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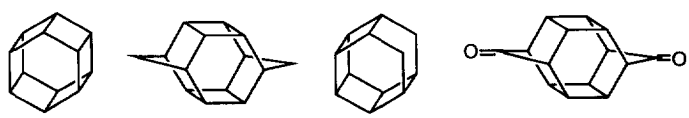
Synthesis and Structure of Bishomohexaprismanedione

Thomas D. Golobish and William P. Dailey*
Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104-6323

Abstract: Synthesis of bishomohexaprimanedione, the D_{2h} dimer of norbornadienone and a potential precursor to hexaprismane, is reported. The synthesis includes an unusual ring contraction of a cycloalkene using a *cis*-hydroxylation/periodate cleavage/aldol sequence. The structure of bishomohexaprimanedione determined from single crystal x-ray analysis is well reproduced by ab initio calculations. Copyright © 1996 Elsevier Science Ltd

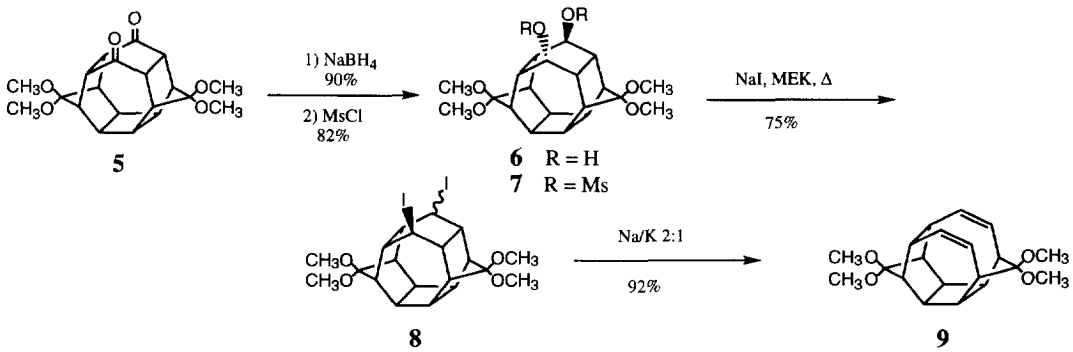
The [n]-prismanes are a novel class of $(CH)_n$ polyhedranes whose architectural structure has attracted the interest of chemists for many years. The synthetic conquest of [3]-prismane (triprismane),[1] [4]-prismane (cubane),[2] and [5]-prismane (pentaprismane),[3] has required diverse synthetic strategies and has shifted the focus to higher order prismanes.[4] Hexaprismane ([6]-prismane) (**1**), the next [n]-prismane in the class, has not yet been prepared. 1,4-Bishomohexaprismane[5] (**2**) and secohexaprismane[6] (**3**) have been synthesized, but efforts to prepare **1** using similar methodology have so far been unsuccessful. In this letter, we report the implementation of several new synthetic strategies that have allowed the first synthesis of the symmetrical face to face dimer of norbornadienone, **4**, a molecule which has been suggested as a precursor to the hexaprismane ring system after bridgehead functionalization and Favorskii ring contraction.[7] Additionally, our synthetic scheme offers a new solution to the problem of bridgehead functionalization of **4**. The structural properties of **4** were determined by x-ray crystallography and calculations at the HF/6-31G* level reproduce the experimental results.



1 **2** **3** **4**

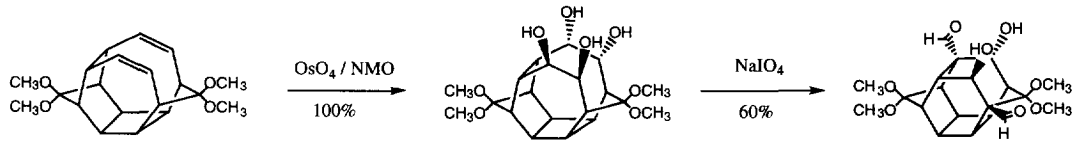
The starting point for our synthesis of **4** was bishomosecoheptaprismanedione **5** which is conveniently available in 8 steps and without resort to any chromatography starting with the Diels-Alder adduct between 5,5-dimethoxycyclopentadiene and benzoquinone.[8] Mehta and Padma[5] had demonstrated that the compound analogous to **5** but lacking methoxy groups could be brominated and converted via Favorskii ring contraction to the bishomohexaprismane ring system and eventually to **2**. However, we reported[8] that the methoxy groups present in **5** adversely effect the reactivity so that functionalization does not proceed. After much

