produce TiF_2. For the TiE_2 reagents prepared from TiE_4 with BuLi or with BuMgEt, the by-product LiE or MgE_2 remains admixed and probably weakly complexed with the TiE_2.

The reaction of $TiCl_4$ with Me_3Al is noteworthy (Eq. (3)).

$$TiCl_4 \; + \; 2 \, Me_3Al \xrightarrow{\text{toluene}} TiCl_2 \cdot Me_2AlCl\downarrow \; + \; Me_2AlCl \qquad (3)$$
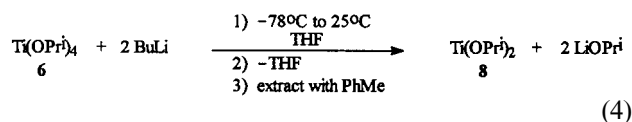$$\text{black (9)}$$

By elemental analysis the black $TiCl_2$ precipitate was found to be complexed with only one equivalent of Me_2AlCl; the other equivalent of Me_2AlCl produced was found free in solution [16]. The ^{27}Al-NMR spectrum ($CDCl_3$) of **9** showed a peak at 101.5 ppm, consistent with a tetracoordinate aluminate anion (cf. the $AlCl_4^-$ signal at 103.3 ppm in $[Cp_2Ti-C(SiMe_3)=CPhMe]^+[AlCl_4]^-$ [17]); the ^1H- and ^{13}C-NMR spectra had signals at 1.37 and 14.2 ppm, respectively. Such evidence is consistent with a polymeric structure of $TiCl^+$ centers bridged by $[Cl-AlMe_2-Cl]^-$.

2.2. Addition of titanium(II) derivatives, TiE_2 (8), to π-bonds involving carbon

2.2.1. To C=C bonds

The interaction of Grignard reagents with catalytic amounts of titanium(IV) isopropoxide (**6**, $E = OPr^i$) has led to remarkable and useful organic chemical transformations, which have been rationalized by Kulinkovich [10] and by Sato [11] as proceeding via titanacyclopropanes of type **2** (Eq. (1)). Our efforts reported here have been directed to verifying this hypothesis by the preparation of titanium(II) isopropoxide (TiE_2 (**8**), E =

Scheme 1.

OPr^i) by alkylative reduction of $Ti(OPr^i)_4$ with *n*-butyllithium (Eq. (4)). The $Ti(OPr^i)_2$ was soluble in toluene and gave ^1H- and ^{13}C-NMR signals for the isopropyl group, which were broadened to obscure ^1H hyperfine splitting, indicative of paramagnetic titanium(II). (Collaborative ESR studies of such titanium(II) derivatives are currently underway with Professor David C. Doetschman of this Department.) Significant by their absence were any absorptions due to complexed THF or 1-butene.

$$Ti(OPr^i)_4 \; + \; 2 \, BuLi \xrightarrow[\substack{2) \; -THF \\ 3) \; \text{extract with PhMe}}]{\substack{1) \; -78°C \; to \; 25°C \\ THF}} Ti(OPr^i)_2 \; + \; 2 \, LiOPr^i$$
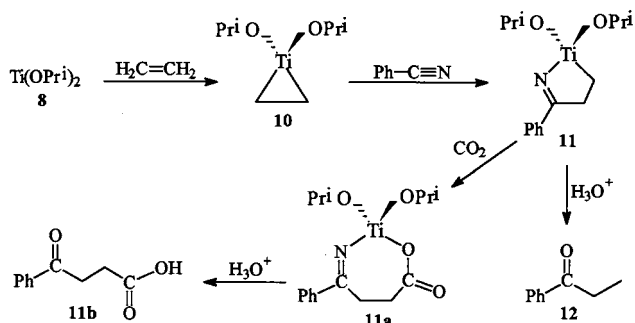$$\mathbf{6} \qquad\qquad\qquad\qquad\qquad\qquad\qquad \mathbf{8}$$
$$(4)$$

