

Synthesis and reactivity of new strained cyclic allene and alkyne precursors*

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Abstract: The synthesis of *ortho*-(trimethylsilyl)vinyl triflates is described. Fluoride-induced decomposition of these triflates leads to the generation of strained cycloallenes and cycloalkynes under mild reaction conditions. The generation rate of these highly reactive intermediates can be modulated by modifying the solubility of the fluoride source. The slow generation of cyclic allenes and alkynes is a prerequisite for their use in homogeneous catalysis.

Keywords: cyclic allenes; cycloalkynes; catalysis; palladium; benzyne.

INTRODUCTION

Strained cyclic allenes [1] and alkynes [2], in which double or triple bonds are present in a ring of seven or fewer atoms, are unstable short-lived intermediates. Due to the strain caused by the deformation of the linear geometry imposed on carbon by *sp* hybridization, the reactivity of such cyclic species is to some extent analogous to the reactivity of arynes [3]. All of these species are potent electrophiles and undergo pericyclic reactions such as [2+2] and [4+2] cycloadditions with alkenes and dienes, respectively. Moreover, since the strain of these intermediates can be relieved by complexation with a transition metal, cycloallenes, cycloalkynes, and arynes can be stabilized as ligands in transition-metal complexes [4–6].

Based on the stabilization effect caused by the coordination of arynes to transition-metal-based fragments, in 1998 we reported the first example of the participation of arynes in a metal-catalyzed reaction, the palladium-catalyzed cyclotrimerization of benzyne [7]. Since then, several examples of metal-catalyzed cycloaddition reactions involving arynes have been described [8]. Bearing in mind the close analogy in terms of organometallic reactivity between arynes, cycloalkynes, and cycloallenes, we decided to explore transition-metal-catalyzed cycloadditions of both cyclic alkynes and allenes. In fact, we recently reported a preliminary example of this principle: the palladium-catalyzed cyclotrimerization of cyclohexyne [9].

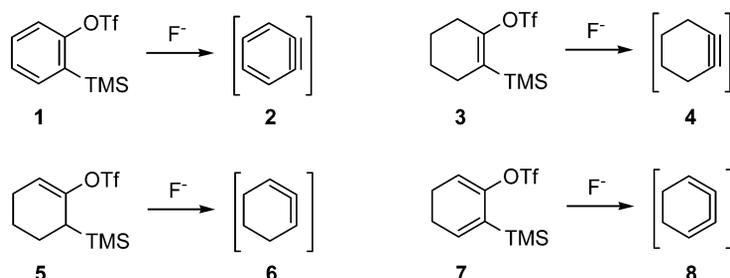
SYNTHESIS OF STRAINED CYCLIC INTERMEDIATE PRECURSORS

An important factor in the design of a metal-catalyzed reaction involving short-lived intermediates is to develop a rate-controlling method for their generation under mild reaction conditions. Our experience in aryne chemistry showed us that fluoride-induced decomposition of *ortho*-(trimethylsilyl)phenyl tri-

*Pure Appl. Chem. **78**, 197–523. An issue of reviews and research papers based on lectures presented at the 13th IUPAC International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS-13), Geneva, Switzerland, 17–21 July 2005.

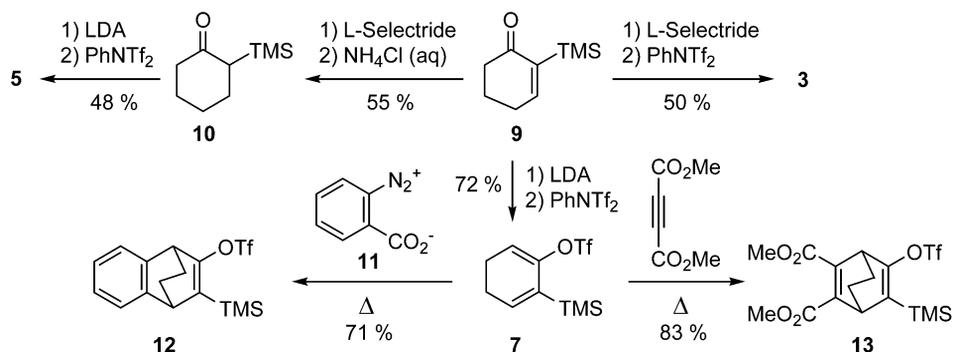
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flate (**1**) [10–11] is an excellent method for the generation of benzyne (**2**) for use in a transition-metal-catalyzed reaction (Scheme 1). The generation rate of benzyne can be modulated by modifying the solubility of the fluoride source. For example, benzyne is generated at room temperature from triflate **1** in acetonitrile (0.25 M) using CsF (2 equiv) in 12 h, while the use of the more soluble tetrabutylammonium fluoride (TBAF, 1.1 equiv) generates benzyne instantaneously. Similarly, *ortho*-(trimethylsilyl)vinyl triflates **3** and **5** should be suitable cyclohexyne (**4**) and 1,2-cyclohexadiene (**6**) precursors, respectively. In fact, the closely related vinyl triflate **7** has been used as a 1,2,3-cyclohexatriene (**8**) precursor [12].



