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Highly Selective Barbier-Type Propargylations and Allenylations Catalyzed by Titanocene(III)

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Abstract: The alkyne functional group is found in many bioactive natural products and is the key to many important chemical transformations developed over recent years. Moreover, allenes have recently gained relevance as versatile reagents in organic synthesis. Mild, catalytic methods to enable the selective introduction of either alkyne or allene motifs into organic molecules are very valuable but, as yet, quite scarce. We describe an extremely mild and selective method for either the propargylation or allenylation of carbonyl compounds catalyzed by the abundant, safe, and inexpensive metal titanium. These reactions can selectively provide homopropargylic alcohols from aldehydes and ketones or α-hydroxy-allenes from aldehydes. The mechanisms involved were also investigated.

Keywords: allenes · carbonyl compounds · homogeneous catalysis · propargylations · titanium

Introduction

The alkyne functional group is present in numerous natural products, bioactive compounds, and interesting new materials,[1] for example, metal–organic frameworks (MOFs).[2] Moreover, in recent years, alkyne chemistry has received renewed interest in the field of organic synthesis, mainly due to the development of efficient alkyne-based carbon–carbon and carbon–heteroatom bond-forming processes, such as Sonogashira couplings,[3] alkyne and enyne metathesis,[4] click chemistry,[5] enyne cycloisomerizations,[6] and enantioselective additions to carbonyl groups,[7] among others.[8] On the other hand, for many years allenes have been considered unstable compounds or simple chemical curiosities but it is now known that the allene motif is present in more than 150 natural products, especially terpenoids and carotenoids.[9] Furthermore, allenes have proved themselves to be important building blocks in organic synthesis, especially in cyclization and cycloaddition reactions.[10] Nevertheless, methods for the synthesis of allenes are still scarce and most are based on alkyne isomerization reactions.[9,10] One of the most straightforward ways of introducing alkyne motifs into organic molecules is by the propargylation of carbonyl derivatives. Within this context, the one-step strategy of Barbier-type propargylations is often more convenient than the two-step strategy (preparation of the propargylic organometallic reagent and subsequent coupling with the carbonyl derivative) characteristic of Grignard-type strategies. This is especially so with propargylic halides because the Grignard reagent may be difficult to prepare in high yields.

Due to the considerable synthetic importance of propargylation reactions,[11] various transition metals, including Mg,[12] Zn,[13] In,[14] Sn,[15] Ce,[16] Sm,[17] and Cr,[18] have been assayed to achieve this reaction by the Barbier-type strategy. Nevertheless, these metals are often required in stoichiometric proportions, which may be expensive and environmentally unfriendly. Additionally, many of them work in the heterogeneous phase, which compromises the reproducibility of results and affords, in many cases, mixtures of homopropargylic and allenic alcohols.

Within this context, we hypothesized that titanocene(III) complexes might provide inexpensive catalysts to mediate Barbier-type propargylations under safe, mild conditions. In fact, titanium is the seventh most-abundant metal on Earth and many titanium compounds are non-toxic and environmentally friendly.[19] Moreover, in previous experiments titanium(III) catalysts had afforded excellent results for Barbier-type allylations.[20] Additionally, preliminary results obtained in our laboratory for propargylation reactions supported our hypothesis.[21]

We report in detail the scope and limitations of the selective Barbier-type propargylation of aldehydes and ketones and the allenylation of aldehydes catalyzed by [$TiClCp_2$] at room temperature under mild conditions compatible with many functional groups. We also present the results of a mechanistic study into these reactions and the catalytic cycle involved.

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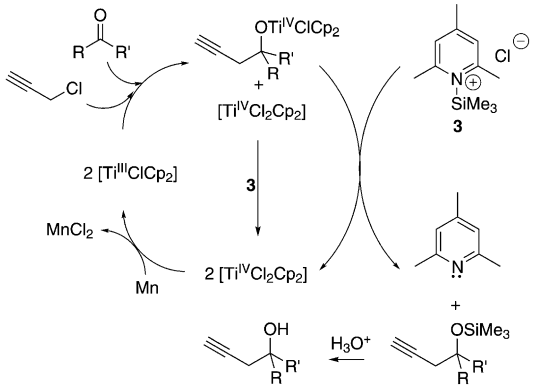
Results and Discussion

Titanocene(III)-catalyzed selective synthesis of terminal homopropargylic alcohols: Terminal alkynes have proved to be very useful intermediates in organic synthesis, especially after the development of the Sonogashira coupling and Carreira's enantioselective alkynylation of aldehydes, among other reactions.[3,7] Therefore, we began this work by studying the selective synthesis of terminal homopropargylic alcohols catalyzed by $[TiClCp_2]$.