Removal of the toluene left **8** as a black solid, which can be readily redissolved in THF. Bubbling ethylene into the latter solution, the subsequent addition of benzonitrile (one-half equivalent based on **8**) and heating the reaction mixture gave upon subsequent hydrolysis 88% of ethyl phenyl ketone (**12**). This outcome is pertinent corroboration of the view that $Ti(OPr^i)_2$ has added to the π-bond of ethylene to form **10**, a process that can be termed epimetallation by analogy with the epoxidation of alkenes in the Prilezhaev reaction [18]. Insertion of benzonitrile into a C–Ti bond of **10** would readily lead to **11**, whose hydrolysis generates **12**.
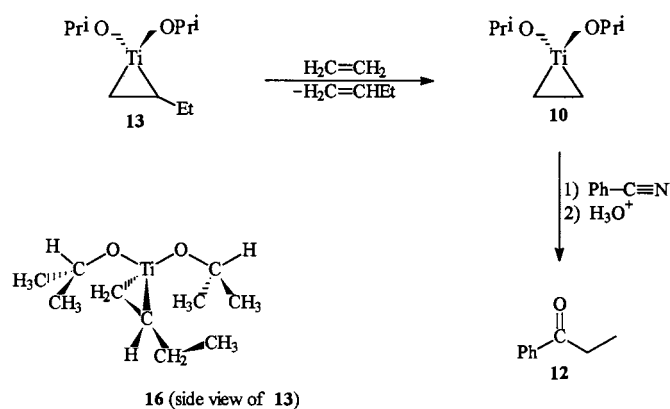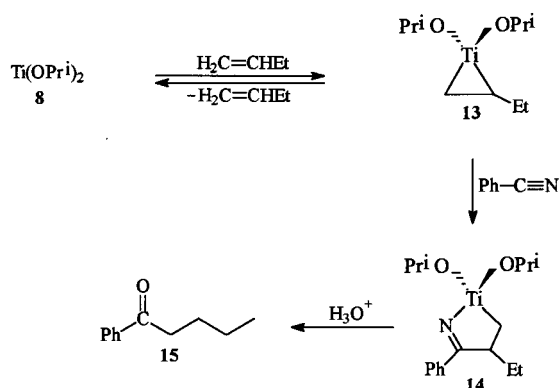
In a modification of this procedure, proof for the existence of the remaining Ti–C bond in **11** was obtained by passing CO_2 into the reaction mixture resulting from **10** and benzonitrile. Evidence that CO_2 had inserted into **11** to form **11a** came from the observation that subsequent hydrolysis of **11a** produced 3-benzoylpropanoic acid (**11b**) in a non-optimized 30% overall yield.

To our knowledge, this sequence of reactions is the first unequivocal proof of the intermediacy of $Ti(OPr^i)_2$ in the reactions discovered and developed by the Kulinkovich and the Sato groups. Furthermore, the $Ti(OPr^i)_2$ is then shown to add to a separately added olefin to form **10**, both of whose two distinct Ti–C bonds can then be identified by individual chemical trapping (Scheme 1).

In a similar manner, it can be shown that the $Ti(OPr^i)_2$ as initially generated in THF (Eq. (4)) immediately coordinates with the 1-butene arising from the alkylative reduction (Eq. (2)) to form **13**: addition of benzonitrile to the THF-solution of $Ti(OPr^i)_2$ yields **14** and subsequent hydrolysis provided a 50% yield of *n*-butyl phenyl ketone (**15**) (Scheme 2). Any concern that some or all of **15** could have resulted from the addition of any residual *n*-butyllithium to benzonitrile was completely allayed by finding that one equivalent of BuLi in THF, when allowed to warm from -78 to $+25°C$ overnight (typical reaction period employed to prepare TiE_2 in Eq. (2)), was completely destroyed by attack on THF [19].

Scheme 2.
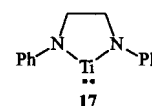

Scheme 3.

greater stability of **10** over **13** most likely arises from the lesser frontal steric strain in **10** between the isopropoxy groups and the hydrogen substituents on the C = C bond (*cf.* **16**) (Scheme 3).

Attempts to detect adducts of 1-butene with either $TiCl_2$ or TiF_2 in the THF solutions in which they are prepared (Eq. (2)) have thus far been unsuccessful. Possibly relevant is that these titanium(II) halides form THF complexes of the type, $TiX_2 \cdot 2THF$. Such complexation may be firmer than that achievable with 1-butene. By contrast, $Ti(OPr^i)_2$ can be isolated free of any complexed THF and thus is sterically capable of complexing with 1-butene readily. Moreover, in preliminary experiments the titanium(II) diamide (**17**) does show the capability of epimetallating C=C and C=O bonds (cf. infra) [20]. Like $Ti(OPr^i)_2$, titanium(II) derivative **17** fails to form an isolable THF complex and thus is capable of adding to C=C and C=O linkages.

2.2.2. To C≡C bonds

Diphenylacetylene (**18**) reacts readily either with isolated $Ti(OPr^i)_2$ (one equivalent), which is free of 1-butene or with $Ti(OPr^i)_2$ as generated in THF where $LiOPr^i$, 1-butene and adduct **13** are still present (Eq. (2)). Hydrolytic work-up yields *cis*-stilbene (**20**) as the major product (90% of product), together with minor amounts of (*E,E*)-1,2,3,4-tetraphenyl-1,3-butadiene **22** and hexaphenylbenzene (5%). The origin of these hydrocarbons can be attributed to the epimetallation adduct **19** and to the insertion of **18** into **19** to form **21** (Scheme 4).

