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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.
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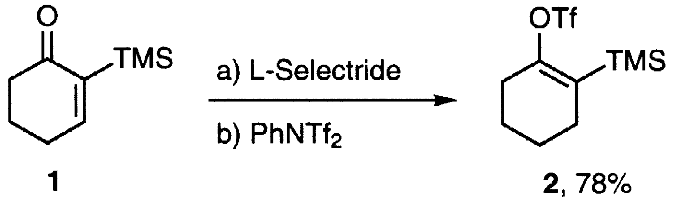
The chemistry of arynes is now so well known that some of their reactions have been included in the arsenal of synthetic chemists.[1] By contrast, most synthetic chemists appear still to consider their close relative cyclohexyne and its derivatives to be chemical curiosities.[2,3] This is probably due 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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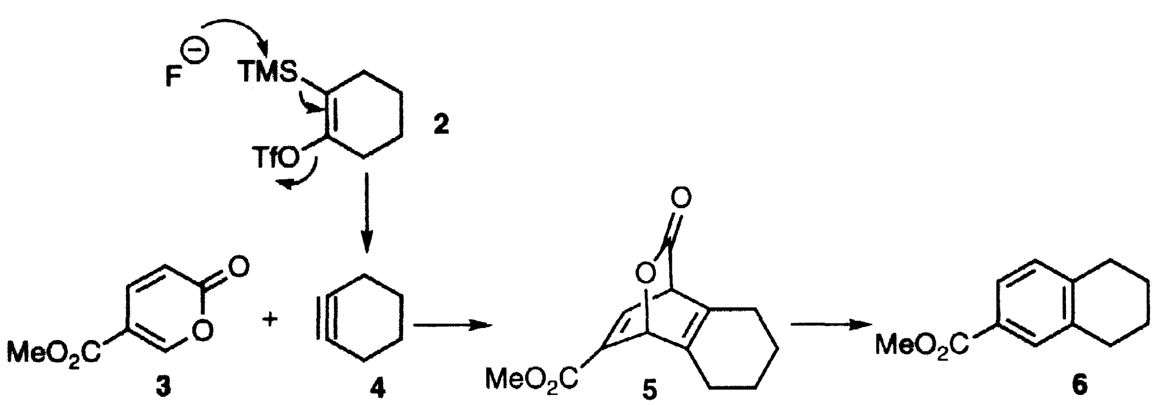
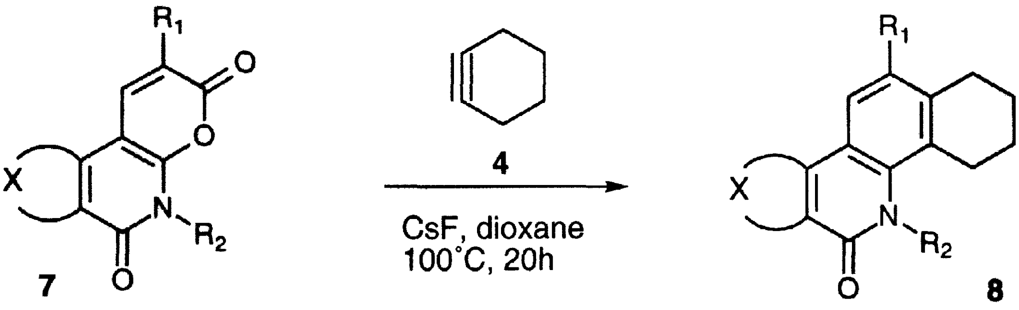


Scheme 2

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.