Coordination-Induced Reductive Elimination and Titanium(II) Carbenoid Transfer in Reactions of Dialkyltitanium(IV) Complexes with Unsaturated Organic Substrates[1]

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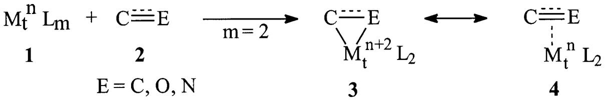
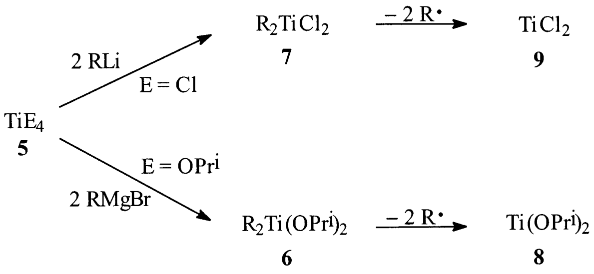
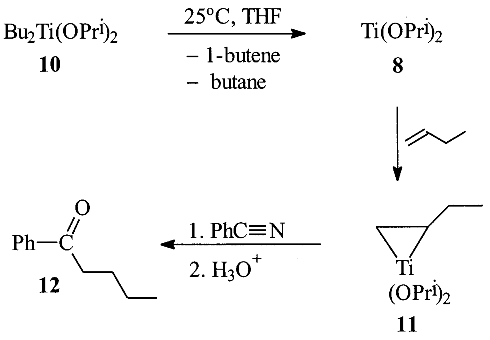
Summary: Dialkyltitanium(IV) derivatives, R_2TiE_2, where $E = X$, OR, react with unsaturated organic substrates, such as olefins, acetylenes, azoarenes, aldehydes, ketones, and imines, to undergo in high yield epimetalation with TiE_2 by transfer. In a general fashion, this finding now permits the stoichiometric generation of these three-membered titanacycles from diverse unsaturated substrates and their transformation into useful, metal-free derivatives by protolysis/deuteriolysis, oxidation, or unsaturated monomer insertion at the C−Ti bond.



Scheme 1



Scheme 2



The oxidative addition of subvalent transition-metal reagents ($M_t{}^nL_m$, **1**) to various $C{=}C$, $C\equiv C$, $C{=}O$, or $C{=}N$ linkages (as in **2**), with the formation of three-membered metallacycles, has been termed epimetalation (eq 1).[2] The bonding character of the metallacyclic adduct can range from a metallacycloprop(en)yl ring (**3**) having two σ-like $C{-}M_t$ bonds and a higher oxidation number for the metal center, $M_t{}^{n+2}$, to a π complex (**4**) having little change in the $M_t{}^n$ oxidation number. Assigning the relative importance of resonance structures **3** and **4** requires careful evaluation of the structural parameters of the individual adduct, if isolated, or of its observed chemical reactions.[2−4] The intermediacy of such metallacycles containing titanium has been postulated for a number of unusual, recently reported reactions:[5] (1) the Kulinkovich synthesis of cyclopropanols from ethyl Grignard reactions with esters catalyzed by $Ti(OPr^i)_4$,[6] (2) the de Meijere modification of the Kulinkovich synthesis, whereby (dialkylamino)cyclopropanes result from the interaction of dialkylamides and alkyl Grignard reagents catalyzed by $Ti(OPr^i)_4$,[7] (3) the Sato modification of the Kulinkovich reaction, in which the coupling of acetylenes and aldehydes, ketones, or imines is promoted by stoichiometric amounts of $Ti(OPr^i)_2$,[8] and (4) our stereoselective, stoichiometric coupling of carbonyl derivatives to pinacols or to olefins and the catalytic cyclotrimerization of acetylenes to benzene derivatives, both effected by $TiCl_2$.[2,9] In all such situations it has been assumed that the requisite titanium(II) reagent (**8** or **9**) has been generated by the alkylative reduction of TiE_4 (**5**) and the subsequent, spontaneous reductive elimination of the two R groups as alkene and alkane from R_2TiE_2

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Table 1. Transfer-Epimetalation of Unsaturated Organic Compounds by Dialkyltitanium(IV) Derivatives