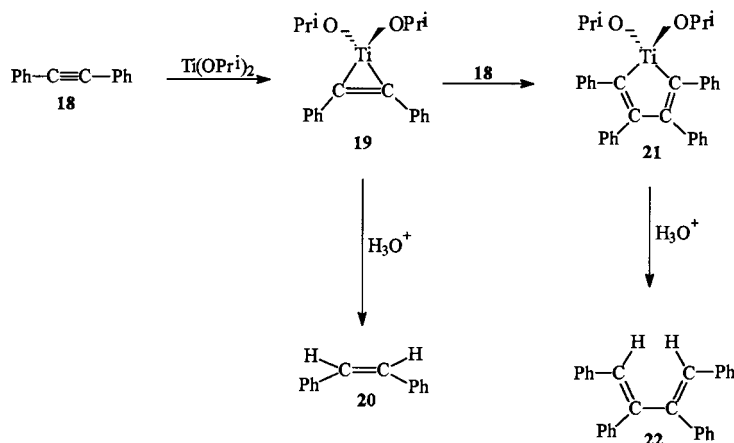This reaction scheme parallels the previously presented mechanism by which $TiCl_2$, especially in toluene

Finally, when the foregoing reaction mixture containing **13** (Scheme 2) is directly treated with ethylene gas, without prior removal of the THF and the 1-butene (**13→8**), and then with benzonitrile, hydrolytic work-up yields only ketone **12** and none of ketone **15**. This result demonstrates that titanacyclopropane **13** is in equilibrium with $Ti(OPr^i)_2$ (**8**) and 1-butene and that **8** bonds more firmly with ethylene in forming **10**. The
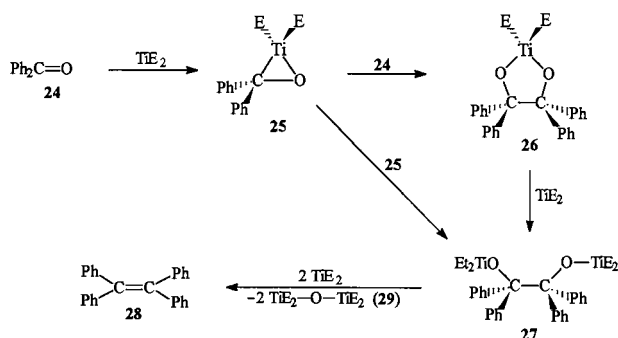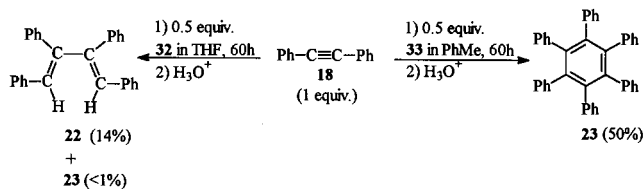

Scheme 4.

Table 1
Products from the reaction of titanium(II) derivatives, TiE$_2$, with benzophenone (24) (2:1) and subsequent hydrolysis (%)

TiE$_2$	Ph$_2$CH–OH (30)	(Ph$_2$C–OH)$_2$ (31)	Ph$_2$C=CPh$_2$ (28)
TiCl$_2$			100
TiF$_2$			100
Ti(OBu^n)$_2$	50	20	30
Ti(OPr^i)$_2$	95	<1	<1
Ti(II) amide 17	60	15	25

Scheme 5.

Scheme 6.

and in the absence of THF, effects the cyclotrimerization of 18 and other alkynes [12,14]. What is significantly different in the reaction of Ti(OPr^i)$_2$ with 18 is the minor amount of hexaphenylbenzene (23), the usual cyclotrimeric product of such reactions, and the preponderance of 20 and hence 19 as a product. In the reactions of TiCl$_2$ not even traces of an olefin like 20 can be detected. We propose that the predominance of 19 and the absence of 23 can be ascribed to the steric effect of isopropoxy groups in 19 and in 21, which would hinder the insertion of 18 into the C–Ti bond of 19 and impede the Diels–Alder addition of 18 to 21 that leads to the production of 23.

2.2.3. To C=O bonds

The titanium(II) reagents, TiCl$_2$, TiF$_2$, Ti(OBu^n)$_2$, Ti(OPr^i)$_2$ and Ti(II) amide 17, were prepared in THF by treating TiE$_4$ with two equivalents of n-butyllithium, first at -78°C and then at gentle reflux until black reaction mixtures resulted. The TiE$_2$ reagent was then treated with 0.5 equivalents of benzophenone (24) and the mixture

heated at reflux. Hydrolytic work-up gave the reduction products given in Table 1 [20].

These results can be understood in terms of the reaction scheme proposed previously for the McMurry-like transformation of 24 into tetraphenylethylene (28) by TiCl$_2$ in THF [12,14]. In Scheme 5 the epimetallation of 24 by TiE$_2$ would first generate 25, which could undergo insertion of 24 to produce pinacolate salt 26 or could simply dimerize directly to pinacolate salt 27. Further reaction of 27 with TiE$_2$ would finally provide 28 with the elimination of E$_2$Ti–O–TiE$_2$ (29). Hydrolysis of 25 and 27 would give rise to benzhydrol (30) and benzpinacol (31), respectively. In light of previous steric effects noted for Ti(OPr^i)$_2$ (cf. supra), it is readily apparent that the epimetallated intermediate 25, where E = OBu^n, OPr^i or one-half of NPh–CH$_2$–CH$_2$–NPh, would be greatly sterically hindered from either autodimerization to 27 or insertion of 24 to yield 26. Accordingly, it would accumulate in the reaction mixture and lead to 30. Similar steric interference would retard the conversion of 27 to 28 by TiE$_2$ (Scheme 5). On the other hand, the failure to detect benzhydrol in reactions of benzophenone with TiCl$_2$ or TiF$_2$ supports the conclusion that 25 (E = Cl, F) is too reactive to persist in solution.

