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1,2,3-Cyclooctatriene

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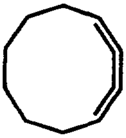
Abstract: 1,2,3-Cyclooctatriene (**3**) has been prepared for the first time by two similar routes. This substance shows moderate kinetic stability, but is readily trapped by cycloaddition with diphenylisobenzofuran or 2,5-dimethylfuran. Total strain in **3** is estimated to be 17.7 kcal/mol.

Cyclic butatrienes comprise a homologous series of hydrocarbons in which decreasing ring size is accompanied by rapid increases in strain and reactivity.[1] Within this series, **1**[2], **2**[3], **4**[4] and **5**[5a] all have been reported. Although 1,2,3-cyclopentatriene remains unknown, a thia analogue, 3,4-dehydrothiophene, very recently has been reported.[5b] Homologues **1** and **2** proved to be isolable, while **4** and **5** undoubtedly are too strained to be isolable under ordinary conditions. Among more unusual examples, the neocarzinostatin chromophore is believed to contain an unstable nine membered ring butatriene.[6] 1,2,3-Cyclooctatriene (**3**) is of interest both to complete this series and to more precisely define limits for isolability. We report here the first synthesis of **3** in addition to preliminary experiments that support its isolability.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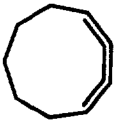
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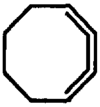
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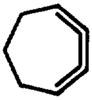
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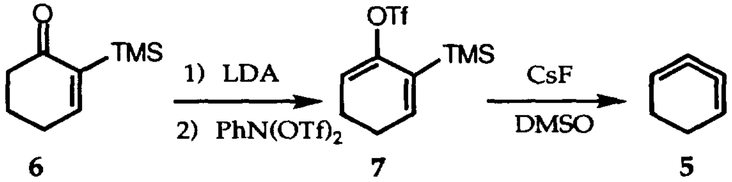
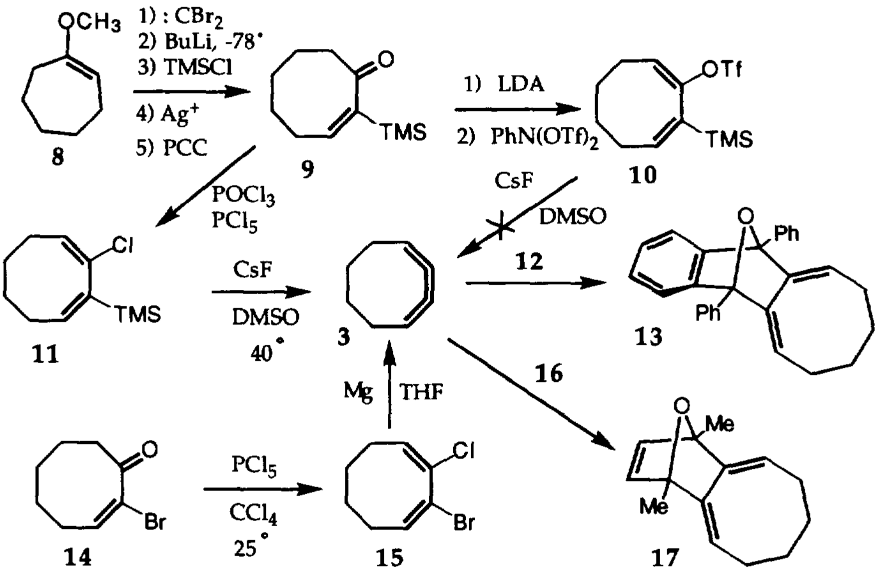
We initially attempted to prepare **3** by the same efficient route we had used previously in the synthesis of 1,2,3-cyclohexatriene (**5**).[5] This earlier work involved synthesis of 1,3-diene **7** as a precursor to the butatriene. The final strained π bond results from fluoride-induced vicinal elimination of trimethylsilyl and triflate groups.[7] In principle, this approach should also be applicable to other ring sizes.



Enone **9** was prepared by ring expansion of methoxycycloheptene (**8**).[8] This was converted to triflate **10** according to the general method described by McMurry.[9,10] However, in contrast to the stability of **7**, diene **10** readily decomposed on attempted purification by chromatography or distillation. We attribute this instability to facile heterolysis of the OTf group, which should give a stabilized β'-silyl vinyl cation.[11,12] Reaction of impure samples of **10** with CsF in the presence of diphenylisobenzofuran (**12**) did not yield evidence for **13**.