Scheme 1 Fluoride-induced generation of strained cyclic intermediates.

Vinyl triflates **3**, **5**, and **7** were prepared from *ortho*-(trimethylsilyl)cyclohexenone (**9**, Scheme 2) [12]. Hydride conjugate addition to enone **9** using L-Selectride followed by trapping of the resulting enolate with a triflating agent afforded the cyclohexyne precursor **3** in 50 % yield [13]. Cycloallene precursor **5** was synthesized from *ortho*-(trimethylsilyl)cyclohexanone (**10**) by trapping the kinetic enolate with PhNTf₂. Similarly, cumulene precursor **7** was prepared from enone **9** in 72 % yield. Remarkably, vinyl triflate **7** can be used to synthesize strained bicyclic alkyne precursors by Diels–Alder cycloaddition with dienophiles. In particular, [4+2] cycloaddition of diene **7** with benzyne, generated by thermal decomposition of benzenediazonium 2-carboxylate (**11**), led to isolation of bicyclic triflate **12** in 71 % yield. Cycloaddition of triflate **7** with dimethyl acetylenedicarboxylate (DMAD) afforded bicyclic triflate **13** in 83 % yield.

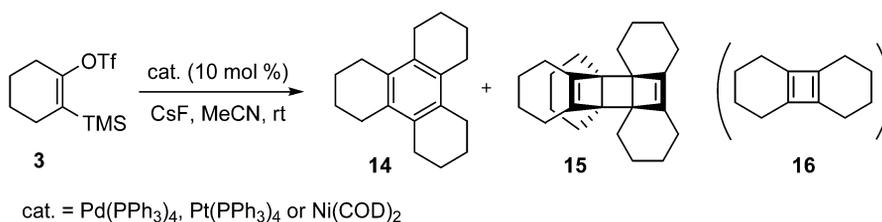


Scheme 2 Synthesis of strained cyclic intermediate precursors.

REACTIVITY OF STRAINED CYCLIC INTERMEDIATE PRECURSORS

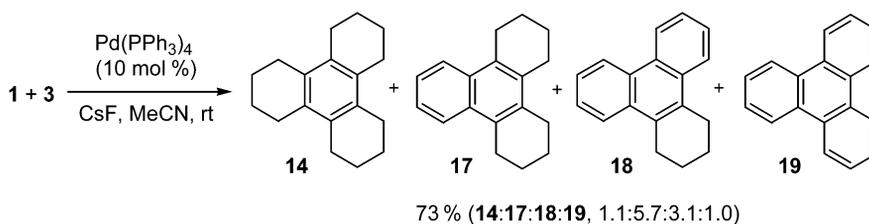
We decided to start studying the generation of cyclohexyne (**4**) in the presence of catalytic amounts of different transition-metal complexes. Conditions similar to those used for the palladium-catalyzed cyclotrimerization of benzyne [7] were employed, with cyclohexyne generated from triflate **3** by the ad-

dition of CsF (2 equiv) in acetonitrile at room temperature during 12 h in the presence of 10 mol % of Pd(PPh₃)₄. This gave dodecahydrotriphenylene (**14**, Scheme 3) in 64 % yield. Generation of cyclohexyne in the presence of Pt(PPh₃)₄ instead of the palladium catalyst, also afforded the [2+2+2] cycloaddition product **14** in a similar yield (62 %). Surprisingly, when cyclohexyne was generated as above using 10 mol % of Ni(COD)₂ as catalyst, the cyclootrimer **14** was isolated in only 10 % yield. Analysis of the reaction mixture showed the presence of tetramer **15** as the major reaction product (27 % yield). This hydrocarbon has previously been isolated from reactions involving cyclohexyne (**4**) [14]. Presumably, the Ni(0)-promoted [2+2] cycloaddition of **4** led to a high concentration of the unstable cyclobutadiene **16**, and subsequent [4+2] cycloaddition of two molecules of **16** afforded the tetramer **15**. Remarkably, generation of cyclohexyne in the absence of catalyst led to the isolation of trimer **14** in a moderate yield (30 %). As previously reported [15], the uncatalyzed cyclootrimerization of cyclohexyne (**4**) is assumed to involve the [2+2] cycloaddition of two molecules of **4** followed by the [4+2] cycloaddition of **16** with cyclohexyne and intramolecular rearrangement to afford **14**.