2.3. Effect of Lewis bases on the reactivity of TiE$_2$ derivatives

The retarding effect of Lewis bases on the epimetallating reaction of TiE$_2$ derivatives is especially evident with TiCl$_2$. When prepared in THF, it can be separated from the LiCl as a complex, TiCl$_2$·2THF (32), soluble in toluene. If the reductive alkylation shown in Eq. (2) is carried out directly in toluene, the TiCl$_2$ forms a partial solution with the LiCl by-product (33). Toward diphenylacetylene (18) in refluxing solvent, 33 proved to be much more reactive in the cyclotrimerization than 32 (Scheme 6). Although the reflux temperatures of the solvents (THF at 66°C and toluene at 111°C) might be considered as responsible for the differences in the conversion of 18 into 23, temperature and time were not decisive factors. Further prolongation of time of reaction for 18 and 32 changed the conversion to 22 and 23 only slightly.

Similar reactivity differences between 33 and 32 were shown in the catalytic cyclotrimerization of 5-decyne (34) (Eq. (5)), and the cyclodimerization of 1,1-diphenylethylene (36) (Eq. (6)).
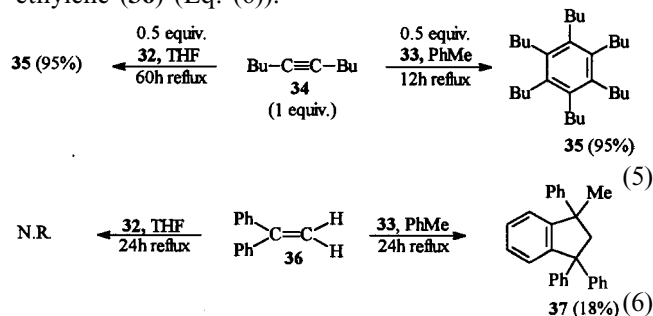
It should be noted that the foregoing comparisons of the reactivity of the reagents, **32** (TiCl$_2$·2 THF dissolved in THF), and **33** (TiCl$_2$ + 2LiCl suspended in toluene) suffer from the heterogeneity of **33** in toluene, a factor that by itself should render reagent **33** less active than reagent **32**, which is homogeneous in THF solution. Despite this hampering influence, therefore, it is all the more striking that in every case reagent **33** has proved to be more reactive than reagent **32**. This finding makes indisputable the retarding influence of THF on the reactivity of TiCl$_2$.

## 2.4. Effect of Lewis acids on the reactivity of TiE$_2$ derivatives

The reactivity of the 1:1 complex of TiCl$_2$ and Me$_2$AlCl (**9**), prepared as shown in Eq. (3) illustrates clearly the accelerating action of Me$_2$AlCl on the epimetallation of C=C and C≡C bonds by TiCl$_2$. Although the structure of the amorphous, apparently polymeric **9** has not yet been determined, its black color supports the presence of a Ti(II) salt and the ^{27}Al-NMR signal at 101.5 ppm indicates the presence of tetracoordinate aluminum. We therefore suggest that **9** has a chain polymeric structure of Ti(II)Cl cationic centers bridged by Cl$_2$AlMe$_2$ anions (**38**).
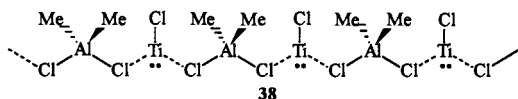
Such a structure would be similar to the known helical polymeric chain structure of [Me$_3$Sn]$^+$[AlCl$_4$]$^-$ [21]. The observed ability of **9** to polymerize ethylene and alpha-olefins at 25°C in toluene, unaided by an
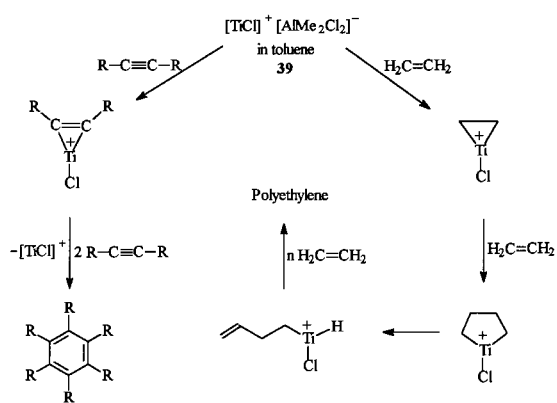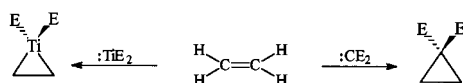
aluminum alkyl co-catalyst such as MAO, and to cyclotrimerize diphenylacetylene (**18**) to hexaphenylbenzene (**23**) at 25°C suggests **9** furnishes [TiCl]$^+$ (**39**) as the potent, electrophilic epimetallating agent to the carbon-carbon π-bond, thereby generating a three-membered titanium(IV) cation capable of rapidly inserting further alkene or alkyne units and leading to polymer or cyclotrimers (Scheme 7) [16].

