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

Diego Peña‡, Beatriz Iglesias, Iago Quintana, Dolores Pérez, Enrique Guitián, and Luis Castedo

Departamento de Química Orgánica, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain

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-
Fluoride (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].

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 1** Fluoride-induced generation of strained cyclic intermediates.

**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-
dation 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 cyclotrimer 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 cyclotrimerization 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](image)

**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](image)

**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).
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.

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.

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