Since its introduction by RajanBabu and Nugent as a mild, single-electron-transfer reagent,[22] $[TiClCp_2]$ has become a formidable tool in organic chemistry. In fact, this complex is capable of catalyzing the homolytic ring opening of epoxides,[23] the pinacol coupling of conjugated aldehydes,[24] stereoselective couplings between aldehydes and conjugated alkenals,[25] Reformatsky-type processes,[26] divergent C–C bond-forming reactions with modulation by Ni or Pd,[27] and other free-radical-based transformations.[28]

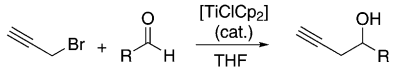
$[TiClCp_2]$ (**1**) can be easily generated in situ, simply by stirring commercially available $[TiCl_2Cp_2]$ with Mn dust in deoxygenated THF. This method was chosen for the present study because it is the most convenient procedure from a practical point of view. When generated by this method, it should be noted that the complex exists as an equilibrium mixture of the monomer **1** and dimeric species $[(TiClCp_2)_2]$ (**2**), presumably with free coordination sites occupied by THF molecules.[29] Moreover, with the aid of a titanocene-regenerating agent, such as **3** (formed by the combination of Me_3SiCl and 2,4,6-collidine, developed in our laboratory),[23f] Ti-catalyzed propargylations could be conducted with substoichiometric amounts of $[TiCl_2Cp_2]$ (Scheme 1).



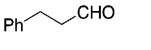
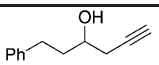
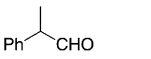
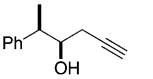
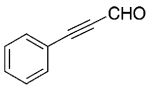
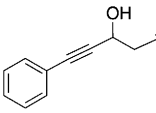
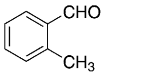
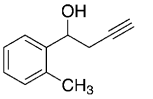
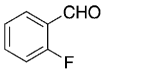
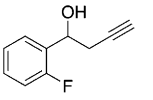
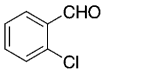
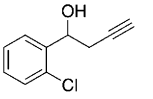
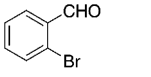
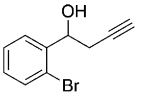
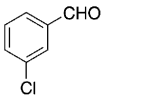
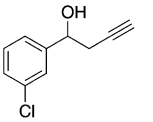
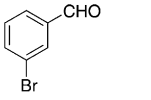
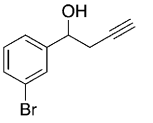
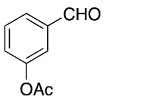
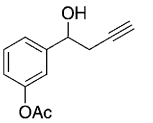
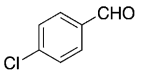
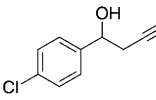
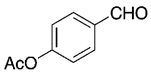
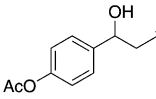
Scheme 1. Anticipated catalytic cycle for Ti-induced Barbier-type propargylations.

To confirm this hypothesis, we treated aldehydes **6–17** with halides **4** and **5** in the presence of substoichiometric $[TiCl_2Cp_2]$ (0.2 equiv), relatively cheap Mn dust, and a combination of Me_3SiCl and 2,4,6-collidine.[30] Thus, we obtained yields in the range of 57–99% for secondary homopropargylic alcohols **18–29** (Table 1). Bromide **4** always afforded better yields than chloride **5**. A control experiment in the absence of titanium did not lead to any coupling product.