3. Discussion

The epimetallation of C=C, C≡C and C=O linkages by subvalent transition metal compounds having at least one unshared electron pair, like :TiE$_2$, :CrCl and :ZrCl$_2$, bears a striking parallel to carbene additions to the same substrates (Scheme 8). In a recent analysis these similarities have induced us to term such reagents as TiE$_2$, (Me$_5$C$_5$)$_2$Ti and Bpy·Ni transition metal carbenoids [4]. The analogy with carbenes has been extended to consider whether such transition metal carbenoids would further exist either as bent singlet complexes (**40**) or linear triplet complexes (**41**).

It has been suggested that the singlet form **40** would be more likely to undergo oxidative additions with π-bonds while **41** would be more responsive to σ-bond insertions.

Finally, with reference to the electronic character of ligand E, electron-withdrawing groups (EWG) should make such carbenoids electrophilic, accepting π-electron density into unfilled d-orbitals (**42**). Conversely, electron-donating groups (**43**) should foster the nucleophilicity and hence the release of the unshared electron pair into the π*-molecular orbital of the π-bond [2,3]. In designating ligands to the M$_t$ carbenoid center as either electron-withdrawing or electron-donating, we consider that such electron-attraction or release would be operative along the σ M$_t$–E bond. With this premise, then, we judge that the Taft σ* parameter would better reflect the electronic effect, rather than the Hammett σ parameter, which measures electronic attraction or release operative via π-bonding. Only with NR$_2$ ligands, for which σ* values are not obtainable, do we propose that its strongly negative σ-value (ca. −0.8) causes it to donate electron density via π-bonding [22].
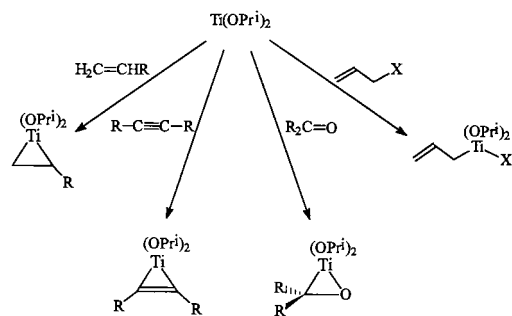

Scheme 7.

Scheme 8.

Scheme 9.

From the present study it is clear that an electrophilic carbene **43** will be deactivated in its epimetallating reactivity by Lewis bases that occupy necessary coordination sites, as with TiCl$_2$·2THF (**32**), which reacts much more slowly with alkynes or with alkenes than TiCl$_2$ in toluene (Scheme 6; Eqs. (5) and (6)). On the other hand, an electrophilic carbene will be activated by Lewis acids towards epimetallation, which acids both open up a coordination site and confer a partial positive charge on the transition metal. This would best explain the enhanced epimetallating and polymerizing action of TiCl$_2$·Me$_2$AlCl (**9**) on alkenes and alkynes (Scheme 7), the higher reactivity readily being ascribable to the generation of the more electrophilic carbenoid cation, [TiCl]$^+$.

Moreover, the failure of Ti(OPr^i)$_2$ to complex with THF, apparently on steric grounds, represents another way by which the electrophilic character and an available coordination site can be preserved for the epimetallation of C=C, C≡C and C=O linkages even in THF solution.

Nucleophilic carbenes of type **43** should be especially prone to reaction with carbonyl linkages, where the unshared electron pair in a d-orbital can be shared with a π*-orbital of the C=O group of (**44**). Coordination of Lewis bases should enhance the nucleophilicity of **43**, so long as the unshared electron pair on M$_t$ is still sterically accessible for coordination to the substrate.
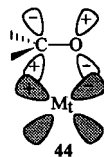
A final structural feature that can enhance the nucleophilicity of **43** is the presence of negative charge. This factor seems to explain why the:CrH$_2$ anion adds readily and extensively to benzophenone (**24**) at −78°C in THF [15]. The presence of the epimetallated adduct, chromaoxacyclopropane **45**, is corroborated by the isolation of dideuteriated benzhydrol **46** in 90% yield (Eq. (7)). Had a hydrochromation of **24** by LiCrH$_2$ ensued instead, then the benzhydrol isolated would have been Ph$_2$CH–OD.