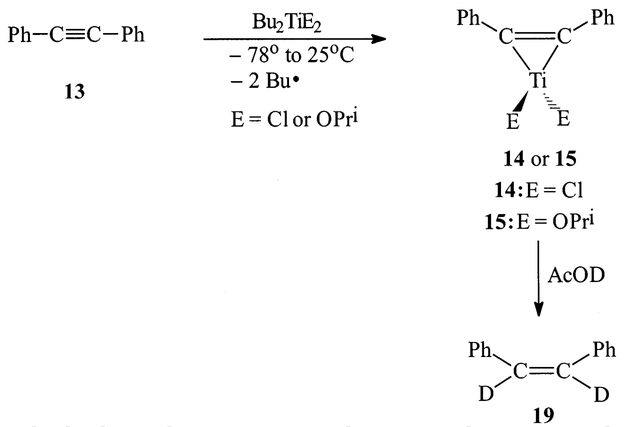
entry	unsaturated substrate	R_2TiE_2	solvent[a]	products	yield (%)
1	diphenylacetylene	$Bu_2Ti(OPr^i)_2$	THF	*cis*-stilbene[b]	99
				bibenzyl	1
2	diphenylacetylene	$Bu_2Ti(OPr^i)_2$	n-C_6H_{14}	*cis*-stilbene[b]	91
				bibenzyl	9
3	diphenylacetylene	Bu_2TiCl_2	THF	*cis*-stilbene	91
				bibenzyl	1
4	diphenylacetylene	Bu_2TiCl_2	n-C_6H_{14}	*cis*-stilbene	85
				bibenzyl	10
5	diphenylacetylene	$Pr^i_2Ti(OPr^i)_2$	Et_2O (−78 °C)	*cis*-stilbene	0
			Et_2O (0 °C)	*cis*-stilbene	3
			Et_2O (25 °C)	*cis*-stilbene	97
6	methylphenylacetylene	$Bu_2Ti(OPr^i)_2$	THF	*cis*-$C_6H_5CH{=}CHMe$	100
7	bis(trimethylsilyl)acetylene	$Bu_2Ti(OPr^i)_2$	THF	*cis*-$Me_3SiCH{=}CHSiMe_3$	100
8	cyclohexylmethylacetylene	$Bu_2Ti(OPr^i)_2$	THF	*cis*-c-$C_6H_{11}CH{=}CHMe$	99
9	di-*n*-butylacetylene	$Bu_2Ti(OPr^i)_2$	THF	*cis*-$C_4H_9CH{=}CHC_4H_9$	100
10	ethoxymethylacetylene	$Bu_2Ti(OPr^i)_2$	THF	*cis*-$EtOCH{=}CHMe$	98
11	*cis*-stilbene	$Bu_2Ti(OPr^i)_2$	THF	bibenzyl	70
				trans-stilbene	30
12	acenaphthylene	$Bu_2Ti(OPr^i)_2$	THF	acenaphthene	97
13	benzophenone	$Bu_2Ti(OPr^i)_2$	THF	benzhydrol	73
				benzopinacol	23
14	9-fluorenone	$Bu_2Ti(OPr^i)_2$	THF	9-fluorenol	100
15	(*d*,*l*)-camphor	$Bu_2Ti(OPr^i)_2$	THF	*endo*-borneol	80
				exo-borneol	16
16	2-benzoylpyridine	$Bu_2Ti(OPr^i)_2$	THF	2(1-hydroxylbenzyl)pyridine	99
				pinacol derivative	1
17	benzamide	$Bu_2Ti(OPr^i)_2$	THF	benzylamine	76
18	benzaldehyde	$Bu_2Ti(OPr^i)_2$	THF	benzyl alchohol	52
				1,2-diphenyl-1,2-ethanediol	31 (*rac*), 17 (*meso*)
19	*N*-benzylideneaniline	$Bu_2Ti(OPr^i)_2$	THF	*N*-benzylaniline	94
				rac,*meso*-1,2-dianilino-1,2-diphenylethane	6
20	azobenzene	$Bu_2Ti(OPr^i)_2$	THF	PhNHNHPh	100

[a] Unless otherwise stated, all reactions employed 5.5 mmol of Bu_2TiE_2 (E = Cl, OPr^i) and 5.0 mmol of the organic substrate in 40 mL of the solvent under an argon atmosphere, were started at −78 °C, and then continued as the mixture was warmed to 25 °C. A standard hydrolytic workup[10] and NMR spectral analysis were used to identify and analyze the products. [b] When this reaction mixture was brought from −78 to 0 °C and held at 0 °C for 2.5 h and during subsequent hydrolysis, the yield of *cis*-stilbene was 42% and that of bibenzyl 1−3%.