Table 1. Barbier-type propargylation of aldehydes **6–17** catalyzed by $[TiClCp_2]$.[a]



4 6-17 18-29

Entry	Aldehyde		Product		Yield[b] [%]
1		**6**		**18**	57
2		**7**		**19**	80[c]
3		**8**		**20**	87
4		**9**		**21**	90
5		**10**		**22**	66
6		**11**		**23**	57
7		**12**		**24**	83
8		**13**		**25**	94
9		**14**		**26**	87
10		**15**		**27**	99
11		**16**		**28**	82
12		**17**		**29**	72

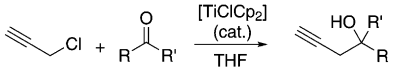
[a] Propargyl halide **4** afforded the best yield in all cases. [b] The homopropargylic alcohol was sometimes accompanied by a minor quantity of the corresponding trimethylsilyl ether, which was easily transformed into the alcohol. [c] *syn*/*anti* 9:1.

The results summarized in Table 1 suggest that this Ti-catalyzed procedure might become a general method for the chemoselective synthesis of terminal alkynes from aldehydes, and thus avoid the formation of allene byproducts

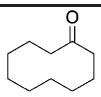
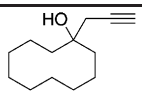
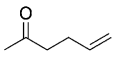
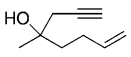
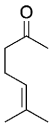
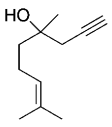
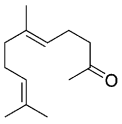
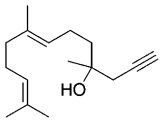
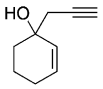
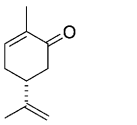
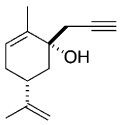
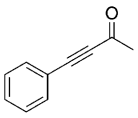
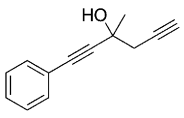
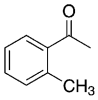
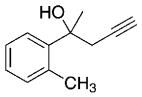
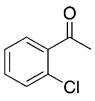
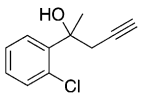
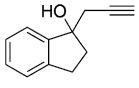
commonly found in previously described propargylation methods.[11–18] Additionally, considerable stereoselectivity was observed for the propargylation of α-substituted aldehyde **7** (Table 1, entry 2; *syn*/*anti* = 9:1), which can be understood by Cram's rule.[31] It should be noted that the reactions took place at room temperature under mild conditions compatible with several functional groups, including conjugated alkynes, esters, fluorides, chlorides, and bromides. Moreover, the reaction worked well with *o*-, *m*-, and *p*-substituted aromatic aldehydes.

The results summarized in Table 2 confirm that the Ti-catalyzed procedure was also useful for the selective propargylation of aliphatic, aromatic, and α,β-unsaturated ketones, to afford tertiary homopropargylic alcohols in yields that ranged from 53–99%. Chloride **5** always led to better results than bromide **4** in the role of pronucleophile.

Table 2. Barbier-type propargylation of ketones **30–39** catalyzed by $[TiClCp_2]$.[a]



5 **30-39** **40-49**

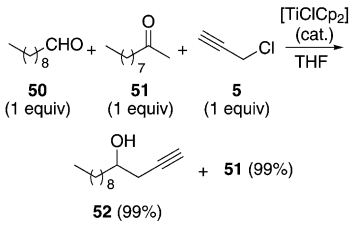
Entry	Ketone		Product		Yield[b] [%]
1		**30**		**40**	73
2		**31**		**41**	85
3		**32**		**42**	96
4		**33**		**43**	89
5		**34**		**44**	63
6		**35**		**45**	81
7		**36**		**46**	80
8		**37**		**47**	53
9		**38**		**48**	99
10		**39**		**49**	92

[a] Propargyl halide **5** provided the best yield in all cases. [b] The homopropargylic alcohol was sometimes accompanied by a minor quantity of the corresponding trimethylsilyl ether, which was easily transformed into the alcohol.

