

Zirconium-promoted Intramolecular Cyclization of Terminal Alkynes and Unusual Carbonylation Reaction

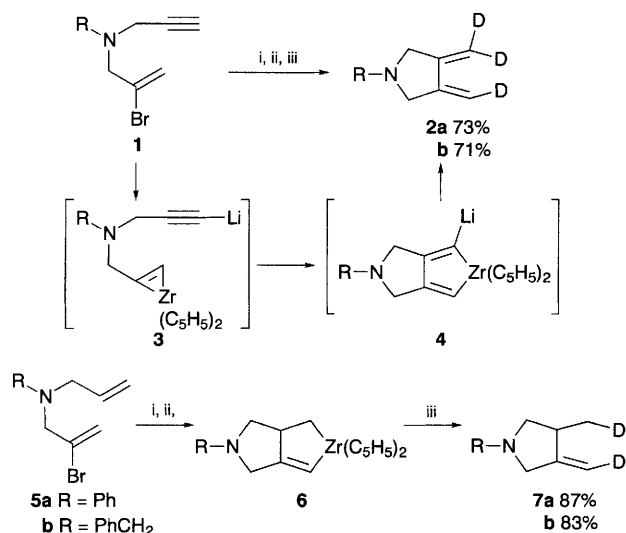
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N-(2-bromoallyl)-*N*-prop-2-ynyl- and *N*-allyl-*N*-(2-bromoallyl)-amines **1** and **5** undergo intramolecular cyclization by using zirconocene methyl chloride to give zirconacycles **4** and **6**, respectively, which are characterized by deuteriolysis affording products **2** and **7**; carbonylation of **6** and further reaction with electrophiles (deuterium oxide, allyl bromide, 4-chlorobenzonitrile, benzaldehyde, benzophenone and benzylideneaniline) leads to compounds **8**, **9** and **11–15**.

Recently the use of zirconium complexes in organic synthesis has been widely recognized.¹ In particular, Negishi *et al.*² and Nugent *et al.*³ independently reported the cyclization of enynes and diynes, using a zirconocene equivalent prepared from zirconocene dichloride and butyllithium, which is a valuable method for the preparation of mono- and bi-cyclic compounds by elaboration of the intermediate zirconabicycles. So, the carbonylation of these intermediates allows the direct and easy obtention of conjugated bicyclic enones.⁴ However, a major limitation of these reactions is that terminal alkynes are not successful substrates, presumably owing to the ready oxidative addition of the electron-rich metallocene to the acidic acetylenic hydrogen.⁵ On the other hand, we have recently reported⁶ the regioselective zirconium-mediated insertion of alkynes, alkenes and electron-rich alkenes in η^2 -prop-2-ynylamine–zirconocene complexes, generated from 2-lithioallylamines.⁷ Here we describe the first zirconium-promoted intramolecular coupling of terminal alkynes and the carbonylation of a new type of zirconacyclopentenes and further elaboration with electrophiles to give different 1-substituted azabicyclooctanones.

Treatment of *N*-(2-bromoallyl)-*N*-prop-2-ynylamines **1** with *tert*-butyllithium at -78°C followed by reaction with zirconocene methyl chloride at temperatures ranging from -78 to 20°C afforded, after addition of deuteriated sulfuric acid, the trideuteriated pyrrolidines **2**. The formation of these compounds can be understood by assuming an intramolecular insertion of the acetylide moiety, generated in the lithiation step, in the zirconacyclopentenes **3** leading to zirconacyclopentadienes **4**, which by deuteriolysis generate the compounds **2**. As far as we know, this is the first time that a terminal alkyne has been used in a zirconium-mediated intramolecular bicyclization (Scheme 1).



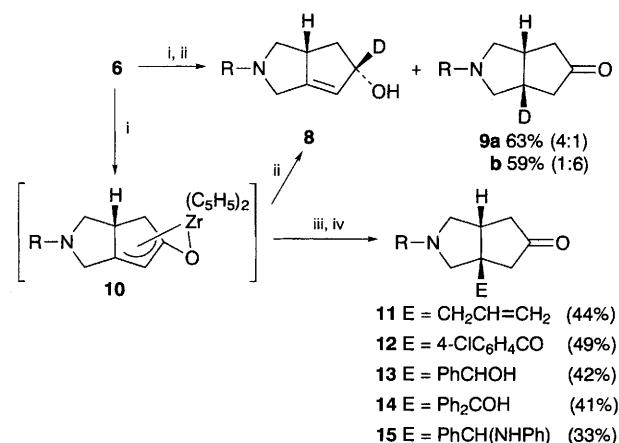
Scheme 1 Reagents and conditions: i, BuLi, -78°C ; ii, Cl(Me)Zr(C₅H₅)₂, -78 to 20°C ; iii, D₂SO₄ (1 mol dm⁻³), 20°C

On the other hand, the successive treatment of *N*-allyl-*N*-(2-bromoallyl)amines **5** with *tert*-butyllithium and zirconocene methyl chloride, under the same reaction conditions as described above, led to zirconabicyclopentenes **6**,[†] which represent a novel type of zirconacycle, although the 8-substituted homologues are known. The intermediates **6** were chemically characterized by deuteriolysis to give pyrrolidines **7** (Scheme 1).

When a diethyl ether solution of zirconacycles **6** was stirred under an atmosphere of carbon monoxide at room temperature for 40 min and then quenched with deuterium oxide, unexpected products, allylic alcohols **8** and saturated cyclopentanones **9**, were obtained. The structures of compounds **8** and **9** were determined by their spectroscopic data and the stereochemistry of **8** was confirmed by NOE experiments on the non-deuteriated form. It is interesting to note that the expected enones were never obtained. We believe that the insertion of carbon monoxide into zirconacycles **6** produces a π -allyl-zirconium complex **10**⁸ by rearrangement of the previously formed η^2 -ketone complex.⁹ The formation of compounds **8** and **9** can be understood by hydrolysis of complexes **10** with the zirconocene unit finishing at the carbon nearest the oxygen or at the bridge carbon.

We think that the different behaviour of **6** in the carbonylation with respect to analogous systems described in the literature is because of the lack of substituents at C-8, which would favour the formation of a π -allyl complex instead of a β -hydrogen abstraction process.

Assuming a π -allyl complex as intermediate we tested its reaction with several electrophiles (allyl bromide, 4-chlorobenzonitrile, benzaldehyde, benzophenone and benzylideneaniline). After hydrolysis and purification 1-substituted-3-azabicyclo[3.3.0]octan-7-ones **11–15** were obtained with yields of ca. 40–50% based on the starting amine **5a** (Scheme 2).



Scheme 2 Reagents and conditions: i, CO, 1 atm, 20°C ; ii, D₂O, 20°C ; iii, electrophile (BrCH₂CH=CH₂, 4-ClC₆H₄CN, PhCHO, Ph₂CO, PhCH=NPh), 20°C ; iv, H₂O, 20°C

The structures of all the compounds were determined by their spectroscopic data. Moreover, we have assigned the stereochemistry of **11–15** on the basis of the results of NOE experiments with **15** that indicated a *cis* ring junction.

In the case of the reaction with benzaldehyde and benzylideneaniline, in which a new chiral centre is generated, a mixture of diastereoisomers is obtained.

This work was supported by the DGICYT (PB 89-0538). R. S. thanks the Ministerio de Educación y Ciencia for a fellowship.

Received, 16th February 1995; Com. 5100936G

Footnote

† The zirconacycles were characterized by ^1H and ^{13}C NMR spectroscopy.

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