



Synthesis and reactivity of polymetallated olefins and functionalized metalloalkynes

Julia Kaftanov, Claudia Averbuj, Natalia Vais-Morlender, Annie Liard, Ilan Marek*

Department of Chemistry and Institute of Catalysis Science and Technology, Technion-Israel Institute of Technology, Technion City, 32 000 Haifa, Israel

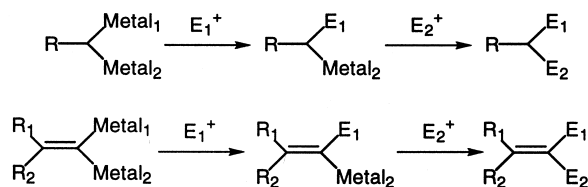
Received 4 October 1999; accepted 19 November 1999

Abstract

The first straightforward synthesis of tris-metallated olefins and functionalized metallated alkynes is reported via the use of low-valent titanium derivatives. ©2000 Elsevier Science Ltd All rights reserved.

Keywords: Alkynes; Functionalized metalloalkynes; Olefins; Polymetallated olefins; Titanium

The development of new strategies in organic syntheses with a minimum of chemical steps is becoming increasingly necessary for the efficient assembly of complex molecular structures [1], and then the combination of multiple reactions in a single operation represents a particularly efficient approach. Among different strategies [2], the synthesis and reactivity of geminated organobismetallics is becoming increasingly useful for the synthesis of molecules with complex architecture [3].



One particular example is the preparation of polysubstituted olefins in a single-pot operation from polymetallated olefins. Indeed, several 1,1-dimetalloalkenes with a large variety of metals (dilithium [4], aluminum and titanium [5,6], aluminum and zirconium [5,6], zinc and zirconium [7,8], zinc and boron [9], copper and boron [9], copper and zirconium [7,8], lithium and boron [10,11] and boron and zirconium [12–14]) have been used as a source of polysubstituted carbon–carbon double bonds with variable stereochemical purities. In this context, we have already reported that the allylmethallation of alkynyl metals [15–18] leads to

sp^2 1,1-bis-metallic derivatives in good overall yield [19,20]. These geminated bis-anions react selectively with two different electrophiles and can be a source of chiral α,α' -disubstituted alkynes [19–21] (Scheme 1).

However, the major drawback of this strategy is the necessary incorporation of the allyl moiety on the carbon skeleton. Also we needed a more general preparation of sp^2 polymetallated derivatives allowing the access to a wide variety of carbon skeletons. To answer this requirement, we thought that some organometallic derivatives might behave, to a certain extent, like a carbon atom. If this assumption is correct, it should then be possible to prepare an organometallic derivative on an already metallated carbon center. In order to test this new concept, we used the pioneering work of Sato and co-workers [22], who demonstrated that various disubstituted alkynes react with diisopropoxy(η^2 -propene)-titanium (**1**), readily generated by the reaction of $Ti(OiPr)_4$ with 2 equivalents of $iPrMgX$, to give the corresponding titanacyclopropene derivatives as described in Scheme 2, path A.

As terminal alkynes failed to participate in the present reaction (path B versus path A), the Sato reagent was ideal for testing this new concept: can a metallated alkyne behave like a disubstituted alkyne (path C identical to path A) and so an organometallic moiety like a carbon atom?

Our initial attempts were to add alkynyl metal derivatives to the preformed $Ti(II)$ complex (**1**) as described in Scheme 3.

The metallated titanacyclopropenes were effectively obtained with moderate chemical yield for $MX_{n-1} =$

* Corresponding author. Tel.: +972-4-8293709; fax: 972-4-8233735; e-mail: chilanm@tx.technion.ac.il

Table 1
Generalization for the synthesis of metallated titanacyclopropenes

Entry	R	X	Compound	Yield (%) ^a
1	oct	Cl	6	90
2	hex	Br	9	75
3	hex	I	10	65
4	hex	SPh	11	70
5	tolyl	Cl	12	95
6	tert- <i>O</i> -amyl(CH ₂) ₂	Cl	13	93

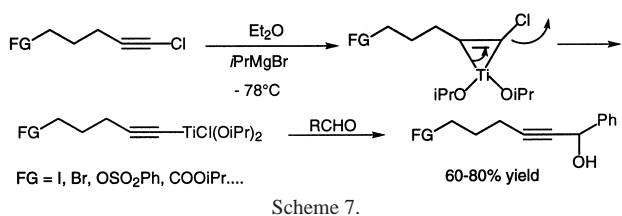
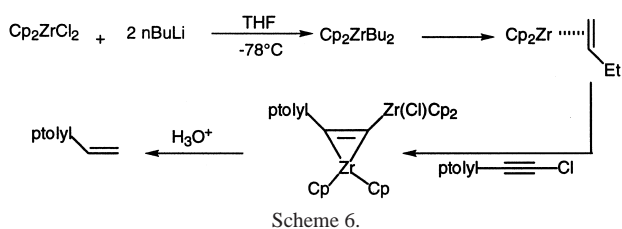
^a Isolated yields after hydrolysis.

yield. The scope of this reaction is broad, as described in Table 1, since alkyl as well as aromatic groups on the alkyne give the polymetallated olefins whatever the nature of the leaving group (compare entries 1, 2 and 3).

The reactivity of zirconocenes [23] and titanocenes [24] was also studied in this process and we found that only the combination zirconocenes/aromatic halogenoalkynes gave good results (Scheme 6).