It should be noted that, once again, we did not detect the formation of any allenic byproduct. Moreover, the regio- and stereoselectivity of the Ti-catalyzed propargylation of carvone (**35**) was noteworthy because it only produced product **45**, derived from axial 1,2-addition (Table 2, entry 6). It is known that the transition state (TS) for the axial addition of organometallic nucleophiles to cyclohexanones has lower energy than the TS for equatorial addition.[32] This is especially so in the case of **35**, which has additional steric bulk in the equatorial plane by virtue of its methyl group.[33] Therefore, the stereochemical outcome of our propargylation suggests that the reaction took place by the 1,2-addition of a bulky titanocene derivative (see mechanistic studies and discussion below).

As for aldehydes, Ti-catalyzed propargylation of ketones took place at room temperature under mild conditions compatible with different functional groups, which included alkenes, conjugated alkenes and alkynes, and chlorides.

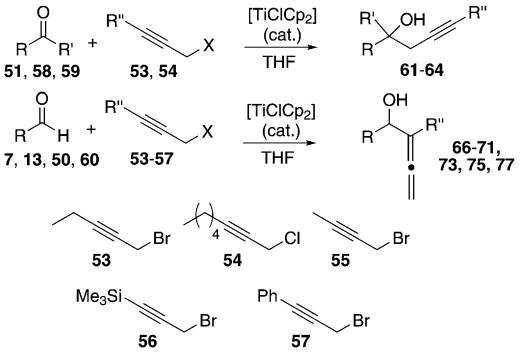
Selectivity is one of the most desirable properties for any method in organic synthesis.[34] Therefore, we assayed the capacity of our procedure for discrimination between aldehydes and ketones. The results of the competition experiment depicted in Scheme 2 indicated that the propargylation of decanal (**50**) was much faster than that of 2-decanone (**51**). This phenomenon could be exploited to advantage in the chemoselective propargylation of aldehydes in the presence of ketones.



Scheme 2. Chemoselective Ti-catalyzed propargylation of decanal.

Titanocene(III)-catalyzed selective synthesis of internal homopropargylic alcohols and α-hydroxy-allenes: Once we were confident about the utility of the Ti-catalyzed method for the synthesis of terminal homopropargylic alcohols we decided to explore the synthesis of the internal analogues. For this purpose, we chose substituted propargyl halides **53–57** as pronucleophiles. As expected, the reactions of ketones **51**, **58**, and **59** with halides **53** and **54**, catalyzed by $[TiClCp_2]$, gave rise mainly to internal alkynes **61–64**, together with a minor quantity of allene **65** in the case of the aromatic ketone **59** (Table 3, entries 1–4). In contrast, the reactions of aldehydes **7**, **13**, **50**, and **60** with pronucleophiles **53–57**, catalyzed by $[TiClCp_2]$, unexpectedly provided α-hy-

Table 3. Internal homopropargylic alcohols and α-hydroxy-allenes from ketones and aldehydes, respectively.



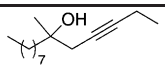
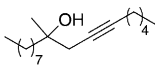
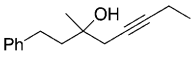
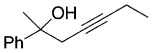
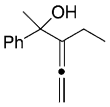
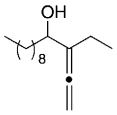
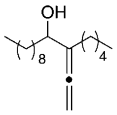
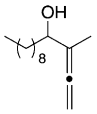
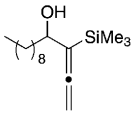
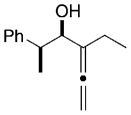
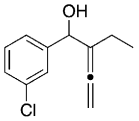
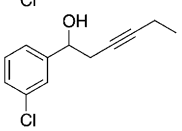
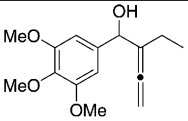
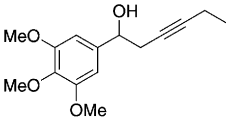
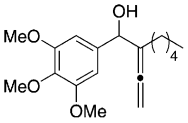
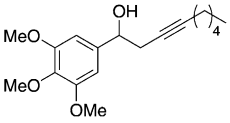
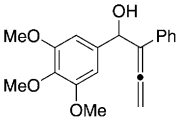
Entry	Substrate	X[a]	Product		Yield [%]
1	**51**	**53**		**61**[b]	77
2	**51**	**54**		**62**	79
3	**58**	**53**		**63**	71
				**64**	58
4	**59**	**53**		**65**	20
5	**50**	**53**		**66**[c]	68
6	**50**	**54**		**67**[c]	91
7	**50**	**55**		**68**[c]	70
8	**50**	**56**		**69**	73
9	**7**	**53**		**70**[d]	71
				**71**	66
10	**13**	**53**		**72**	19