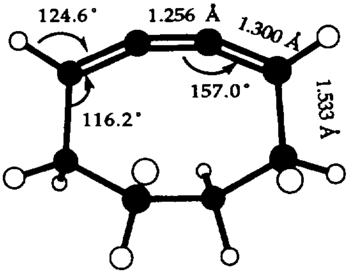


Two alternative routes were then developed. Conversion of **9** to diene **11** was effected in 22% yield by reaction with $PCl_5/POCl_3$. Reaction of **11** with CsF and **12** in DMSO afforded 7% of a crystalline substance that was characterized securely as **13** by spectral data.[13] In a second approach, bromoenone **14**[14] was converted to diene **15**. Numerous attempts did not raise the yield of this reaction beyond 10%. However, treatment of **15** with magnesium in THF at 35°, in the presence of two equivalents of **12**, led smoothly to **13** in 49% yield. Similar trapping was observed with 2,5-dimethylfuran (**16**) to give **17** in a yield of 14%.

As with our earlier work[5a] on **5**, these experiments are consistent with the intermediacy of butatriene **3**, which is trapped at the strained central π bond by Diels-Alder cycloaddition with **12**. To assess the kinetic stability of **3**, diene **15** was reacted with magnesium in the absence of **12**. After 20 min, the mixture was quenched with water to ensure that no Grignard reagent remained. Immediate addition of one equivalent of **12** resulted in a 15% yield of **13**. These experiments demonstrate moderate kinetic stability of **3** in solution; further experiments to obtain spectral evidence are in progress.

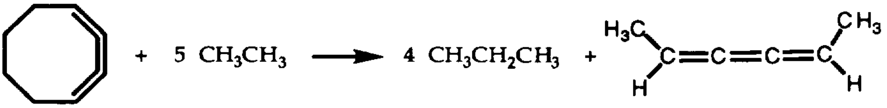
Strain in butatriene **3** was assessed by ab initio calculations.[15,16] Figure 1 shows the optimized structure, which has C_2 symmetry. The butatriene unit is predicted to be nearly planar but is bent by 23°, in good agreement with our previous semiempirical calculations.[3]

Figure 1. HF/3-21G Optimized Geometry for 1,2,3-Cyclooctatriene

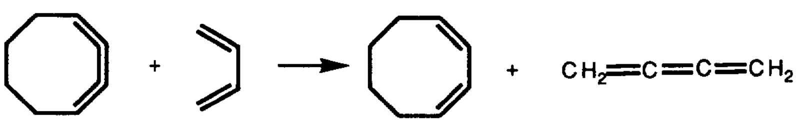


Total strain in **3** was estimated at the MP2/6-31G*//HF/3-21G level according to homodesmic equation [1] to be 17.7 kcal/mol, while strain in the butatriene central π bond was estimated from isodesmic equation [2] to be 12.4 kcal/mol.[17] At the SCF level, these values increase by ca. 4 kcal/mol. Both estimates indicate only modest levels of strain, most of which clearly is due to the bent in-plane π bond.

Eq [1] Homodesmic Estimate of Total Strain in **3** $\Delta E = -17.7$ kcal/mol



Eq [2] Isodesmic Estimate of Butatriene Strain in **3** $\Delta E = -12.4$ kcal/mol



We are working to improve the efficiency of this synthesis so that **3** might become a readily used intermediate in the synthesis of eight membered rings.

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(13) Data for **13** include : mp 83 - 85°, ^{1}H NMR(360 MHz, CDCl3) δ 7.81-7.84 (dt, 4H, J = 1.4, 7.1 Hz), 7.51 (tt, 4H, J = 7.2 Hz), 7.43(tt, 2H, J = 7.3 Hz), 7.38(dd, 2H, J = 3.0, 5.4 Hz), 7.17 (dd, 2H, J = 3.0, 5.4 Hz), 5.65 (t, 2H, J = 6.5 Hz), 2.27-2.31(m, 2H), 2.16-2.22(m, 2H), 1.60-1.63(m, 4H); ^{13}C NMR δ 147.3, 141.8, 135.8, 128.3, 128.0, 127.6, 126.4, 123.8, 119.4, 90.4, 27.2, 24.7. HRMS for $C_{28}H_{24}O$ calcd 376.1827, found 376.1840.

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