(7)
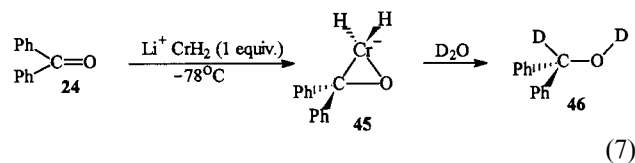
From a preparative standpoint in organic synthesis, it is noteworthy that the Ti(OPr^i)$_2$ necessary for the many synthesis applications discovered by the groups of Kulinkovich and of Sato can be made most readily and conveniently from Ti(OPr^i)$_2$ according to Eq. (2) and can be freed of any 1-butene or THF contaminants. Its adducts with alkenes, alkynes, carbonyl derivatives and allylic halides are then directly accessible (Scheme 9).

4. Conclusions

A series of titanium(II) derivatives of the type, TiCl$_2$, TiF$_2$, Ti(OPr^i)$_2$ and Ti(NPh–CH$_2$–CH$_2$–NPh) have been generated by the alkylative reduction of the corresponding titanium(IV) derivative by two equivalents of n-butyllithium in THF at −78°C. The titanium(II) derivatives can usually be obtained free of the LiE by-product and any complexed 1-butene. The TiCl$_2$ and TiF$_2$ remained complexed with THF (2 mol), while Ti(OPr^i)$_2$ and Ti(NPh–CH$_2$–CH$_2$–NPh) can be obtained free of THF.

All Ti(II) derivatives can effect the epimetallation and oligomerization of C=C, C≡C and C=O derivatives with varying facility. Lewis bases retard such reactions and Lewis acids, such as Me$_2$AlCl, can greatly accelerate such epimetallations.

Steric factors in such derivatives as Ti(OPr^i)$_2$ and Ti(NPh–CH$_2$–CH$_2$–NPh) can greatly hinder the coordination with Lewis bases as well as with π-bonds in unsaturated substrates.

Finally, the hypothesis has been corroborated that Ti(OPr^i)$_2$ forms key titanacyclopropane complexes with olefins in the Ti(OPr^i)$_4$-catalyzed reactions of Grignard reagents with esters in the Kulinkovich synthesis of cyclopropanols. As a bonus in convenience, it has been found that the Ti(OPr^i)$_2$ necessary for the Kulinkovich reaction and related reactions uncovered by Sato can be readily generated from Ti(OPr^i)$_4$ and n-butyllithium in THF.

5. Experimental

5.1. Instrumentation, analysis and starting reagents

All reactions were carried out under a positive pressure of anhydrous, oxygen-free argon. All solvents employed with organometallic compounds were dried and

distilled from a sodium metal-benzophenone ketyl mixture prior to use [23]. The IR spectra were recorded with a Perkin–Elmer instrument, model 457 and samples were measured either as mineral oil mulls or as KBr films. The NMR spectra (^{1}N and ^{13}C) were recorded with a Bruker spectrometer, model EM-360, and tetramethylsilane (Me_4Si) was used as the internal standard. The chemical shifts reported are expressed in the δ-scale and in parts per million (ppm) from the reference Me_4Si signal. The GC/MS measurements and analyses were performed with a Hewlett–Packard GC 5890/Hewlett–Packard 5970 mass-selective-detector instrument. The gas chromatographic analyses were carried out with a Hewlett–Packard instrument, model 5880, provided with a 6 ft. OV-101 packed column or with a Hewlett–Packard instrument, model 4890, having a 30 m SE-30 capillary column, respectively. Melting points were determined on a Thomas–Hoover Unimelt capillary melting point apparatus and are uncorrected.

The $TiCl_4$, TiF_4, $Ti(OPr^i)_4$, $Ti(OBu^n)_4$, ethyl (n-butyl)magnesium, trimethylaluminum and n-butyllithium were obtained from commercial sources. The titanium(IV) bis(1,2-ethane-dianilide), $Ti(NPhCH_2CH_2CH_2NPh)_2$ was prepared in toluene by heating two equivalents of 1,2-dianilinoethane with four equivalents of n-butyllithium, and then adding one equivalent of $TiCl_4$ to the resulting sodium salt, $Li_2(NPh–CH_2–CH_2NPh)$. The slurry was stirred at reflux and the LiCl filtered from the hot toluene solution. The cooled toluene solution deposited colorless $Ti(NPh–CH_2–CH_2–NPh)_2$ in 75% yield [20].

5.2. Preparation of titanium(II) derivatives, TiE$_2$, by alkylative reduction of titanium(IV) derivatives

5.2.1. With n-butyllithium

The preparation of the titanium(II) derivatives, TiE$_2$, where E = Cl, F, OPr^i, OBu^n and 0.5 NPh–CH$_2$–CH$_2$–NPh, from the TiE$_4$ derivative was conducted analogous to the published preparation of TiCl$_2$ in THF solution containing the two equivalents of LiCl by-product [12]. Given below is the model procedure for the preparation of titanium(II) isopropoxide, which was followed for all other titanium(II) derivatives as well.