Table 3. (Continued)

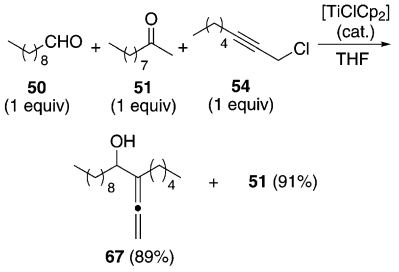
Entry	Substrate	X[a]	Product		Yield [%]
11	**60**	**53**		**73**	52
				**74**	20
12	**60**	**54**		**75**	61
				**76**	20
13	**60**	**57**		**77**	84

[a] Propargyl halide. [b] A trace of an allene was detected. [c] A trace of an internal alkyne was detected. [d] *syn*/*anti* 2:1.

droxy-allenes **66**–**71**, **73**, **75**, and **77**, accompanied by minor quantities of alkynes **72**, **74**, and **76** in the cases of aromatic aldehydes **13** and **60** (Table 3, entries 5–13).

The unexpected difference in behavior between aldehydes and ketones was intriguing and is discussed below. Aside from mechanistic considerations, it should be noted that this reaction constitutes a novel and convenient method for the straightforward synthesis of α-hydroxy-allenes from aldehydes. Also notable is that the α-hydroxy-allene motif is present in several bioactive natural products and its chemical synthesis is hard to achieve by any other method.[9] Moreover, our procedure requires only catalytic proportions of a non-toxic titanium complex, takes place at room temperature under very mild conditions, and is compatible with numerous functional groups.

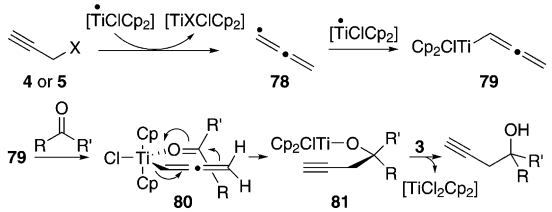
Finally, we assayed the Ti-catalyzed chemoselective allenylation of **50** in the presence of **51** with internal chloroalkyne **54** as the pronucleophile (Scheme 3). We obtained an



Scheme 3. Competition experiment between decanal and 2-decanone.

89% yield of α-hydroxy-allene **67** and **51** was recovered unchanged. Moreover, homopropargylic alcohol **62**, potentially derived from ketone **51**, was not detected.

Mechanistic studies and discussion: Ti-catalyzed reactions of terminal propargyl halides **4** and **5** with aldehydes and ketones (Tables 1 and 2) exclusively afforded homopropargylic alcohols in all cases assayed. These results can be rationalized by the formation of an allenyl radical (**78**), which would be trapped by a second [$TiClCp_2$] species to give an organometallic allenyltitanium species (**79**). Intermediate **79** would eventually attack the carbonyl compound present via an intermediate such as **80** (Scheme 4), in a similar manner to that previously proposed for Nozaki–Hiyama propargylations.[18]



Scheme 4. Proposed mechanism for the selective formation of terminal homopropargylic alcohols.

To test this hypothesis, we reacted propargyl chloride **5** with [$TiClCp_2$] in [D_8]THF in the absence of any carbonyl compound. After 1 h stirring, we analyzed the reaction mixture by NMR spectroscopy. The ^{13}C NMR spectrum showed signals at $\delta = 78.2$ (CH_2), 122.2 (CH), and 218.1 ppm (C), which could be assigned to **79**, and supports the mechanism proposed in Scheme 4. On the other hand, signals assignable to a potential propargyltitanium species were not observed.

The above mechanism may also account for the observed chemoselectivity towards aldehydes (Scheme 2). The transition state (TS) between **80** and **81** would presumably involve six delocalized electrons in a flat arrangement (Figure 1).