In a parallel study, we have also investigated the reactivity of tribromo olefins such as compound **8** (see Scheme 5) and found that this compound can undergo specific coupling reaction with various organometallics in the presence of a catalytic amount of transition metal [25].

We finally turned our attention to the new preparation of metalloalkyne (**4**) (Scheme 5) via diisopropoxy(η^2 -propene)titanium (**1**). Indeed, it is known that triisopropoxy-alkynyl titanium derivatives react chemoselectively with carbonyl compounds to give the corresponding carbinols in high yield [26]. However, and to the best of our knowledge, these metallated alkynes were always prepared by transmetallation between alkynyl lithium and ClTi(OiPr)₃, which precludes the presence of sensitive moieties on the carbon skeleton [27]. It then appeared to us that this new methodology established for the synthesis of **4** could be an interesting alternative for the formation of chlorodiisopropoxyalkynyl



titanium possessing sensitive groups [28]. This was effectively the case, as described in Scheme 7.

The metallated alkyne (**14**) shows a remarkable functional group tolerance, and several classical functional organic moieties can be present during the formation of the chlorodiisopropoxyalkynyl titanium derivatives.

In conclusion, this new concept (organometallic derivative can behave like a carbon atom) enabled us to describe the first and straightforward preparation of tris-metallated olefins in high chemical yield. Moreover, during the preparation of the latter, we found a new preparation of metallated alkynes possessing functional groups.

Acknowledgements

I.M. is the Holder of the Lawrence G. Horowitz Career Development Chair, is a Ygal Alon Fellow and Evelyn and Salman Grand Academic Lectureship — USA. This research was supported in part by The Israel Science Foundation founded by The Academy of Sciences and Humanities (No. 060-471) and by the fund for the promotion of research at the Technion. Acknowledgment is also made to the donors of The Petroleum Research Fund, administered by the ACS, for partial support of this research (PRF 33747-AC1). The authors thank also P. and E. Nathan Research Fund, N. Haar and R. Zinn Research Fund. J.K. thanks the Ministry of Immigrant Absorption for financial support.

References

- [1] E.J. Corey, X. Cheng, *The Logic of Chemical Synthesis* (1989) Wiley-Interscience, New York.
- [2] *Frontiers in Organic Synthesis, Chem. Rev.* 1 (1996) 96.
- [3] I. Marek, J.F. Normant, *Chem. Rev.* 96 (1996) 3241.
- [4] J. Barluenga, M.A. Rodriguez, P.J. Campos, G. Asensio, *J. Am. Chem. Soc.* 110 (1988) 5567 and references cited therein.
- [5] T. Yoshida, E.I. Negishi, *J. Am. Chem. Soc.* 103 (1981) 1276.
- [6] E.I. Negishi, *Pure Appl. Chem.* 53 (1981) 2333.
- [7] C.E. Tucker, P. Knochel, *J. Am. Chem. Soc.* 113 (1991) 9888.
- [8] C.E. Tucker, B. Greve, W. Klein, P. Knochel, *Organometallics* 13 (1994) 94.
- [9] J.R. Waas, A.R. Sidduri, P. Knochel, *Tetrahedron Lett.* 33 (1992) 3717.
- [10] A. Pelter, E.M. Colclough, *Tetrahedron* 51 (1995) 811 and references cited therein.
- [11] M.P. Cooke Jr., *J. Org. Chem.* 59 (1994) 2930.
- [12] M. Srebnik, L. Deloux, M. Sabat, *J. Org. Chem.* 69 (1995) 3276.
- [13] L. Deloux, M. Srebnik, *J. Org. Chem.* 59 (1994) 6871.
- [14] L. Deloux, E. Skrzypczak-Jankun, B.V. Cheesman, M. Srebnik, M. Sabat, *J. Am. Chem. Soc.* 116 (1994) 10302.
- [15] M. Gaudemar, *C.R. Acad. Sci., Ser. C* 273 (1971) 1669.
- [16] Y. Frangin, M. Gaudemar, *C.R. Acad. Sci., Ser. C* 278 (1974) 885.
- [17] Y. Frangin, M. Gaudemar, *Synthesis* (1977) 205.
- [18] J. Auger, G. Courtois, L. Miginiac, *J. Organomet. Chem.* 133 (1977) 285.
- [19] I. Creton, I. Marek, J.F. Normant, *Tetrahedron Lett.* 36 (1995) 7451.
- [20] I. Creton, I. Marek, J.F. Normant, *Synthesis* (1996) 1499.
- [21] I. Creton, H. Rezaei, I. Marek, J.F. Normant, *Tetrahedron Lett.* 40 (1999) 1899.

- [22] K. Harada, H. Urabe, F. Sato, *Tetrahedron Lett.* 36 (1995) 3203.
- [23] E.I. Neghishi, T. Takahashi, *Bull. Chem. Soc. Jpn.* 71 (1998) 755 for the use of dialkylzirconocenes in synthesis.
- [24] S.L. Buchwald, R.B. Nielsen, *Chem. Rev.* 88 (1988) 1047 for the use of dialkyltitanocenes in synthesis.
- [25] A. Liard, I. Marek, unpublished results.
- [26] N. Krause, D. Seebach, *Chem. Ber.* 120 (1987) 1845.
- [27] M. Reetz, M. Schlosser, *Organometallics in Synthesis*, 1998, Wiley, New York, p. 195.
- [28] N. Morlender-Vais, J. Kaftanov, I. Marek, in preparation.