To a solution of titanium(II) isopropoxide (5.95 ml, 20 mmol) dissolved in anhydrous, deoxygenated THF (30 ml) at −78°C was added slowly n-butyllithium (25 ml in hexane, 40 mmol) whereupon the solution turned light brown and then brown. The reaction mixture was stirred overnight (18 h) as the reaction temperature was allowed to rise to room temperature. At this point, a black solution of titanium(II) isopropoxide was obtained. In the analogous preparation of TiF$_2$ it was necessary to warm the THF reaction mixture to com-

plete the conversion of the brown mixture (Bu$_2^n$TiF$_2$) to the black TiF$_2$.

Such TiE$_2$ reagents in THF, still containing the LiE by-product, can be used directly for epimetallation and oligomerization reactions of unsaturated organic substrates. In fact, the results obtained with benzophenone and given in Table 1 were obtained with such reagents.

When the LiE by-product is to be removed, one can do so by the procedure used to isolate pure TiCl$_2$·2THF and previously reported [12]. This procedure applied to isolation of titanium(II) propoxide is a given as a model method for separating LiE from the other foregoing TiE$_2$ derivatives. Thus, the previously obtained black solution of titanium(II) isopropoxide in THF was subjected to reduced presence with warming at 40°C, until all volatiles (THF, 1-butene) were removed. The residue black solid was successively slurried with 3×20 ml portions of anhydrous, deoxygenated toluene and filtered. Evaporation of the toluene filtrate gave the $Ti(OPr^i)_2$ as a black solid admixed with LiOPr^i. Dissolution of a sample of $Ti(OPr^i)_2$ in THF-d_8 gave an ^{1}H-NMR spectrum showing an intense, but broad (0.4 ppm) signal centered at 1.2 ppm ($–CH(CH_3)_2$), and a weak, broadened (0.3 ppm) signal at 3.7 ppm ($–CH(CH_3)_2$), expected for the isoproxyl group. Noteworthy is the absence of any signals ascribable to THF or to 1-butene.

In a similar manner, the lithium salt-free TiF$_2$ was shown to have coordinated THF (probably two equivalents) and the $Ti(OBu^n)_2$ and $Ti(NPh–CH_2–CH_2–NPh)$ shown not to have coordinated THF.

Because of the solubility of titanium(II) isopropoxide in toluene, the reagent can be prepared directly in this solvent. Thus, to a solution of $Ti(OPr^i)_4$ (5.95 ml, 20 mmol) dissolved in 30 ml of anhydrous, deoxygenated toluene was slowly added at −78°C n-butyllithium (25 ml, 1.6 M). The initially brown-colored solution turned black over 18 h of rising to 20°C. The solution of $Ti(OPr^i)_2$ may be used directly.

5.2.2. With trimethylaluminum

The alkylative reduction of a titanium(IV) derivative with either trimethylaluminum in toluene or ethyl(-butyl)magnesium in heptane has thus far been applied only to TiCl$_4$. A detailed procedure employing Me$_3$Al is given below.

To 15.0 ml of 1.0 M TiCl$_4$ (15 mmol) in toluene and 80 ml of anhydrous, deoxygenated toluene at −78°C were slowly added 15 ml of 2.0 M Me$_3$Al (30 mmol) in toluene over 90 min. The resulting reaction mixture was allowed to warm to 20°C over 24 h to produce a black suspension. The black suspension was filtered off (3.1 g) and the ^{1}H-NMR spectrum of the light yellow filtrate showed the presence of one equivalent (ca. 15 mmol) of uncomplexed $(CH_3)_2AlCl$ (^{27}Al-NMR) signal at 175 ppm.

The black solid was analyzed for titanium and for chlorine as previously published for TiCl$_2$ [12]. (Found: Cl, 50.49; Ti, 22.50. C$_2$H$_6$Cl$_3$AlTi Calc.: Cl, 50.37; Ti, 22.68%). The black solid (9) dissolved in dry, deoxygenated CDCl$_3$ gave the following NMR signals: ^{27}Al, + 101.5 ppm, ^{1}H, 1.37 ppm and ^{13}C, 14.2 ppm.

5.3. Reactions of titanium(II) derivatives prepared in THF with benzophenone

The following titanium(II) derivatives were prepared on a 20-mmol scale in THF by alkylative reduction with *n*-butyllithium (Section 5.2): TiCl$_2$, TiF$_2$, Ti(OBu^n)$_2$, Ti(OPr^i)$_2$ and Ti(II) amide 17. To such solutions were added 1.82g (10 mmol) of benzophenone. The reaction mixture was heated under reflux for 24 h and a hydrolysis with aqueous 3 N HCl ensued. Usual separation and drying of the organic layer, solvent removal and a combined NMR spectral and chromatographic analysis yielded the results compiled in Table 1.