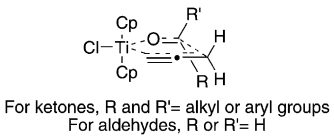
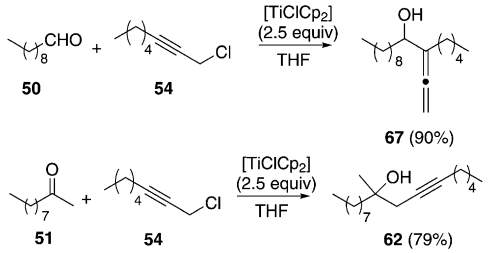


Figure 1. TS formed between **80** and **81**.

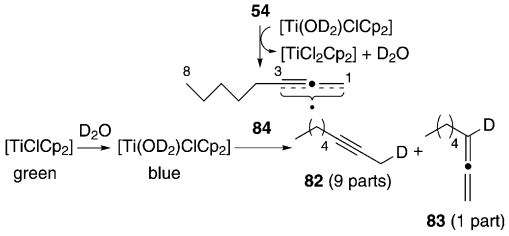
From a thermodynamic point of view, this could represent quite a favorable situation and, in fact, reactions conducted at room temperature afforded good-to-excellent yields. Nevertheless, in ketones the R and R′ substituents are alkyl or aryl groups and are both eclipsed by the adjacent hydrogen atoms. However, in aldehydes either R or R′ is a hydrogen atom and, therefore, only one bulky alkyl or aryl group is eclipsed. Thus, steric hindrance in the TS is lower for aldehydes and consequently the activation energy (E_a) is also lower, hence the reaction rate is faster than for ketones.

The mechanism depicted in Scheme 4, however, cannot explain the formation of α-hydroxy-allenes **66**–**71**, **73**, **75**, and **77** from aldehydes (Table 3, entries 5–13). Therefore, we decided to clarify the difference in behavior between aldehydes and ketones in reactions with the substituted pronucleophiles **53**–**57**. Nevertheless, the titanocene(III)-based catalytic system involves many experimental variables and, as a consequence, the experimental results might become too complicated to be interpreted in a straightforward way. So, we decided to assay the reactions of **50** and **51** with substituted pronucleophile **54** promoted by an excess of [$TiClCp_2$], thus simplifying the reaction system by removal of the titanocene-regenerating agent **3** (Scheme 5). Gratifyingly, the results obtained under these conditions were very similar to those obtained with the catalytic system (Table 3). These observations not only allowed us to use a simpler system for our mechanistic studies but also suggested that the relative proportions of the monomeric and dimeric forms of the titanocene complex in the equilibrium **1**⇌**2**[29] do not substantially affect the reaction mechanism.



Scheme 5. Reactions between aldehyde **50** and ketone **51** with pronucleophile **54** promoted by an excess of [$TiClCp_2$].

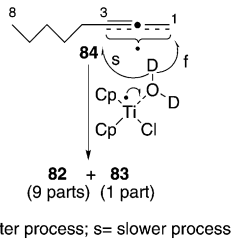
The formation of α-hydroxy-allenes from aldehydes might be put down to the direct attack of an allenyl radical, similar to the reaction between prenyl radicals and some aldehydes.[20b] Therefore, we decided to trap these potential allenyl radicals. It is known that radicals can be reduced by hydrogen atom transfer (HAT) from [$Ti(OH_2)ClCp_2$].[35] We treated propargyl halide **54** with [$Ti(OD_2)ClCp_2$] (deep blue) prepared in situ from [$TiClCp_2$] (lime green) and D_2O (Scheme 6). In this way, we obtained a 9:1 mixture of isotopomers **82** and **83** with deuterium incorporation (DI)



Scheme 6. Reaction between **54** and [$Ti(OD_2)ClCp_2$].

greater than 95% in both compounds. It is noteworthy that no dimerization products were detected (GC-MS analysis), which indicated that, under the experimental conditions employed, deuterium atom transfer (DAT) was faster than the potential radical–radical coupling that would have led to the formation of dimers.