experimentation we have discovered that ring contraction of the bishomosecoheptaprismane system of **5** to the bishomosecohexaprismane system can be accomplished in the following manner. Dione **5** was converted to diol **6** using $NaBH_4$, and this was converted to dimesylate **7**.[9] Dimesylate **7** was converted to diiodide **8** as a mixture of diastereomers which when treated with Na/K alloy produced diene **9** in good yield via Grob fragmentation.[10] As expected based on literature precedent, diene **9** was resistant to photochemical [2+2] ring closure under sensitized or direct irradiation conditions.[10]



5 **6** R = H, **7** R = Ms, **8**, **9**

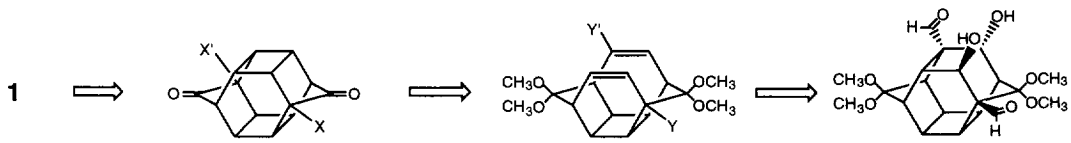
Diene **9** was converted to the highly water soluble tetraol **10** in quantitative crude yield using catalytic OsO_4. Attempts to induce ring contraction of **10** using pinacol chemistry under acid or base conditions (TsCl/pyridine) have so far been unsuccessful. However, treatment of crude tetraol **10** with periodic acid leads to formation of **11**, the doubly ring contracted product, in 60% yield. Remarkably only the unsymmetrical product **11** was obtained. The structure and stereochemistry of **11** were confirmed by single crystal x-ray analysis. The mechanism of formation of **11** from **10** presumably involves stepwise cleavage of each diol to dialdehyde, enolization of one of the resulting aldehydes, and aldol ring closure. It is not clear why only this isomer is formed. An exhaustive search has failed to provide evidence for any of the other possible regio- and stereoisomers of **11**.



9 **10** **11**

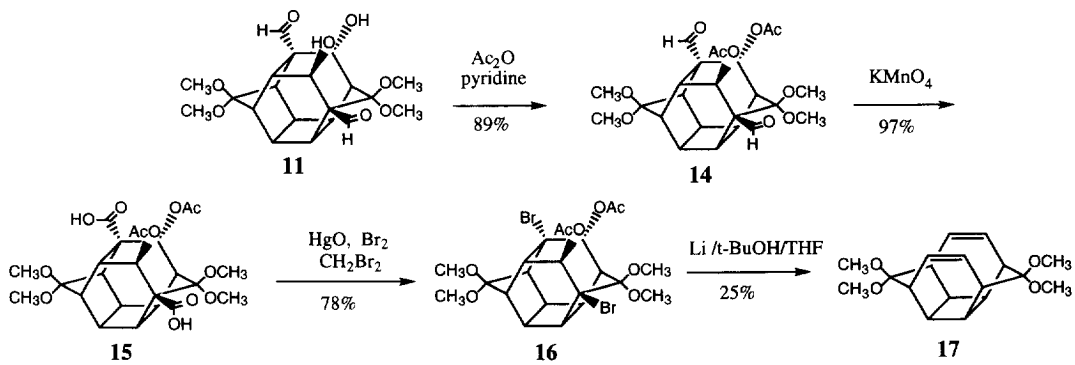
With **11** in hand, we turned our attention to its further manipulation towards hexaprismane (**1**). Our retrosynthetic analysis is shown below. It includes conversion of the hydroxyl groups in **11** to leaving groups, since analysis of compound **11** reveals that the stereochemistry of the two alcohol groups are perfectly aligned for a Grob fragmentation of the ring to produce the ring fragmented diene **12**. Photochemical ring closure of diene **12** was expected to be straightforward since the increase in strain energy would be within acceptable limits.[10] As an added bonus to this strategy, the dienedione derived by hydrolysis of diene **12** could offer a new method for future bridgehead functionalization using enolate chemistry. While one of the aldehyde groups from **11** will have the correct regiochemistry in **12** (Y) and could be converted to an appropriate leaving group X in **13**, the other aldehyde will be in an undesired position Y', and would eventually need to be removed. Although

it may be possible to chemically differentiate between the two aldehyde groups, we chose to remove both of them as an initial strategy.