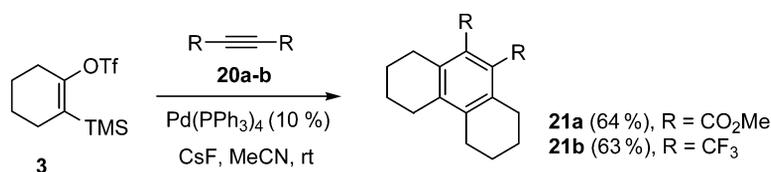
Scheme 3 Metal-catalyzed cycloaddition of cyclohexyne.

The similar reactivity of benzyne and cyclohexyne in the presence of palladium catalysts, prompted us to explore the [2+2+2] cocycloaddition of cyclohexyne and benzyne to give partially hydrogenated triphenylenes (Scheme 4). In particular, when a 1:1 mixture of triflates **1** and **3** was added to a suspension of CsF in acetonitrile at room temperature in the presence of 10 mol % of Pd(PPh₃)₄, a mixture of the four possible cyclotrimers was obtained in 73 % yield.



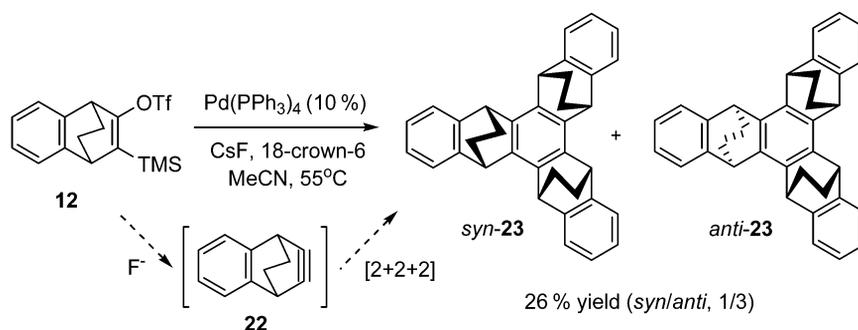
Scheme 4 Palladium-catalyzed [2+2+2] cocycloaddition of cyclohexyne and benzyne.

We also observed that cocyclization of cyclohexyne and electron-poor alkynes can be catalyzed by palladium complexes. Generation of cyclohexyne (**4**) from triflate **3** in the presence of alkynes **20a–b** and 10 mol % of Pd(PPh₃)₄ led to the isolation of octahydrophenanthrenes **21a–b**. These products, resulting from the [2+2+2] cycloaddition of two molecules of cyclohexyne and one molecule of alkyne (Scheme 5).



Scheme 5 Palladium-catalyzed [2+2+2] cycloaddition of cyclohexyne and alkynes.

Strained bicyclic alkynes can also participate in the palladium-catalyzed cyclotrimerization. For example, generation of cycloalkyne **22** from vinyl triflate **12** by reaction with CsF in acetonitrile in the presence of Pd(PPh₃)₄ led to the isolation of the two possible cyclotrimerization products, *syn*- and *anti*-**23** in 26% yield (Scheme 6). The additional strain inherent in this bicyclic alkyne made its generation in solution especially difficult. Therefore, harsher reaction conditions were established by heating the mixture at 55 °C and adding crown ether. In this way, the solubility of the fluoride salt was enhanced, forcing the generation of the strained bicyclic alkyne **22**.



Scheme 6 Palladium-catalyzed [2+2+2] cyclotrimerization of strained bicyclic alkyne **22**.

In conclusion, *ortho*-(trimethylsilyl)vinyl triflates are suitable precursors to generate strained cyclic intermediates such as cycloalkynes under mild reaction conditions. If these short-lived intermediates are generated in the presence of catalytic amounts of transition-metal complexes, structurally interesting cycloaddition products can be obtained. Our group is currently focusing on similar metal-catalyzed cycloaddition reactions involving cycloallenes.

ACKNOWLEDGMENTS

Financial support from the DGES (BQU2000-0464) and PGIDT (01PXI20902PN) is gratefully acknowledged. D. Peña also thanks MCyT for the award of a Ramón y Cajal research contract.

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