(**6** or **7**) (Scheme 1).[10] Thereupon, **8** or **9** would epimetalate the organic substrate, the olefin, acetylene, or carbonyl derivative,[6−9] directly or indirectly via the olefin complex formed during its generation.[8a,11] Evidence for the epimetalated olefin intermediate **11** formed in the decomposition of dibutyltitanium diisopropoxide (**10**) in THF has been adduced by capturing **11** chemically with benzonitrile and isolating ketone **12** (Scheme 2).

However, very recent and unexpected observations with isolated titanium(II) reagents have now raised serious objections to the operation of solely a direct epimetalation process as depicted in eq 1. Noteworthy, for example, is the slow reaction between $TiCl_2$ (**9**) and diphenylacetylene (**13**): there was no epimetalation whatsoever at 25 °C, and even after 60 h in refluxing THF, hydrolysis revealed the presence of only 14% of (*E*,*E*)-1,2,3,4-tetraphenyl-1,3-butadiene (**16**) and a trace of hexaphenylbenzene but no *cis*-stilbene at all. Also after contact with $Ti(OPr^i)_2$ (**8**) in THF at 25 °C for 24 h diphenylacetylene (**13**) was only partly reduced to *cis*-stilbene (**17**, 31%) and to bibenzyl (**18**, 3%). Precursors to the hydrocarbons **16**, **17**, and **18** were the titanacyclic intermediates, such as **14** or **15** for *cis*-stilbene, as deuteriolytic workup was able to demonstrate.[12]

Scheme 3



By dramatic contrast, however, when either Bu_2TiCl_2 or $Bu_2Ti(OPr^i)_2$ was generated either in THF or in hexane at −78 °C and 0.9 equiv of diphenylacetylene (**13**) was then added, a subsequent warming to 25 °C and treatment with D_2O gave a 91−99% yield of *cis*-stilbene-$d_{1,2}$ (**19**), a clear indication that the epimeta-

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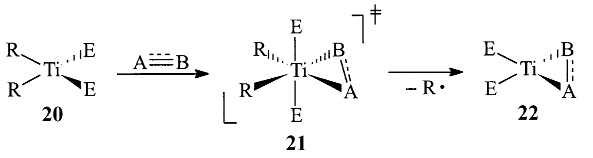
[10] (a) The preparation of $TiCl_2$, $ZrCl_2$, and $HfCl_2$, as THF solvates, has been achieved by the treatment of the appropriate M_tCl_4 with 2 equiv of *n*-butyllithium in THF at −78 °C. Eisch, J. J.; Shi, W.; Owuor, F. A. *Organometallics* **1998**, *17*, 5219. (b) In a completely analogous procedure, $Ti(OPr^i)_2$ has been prepared from $Ti(OPr^i)_4$ and 2 equiv of *n*-butyllithium in THF.[11]

[11] Eisch, J. J.; Gitua, J. N.; Otieno, P. O.; Shi, X. *J. Organomet. Chem.* **2001**, *624*, 229.

[12] Thus, workup of the individual reaction mixtures of diphenylacetylene with $TiCl_2$ (**8**) and with $Ti(OPr^i)_2$ (**9**) with D_2O isolation of the organic products, and analysis by ^1H and ^2H NMR spectroscopy and by mass spectrometry revealed that **16** was 1,4-dideuterated, **19** was 1,2-dideuterated, and **18** was 1,1,2,2-tetradeuterated.

lated adduct had been rapidly and selectively formed without oligomerization (Scheme 3). From entries 1, 3, and 5 it is further evident that the rate of transfer-epimetalation becomes significant at 0 °C or above. From the slow reaction of $TiCl_2$ in THF or of $Ti(OPr^i)_2$ in either THF or hexane with diphenylacetylene, it is clear that the high yield of epimetalated product obtained under these conditions cannot be ascribed to **8** or **9**. In fact, in the temperature range of −78 to +25 °C, the solution is light *brown* in color, typical of Bu_2TiE_2, and has not yet taken on the characteristic *black* color of TiE_2 derivatives. This leads us to propose that the epimetalating agent under these reaction conditions is the Bu_2TiE_2 derivative itself.