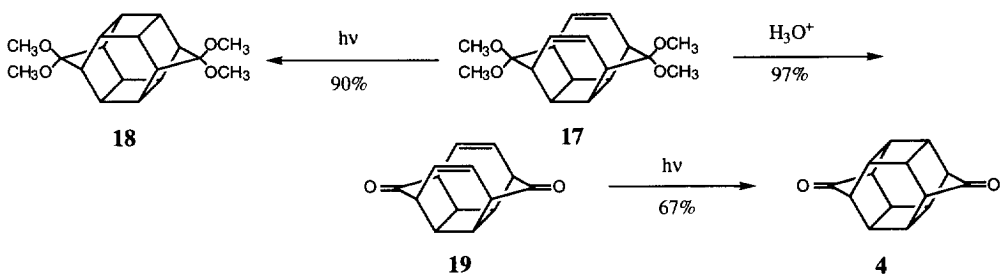
13 12 11

The hydroxyl groups in **11** were protected as the acetates to give **14**, and the aldehyde groups were oxidized with $KMnO_4$ to produce diacid **15**. Decarboxylation using Barton methodology[11] proved troublesome, so instead the carboxylic acid groups were converted to bromides via Hunsdiecker reaction to give **16**. Treatment of **16** with lithium dispersion in *t*-BuOH/THF solution resulted not only in reductive debromination as we had anticipated but also reductive fragmentation to form diene **17** in 25% overall yield. Much to our surprise, control experiments have demonstrated that the debrominated diacetate derived by tributyltin hydride reduction of **16** does not undergo fragmentation to **17** when treated under the lithium dispersion conditions. The mechanism of the fragmentation reaction is currently under study in an attempt to improve the yield of **17**.



11 14 15 16 17

Irradiation of **17** in a 4:1 benzene/acetone solution cleanly led to the ring closed product **18** in high yield. Hydrolysis of **17** produced dienedione **19** which also underwent photochemical ring closure to the highly sought-after norbornadienone dimer **4**.[12]

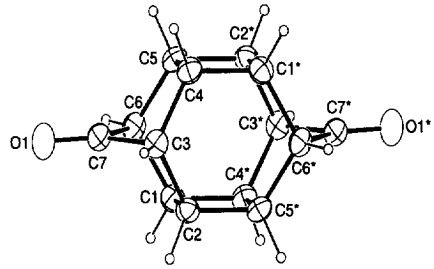


18 17 19 4

The structure of **4** was determined by single crystal x-ray analysis and some of the results are compared with those obtained from geometry optimized ab initio calculations at the HF/6-31G* level (Table I). The agreement is outstanding.

Table I. Experimental and Calculated Bond Lengths in **4**.

Bond	X-ray(Å)	HF/6-31G*
C1*- C4	1.546	1.546
C3-C4	1.530	1.538
C3-C7	1.535	1.536
C4-C5	1.574	1.569
C7-O1	1.206	1.183



Recently Eaton and Spitz have described a new method for the bridgehead functionalization of non-enolizable ketones. Their method converts the ketone to an auxiliary group which then directs radical substitution to the bridgehead position.[7] While the yield reported for bridgehead functionalization of norbornanone was modest, the required directing group is not trivially prepared, and conversion of the auxiliary back to a carbonyl group may be problematic with more highly strained systems. In principle this method could be applied to **4**. However as an attractive alternative method for bridgehead functionalization, our preliminary experiments have demonstrated that **19** can undergo enolate chemistry when methyl iodide is used as the electrophile. Our future efforts directed toward similar functionalization of **19** with appropriate leaving groups and subsequent conversion to hexaprismane will be reported in due course.

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