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Generation of Cyclohexyne and its Diels-Alder Reaction with α-Pyrones

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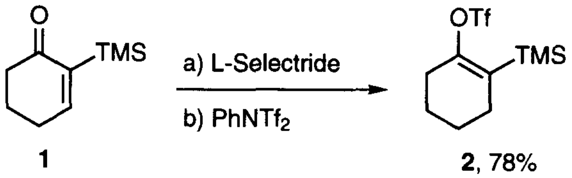
Abstract. Cyclohexyne, which was generated from 2-(trimethylsilyl)cyclohexenyltriflate by fluoride-promoted β-elimination, reacts with α–pyrones to afford the corresponding tetrahydronaphthalenes.

The chemistry of arynes is now so well known that some of their reactions have been included in the arsenal of synthetic chemists.[1] By contrast, most synthetic chemists appear still to consider their close relative cyclohexyne and its derivatives to be chemical curiosities.[2,3] This is probably due to the low stability of these species,[4] and to the fact that mild, efficient procedures for their generation[5] have only recently become available. Although these procedures which are based on fluoride-promoted β–elimination of *o*-substituted arylsilanes, have been used to prepare arynes, strained cycloalkenes and cycloalkynes,[6] to the best of our knowledge the milder variant involving β–elimination of TMS and OTf has not yet been used to prepare cyclohexyne.[7] In this work we examined this approach, applying it to the generation of cyclohexyne for use as a dienophile in Diels-Alder reactions. The dienes were some α–pyrones previously prepared by us, because of the known reactivivity of α–pyrones towards arynes,[8] and because the reaction products were of potential pharmacological interest.

Cyclohexyne precursor **2** was prepared in 78% yield by reducing **1**[6] with L-Selectride and trapping the resulting enolate with $PhNTf_2$ as shown in Scheme 1.



Scheme 1

To test the feasibility of cycloaddition of cyclohexyne to α–pyrones, we examined the reaction of the simple pyrone **4**. Cyclohexyne **3** was generated in the presence of pyrone **4** by treatment of **2** with CsF at 90-100 °C for 30 h. Work-up of the reaction mixture afforded tetrahydronaphthalene **6** in 82% yield.[9] The initial adduct **5** was not detected.

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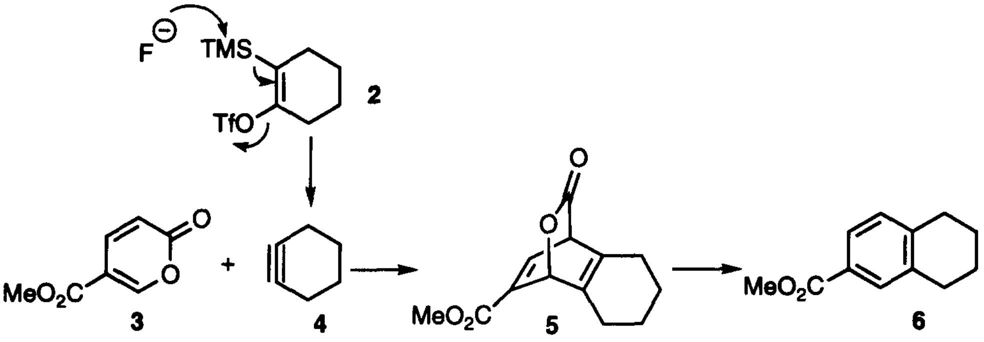
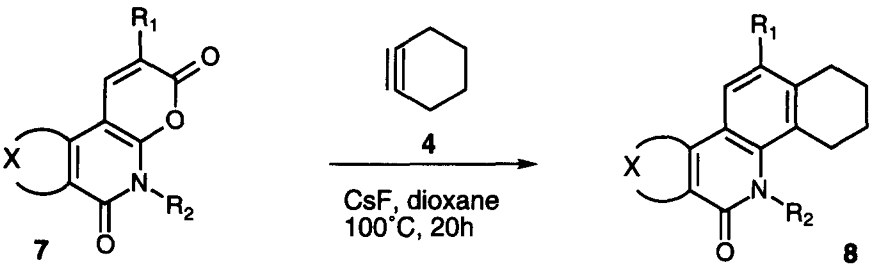


Scheme 2

Next, without optimizing the conditions, we applied the reaction to the more elaborate pyrones **7a-d**. To our delight the corresponding tetrahydronaphthalenes **8a-d** were obtained in 81-86% yield.



a, X= -$(CH)_4$, R_1=CO_2Et, R_2=Me, 86%; **b**, X= -$(CH)_4$, R_1=CO_2Et, R_2=Bn, 82%;
c, X= -$(CH_2)_4$, R_1=CO_2Me, R_2=Bn, 81%; **d**, X= -$(CH_2)_4$, R_1=OMe, R_2=Bn, 86%;

Scheme 3

Compounds **8a** and **b** can be considered reduced analogues of benzophenanthridines, and compounds **8c** and **d** analogues of the planar framework of dynemicin A.

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2. Krebs, A.; Wilke, J. *Angle Strained Cycloalkynes* in *Topics in Current Chemistry* **1983**, *109*, 189.
3. Over the last 20 years research into cycloalkyne chemistry has focused mainly on metal-cycloalkyne complexes, which has resulted in the preparation and characterization of stable cyclohexyne complexes with W, Co, Zr, Pt, Os and Ni. See Bennett, M. A.; Wenger, E. *Chem. Ber./Recueil* **1997**, *130*, 1029 and references therein.
4. Olivella, S.; Pericás, M. A. ; Riera, A; Solé, A. *J. Org. Chem.* **1987**, *52*, 4160.
5. Hitherto, the methods used to generate cycloalkynes, specially cyclohexyne, have been those used for the formation of benzyne. See references 1 and 2.
6. See Shakespeare, W. C.; Johnson, R. P. *J. Am. Chem. Soc.* **1990**, *112*, 8578 and references therein.
7. A similar procedure has been used to generate of 1,2,3-cyclohexatriene in ref. 6.
8. Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Tetrahedron Lett.* **1997**, *38*, 5375.
9. All new compounds show correct spectroscopic data.