5.4. Reaction of titanium(II) isopropoxide in THF with benzonitrile

To the black solution of titanium(II) isopropoxide in THF was added benzonitrile (1.02 ml, 10 mmol) at 25°C. The solution was stirred at 25°C for 12 h. This period was followed by hydrolysis with aqueous 3 N HCl, extraction of the organic products in Et$_2$O (3 × 30 ml) and neutralization of the combined organic extracts with NaHCO$_3$. The extracts were dried with anhydrous MgSO$_4$ and the removal of the solvent under reduced pressure gave a thick brown liquid. Yield of the crude product = 0.82 g. From the ^{1}H-NMR spectrum, 50% of *n*-butyl phenyl ketone was found to result.

5.5. Reaction of titanium(II) isopropoxide in THF with ethylene and benzonitrile

Into 20 mmol of titanium(II) isopropoxide in THF at 25°C was passed an excess of dry ethylene gas. Then 1.05g (10 mmol) of benzonitrile was introduced and the resulting reaction mixture was stirred at room temperature for 12 h. Hydrolytic work-up and NMR spectral analysis showed that 88% of ethyl phenyl ketone had resulted and no trace of *n*-butyl phenyl ketone could be detected.

In a modification of the foregoing procedure, after the reaction between titanium(II) isopropoxide (20 mmol) and benzonitrile (10 mmol) had been permitted to react at 25°C for 10 h, the reaction mixture was cooled to − 78°C and treated with anhydrous, gaseous CO$_2$ for 2 h. Usual hydrolytic work-up with aqueous 3 N HCl and diethyl ether produced an organic extract

that was extracted with 3 × 20 ml portions of aqueous NaHCO$_3$. The combined aqueous extracts were acidified with aqueous 6 N HCl and the liberated carboxylic acid taken up in ether. The isolated acid, 3-benzoylpropanoic acid (11b), was obtained in a non-optimized 30% yield. ^{1}H-NMR (CDCl$_3$) δ 2.8 (2H, t), 3.3 (2H, t), 7.4–7.6 (8H, m), 7.9–8.0 (2H, m); ^{13}C-NMR (CDCl$_3$) δ 28.0, 33.2, 128, 128.5, 133.2, 136.4, 198.1, 198.2.

5.6. Reaction of titanium(II) isopropoxide in THF with benzophenone

The reaction of 20 mmol of titanium(II) isopropoxide in THF with 0.5 equivalents (1.82 g, 10 mmol) of benzophenone gave, after 24 h at 25°C and hydrolytic work-up, 1.65 g of product, which by NMR spectral analysis was shown to consist of 95% *cis*-stilbene, 5% of remaining benzophenone and < 1% of benzpinacol and tetraphenylethylene.

5.7. Reactions of the 1:1 complex, TiCl$_2$·Me$_2$AlCl (9)

5.7.1. With ethylene

The reaction mixture of 9 with the Me$_2$AlCl by-product resulting from admixing 1.0 mmol of TiCl$_4$ with 2.0 mmol of Me$_3$Al in 100 ml of toluene was filtered to separate 9. Black solid 9 was resuspended in 100 ml of toluene and treated with ethylene gas at 25°C and at 40 psi for 1 h. Usual hydrolytic work-up yielded 7.10 g of polyethylene, representing an activity of 54.6 g Ti^{-1} h^{-1} bar^{-1}.

5.7.2. With 1-hexene

Black 9 (1 mmol) suspended in 150 ml of cyclohexane was treated with 10 mmol of 1-hexene for 48 h at room temperature. Usual hydrolytic work-up and removal of volatiles under reduced pressure left 31 g (78%) of clear, pale yellow viscous liquid, whose ^{1}H-NMR spectrum in toluene-d_8 had two broad signals at 0.9–1.00 ppm and at 1.30–1.40 ppm in an area ratio of 3:7, consistent with the presence of a polyalkane.

5.8. Reaction of titanium(II) isoproxide with diphenylacetylene

To 20 mmol of titanium(II) isopropoxide in THF was added one equivalent of diphenylacetylene (3.56 g, 20 mmol) and the resulting solution stirred at 25°C for 24 h. Usual hydrolytic work-up and NMR spectral analysis revealed that 50% of the alkyne was recovered, 45% of the product was *cis*-stilbene and the remaining 5% was a mixture of (*E,E*)-1,2,3,4-tetraphenyl-1,3-butadiene and hexaphenylbenzene.

5.9. Reaction of titanium(II) chloride with 5-decyne

Two parallel reactions were carried out: (1) 20 mmol of $TiCl_2 \cdot 2$ THF (**32**) in 80 ml of anhydrous THF was heated at reflux with 40 mmol of 5-decyne. By intermittent sampling and GC analysis after hydrolysis it was found that a 95% yield of hexa-*n*-butylbenzene was attained after 60 h; (2) 20 mmol of $TiCl + 2LiCl$, prepared as a suspension in 80 ml of toluene, was allowed to react at reflux with 40 mmol of 5-decyne. Similar analytical sampling showed that a 95% yield of trimer was attained after 12 h.

Acknowledgements

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