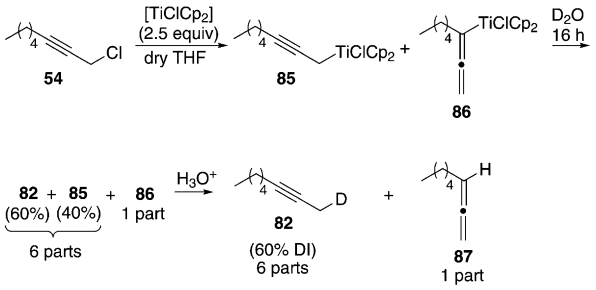
To the best of our knowledge this is the first evidence that suggests that, in contrast to allylic and benzylic radicals,[35d] propargylic radicals can be effectively reduced by HAT from water in a reaction promoted by $[TiClCp_2]$. Moreover, the relative proportions of **82**/**83** indicate that the C1 radical tautomer of **84** is more reactive than its C3 counterpart against $[Ti(OD_2)ClCp_2]$ (Scheme 7). In other words, the E_a of DAT to the C1 radical is substantially lower than the E_a of DAT to the C3 radical.



Scheme 7. DAT from $[Ti(OD_2)ClCp_2]$ to propargylic radical **84**.

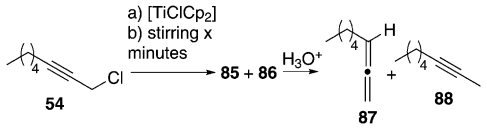
The above observations cast doubt on the possibility of radical attack being responsible for the formation of α-hydroxy-allenes from aldehydes. Nevertheless, it is known that conjugated aldehydes are more susceptible than non-conjugated aldehydes to attack by free radicals generated by $[TiClCp_2]$[20b] and thus the possibility of minor propargylic alcohols **72**, **74**, and **76** (Table 3, entries 10–12) derived from attack by the propargylic radical **84** on aromatic aldehydes cannot be ruled out.

A second way to explain the formation of α-hydroxy-allenes **66**–**71**, **73**, **75**, and **77** might be via propargyltitanium intermediates. To study these potential organometallic intermediates we treated propargyl chloride **54** with an excess of $[TiClCp_2]$. Once all of the starting material was consumed we added D_2O, stirred the reaction mixture for 16 h, and obtained a 1:6 mixture of allene **87** and deuterium-labeled alkyne **82** (60% DI) (Scheme 8).



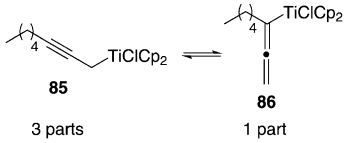
Scheme 8. Neutral D_2O-promoted hydrolysis of propargyltitanium species **85**.

These observations indicated that allenyltitanium species **86** was inert to neutral hydrolysis with D_2O and, under these conditions, was more robust than propargyltitanium species **85**, 60% of which underwent neutral deuterolysis. Within this context, we performed a series of six experiments by treating **54** with $[TiClCp_2]$, followed by an acidic hydrolysis quench after 0.5, 2, 10, 30, 60, and 120 min (Scheme 9).



Scheme 9. Preparation and acidic hydrolysis of the **85**/**86** mixture.

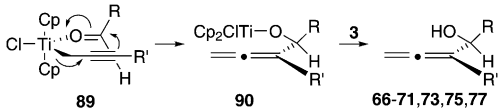
At the respective time points we obtained 1:1, 1:1.5, 1:2, 1:3, 1:3, and 1:3 mixtures of products **87** and **88**. These results suggest that 30 s after the addition of $[TiClCp_2]$, an equimolar mixture of complexes **85** and **86** is formed. This mixture gradually evolves to an equilibrium in which **85** predominates over **86** in a proportion of 3:1 (Scheme 10). This



Scheme 10. Equilibrium between complexes **85** and **86**.

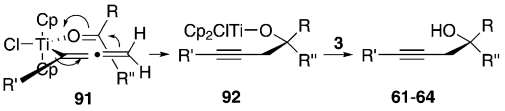
equilibrium is reached by 30 min after the addition of $[TiClCp_2]$. The equilibrium between propargyltitanium and allenyltitanium species has been hypothesized previously[36] but, to the best of our knowledge, our results represent the first experimental evidence to support this hypothesis and determine the relative proportions in the equilibrium.