Similar, smooth epimetalations, in a process that may be termed *transfer-epimetalations induced by coordination*, were also readily achieved by treating Bu_2TiCl_2 or $Bu_2Ti(OPr^i)_2$ in THF or in hydrocarbon medium with a variety of olefins, acetylenes, azoarenes, imines, and carbonyl derivatives, and the gratifying results are presented in Table 1. Although the product shown is the product obtained after protolytic treatment, the product upon a parallel deuteriolytic workup contained deuterium on all the sites corresponding to any new hydrogen introduced by reaction. This finding confirms that the epititanacycle **24** was the primary reaction product of the action of Bu_2TiE_2 on the unsaturated substrate, as generalized in eq 2. It is again most noteworthy that the yields of epimetalated product obtained from the same substrates with isolated **8** or **9** itself were low (10−30%) and the reduced dimers and/or cyclotrimers were found in greater proportion.[2]



(2)

The remarkable ease of such epimetalations when the unsaturated substrates are exposed to the dialkyltitanium(IV) derivatives (**20**) (eq 2) appears likewise to lie in the coordinating ability of these substrates to form the octahedral-like transition state **21**, in which the coordinated substrate weakens the alkyl−titanium bonds and thereby induces reductive elimination, leading to the epimetalated adduct **22**.[13] Such labilization of group 4 metal−carbon bonds by Lewis bases had previously been reported by us for the allyltitanocene(III) system[14] and most recently for dibutylmetal(IV) dichlorides (**25**),[15] where the thermal reductive elimination of the allyl group or of the butyl groups, respectively, to produce a titanium(II) derivative occurred more rapidly and at a lower temperature in THF than in hydrocarbon media. The octahedral coordination attainable by Bu_2TiCl_2 in THF was held responsible for the facile homolytic reductive elimination to **9** occurring in THF. Conversely, the much lower reactivity of $Ti(OPr^i)_2$ (**8**) and of $TiCl_2$ (**9**) in direct epimetalation may be due to their association into dimers or trimers, as ongoing ESR studies now indicate.[16]

In a general manner, transfer-epimetalation affords stoichiometric quantities of three-membered titanacycles derived from diverse unsaturated substrates. In further stoichiometric reactions these metallacycles can be converted into a variety of metal-free organic derivatives, often stereoselectively. The scope and potential utility of such reactions will be exemplified with 1,1-diisopropoxy-2,3-diphenyl-1-titanacyclopropene (**17**). In addition to a number of useful transformations already reported,[17] such as protolysis (ref 8a, Scheme 3) and insertions of aldehydes, ketones, and imines into the C−Ti bond,[8b] here we report further useful derivatizations. Oxidation with 1 and 2 equiv of Me_3NO yields benzyl phenyl ketone and benzoin, respectively, 2 equiv of phenylacetylene produces 1,2,4,5-tetraphenylbenzene, and insertion of CO_2 gives (*E*)-2,3-diphenyl-2-propenoic acid.[18]

In summary, the epimetalation of olefins, acetylenes, azoarenes, imines, or carbonyl derivatives has been shown generally to be readily achieved via coordination of the organic substrate with the R_2TiE_2 derivative and the reductive elimination of the R groups, thereby effecting a direct epimetalation by transfer. The three-membered titanacycles can thereby be obtained in preparatively useful quantities and can be smoothly and stereoselectively converted into organic derivatives by various stoichiometric reactions, such as protolysis or deuteriolysis, oxidation, and insertion of an unsaturated monomer into the titanacycle.

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(13) Weakening of the alkyl−titanium bonds in an octahedral transition state such as **21** could readily be ascribed to the injection of electron density from the π bond of unsaturated substrate **2** into the σ antibonding orbitals.

(14) Eisch, J. J.; Boleslawski, M. P. *J. Organomet. Chem.* **1987**, *334*, C1.

(15) Eisch, J. J.; Owuor, F. A.; Shi, X. *Organometallics* **1999**, *18*, 2930.

(16) Doetschman, D. C.; Eisch, J. J.; Gitua, J. N. Unpublished studies in this department, 2001.

(17) In several applications of the Kulinkovich reactions to alkyne substrates, adducts such as **17** have been produced from 2 equiv of Pr^iMgCl in ether and one of $Ti(OPr^i)_4$.[8] In the formation of such titanacyclopropenes from $Pr^i{}_2Ti(OPr^i)_2$, it has been assumed without proof that $Pr^i{}_2Ti(OPr^i)_2$ first decomposes to produce 1,1-diisopropoxy-2-methyltitanacyclopropane (**a**), which then transfers $Ti(OPr^i)_2$ to the alkyne. However, current studies in our laboratory designed to trap **a** chemically with benzonitrile have failed to detect **a** in the decomposition of $Pr^i{}_2Ti(OPr^i)_2$. In contrast, note that such an analogous intermediate, **11**, can be trapped as **12** in the decomposition of $Bu_2Ti(OPr^i)_2$ (Scheme 2).

(18) These reactions were carried out with THF solutions of **17** prepared according to footnote *a* of Table 1. In unoptimized trial reactions, the given products were obtained in yields ranging from 60 to 95%.