In this scenario, it is not too far-fetched to suppose that α-hydroxy-allenes **66**–**71**, **73**, **75**, and **77** might be formed by reaction between propargyltitanium complexes, such as **85**, and the appropriate aldehyde via intermediate **89**, depicted in Scheme 11.



Scheme 11. Proposed mechanism for the selective formation of α-hydroxy-allenes from aldehydes.

Nevertheless, reactions with ketones **51**, **58**, and **59** mainly afforded internal homopropargylic alcohols **61**–**64** (Table 3, entries 1–4). Formation of these alkynes cannot be justified via an intermediate such as **89**. Instead, these products could derive from allenyltitanium species analogous to **86** via intermediates of type **91** (Scheme 12).



Scheme 12. Proposed mechanism for the selective formation of internal homopropargylic alcohols from ketones.

In the case of ketones, it would seem that TS **93** (Figure 2), derived from attack by a propargyltitanium species, such as **85**, would be energetically disfavored due to steric hindrance from R′, which is in gauche orientation with respect to both R and R″ (in ketones, R and R″ are bulky alkyl or aryl groups). Thus, TS **94** (Figure 2)—formed between intermediates **91** and **92**), in which this steric hindrance does not exist—would be energetically more favorable and lead mainly to homopropargylic alcohols **61**–**64**.

Whatever the case, the formation of the minor product **65** (Table 3, entry 4) from attack by a propargyltitanium species via TS **93** cannot be ruled out.

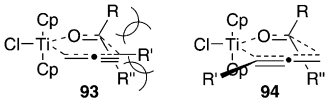


Figure 2. Potential transition states **93** and **94**.

In summary, [$TiClCp_2$] reacts with unsubstituted propargyl halides (such as **4** and **5**) to give allenyltitanium species **79**, which, in turn, attacks aldehydes and ketones to exclusively provide terminal homopropargylic alcohols. On the other hand, [$TiClCp_2$] reacts with substituted propargyl halides (such as **53**–**57**) to give an equilibrium mixture of propargyltitanium and allenyltitanium complexes, such as **85** and **86**. Aldehydes react faster with propargyltitanium species than with allenyltitanium species, thus mainly generate α-hydroxy-allenes. In contrast, ketones react faster with allenyltitanium species, thus mainly afford internal homopropargylic alcohols.

Conclusion

Titanium is one of the most abundant, safe, and environmentally friendly transition metals on Earth. We have described a novel, selective method for either the propargylation or allenylation of aldehydes and ketones catalyzed by titanocene(III). Reactions proceed at room temperature under extremely mild conditions, compatible with numerous functional groups, and provide terminal homopropargylic alcohols from aldehydes and ketones, internal homopropargylic alcohols from ketones, and α-hydroxy-allenes from aldehydes, in yields of up to 99%. Mechanistic studies strongly suggest that these processes occur mainly by the formation of organometallic propargyltitanium or allenyltitanium species and subsequent attack on a carbonyl compound. We also present, for the first time, experimental evidence for the chemical equilibrium between propargyltitanium and allenyltitanium species. Additionally, the unprecedented reduction of propargyl radicals by hydrogen atom transfer from water promoted by [$TiClCp_2$] is shown.

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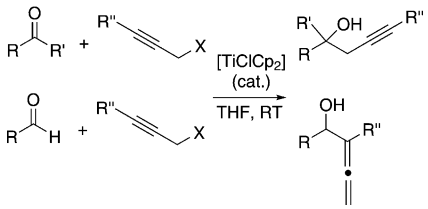
Effectiveness, selectivity, and sustainability are key properties of this novel method for Ti-catalyzed Barbier-type propargylation/allenylation. The reaction proceeds at RT under mild conditions compatible with numerous functional groups and affords homopropargylic alcohols from aldehydes and ketones and α-hydroxy-allenes from aldehydes (see scheme).



Synthetic Methods

J. Muñoz-Bascón, I. Sancho-Sanz, E. Álvarez-Manzaneda, A. Rosales, J. E. Oltra** ..... ▮▮▮▮–▮▮▮▮

Highly Selective Barbier-Type Propargylations and Allenylations Catalyzed by Titanocene(III)