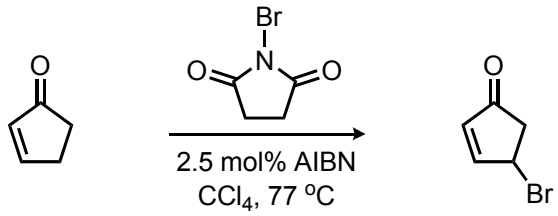
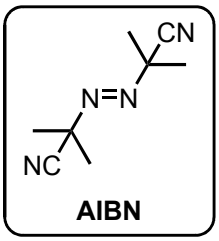
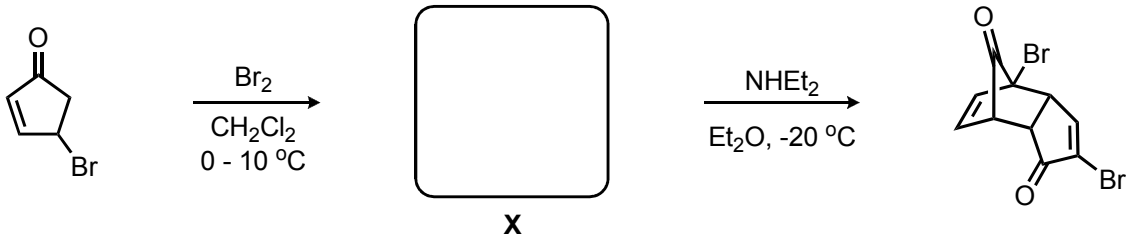
Keith Reber
5/13/2010

1) The compound *N*-bromosuccinimide is frequently used in combination with a radical initiator to perform the allylic bromination of alkenes. Write a mechanism for this reaction, and identify the intermediate that serves as the radical chain carrier. What is the origin of the regioselectivity in this bromination reaction?





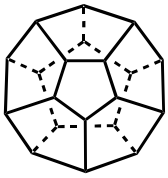
2) When the product of the allylic bromination is treated with one equivalent of molecular bromine, compound **X** is formed. When this isolable intermediate is treated with diethylamine at low temperature, the indicated bicyclic compound is formed as a single diastereomer. Identify compound **X**, and write a mechanism for the formation of the bicycle.



3) Organic chemists have long been fascinated by the so-called Platonic hydrocarbons; that is, molecules corresponding to the Platonic solids where each vertex is a methine carbon, each edge is a carbon-carbon bond, and each face is carbocyclic ring. These "un-natural" products are of great theoretical interest due to their considerable ring strain and unusual bonding characteristics; however, true synthetic chemists are drawn to these compounds based solely on their aesthetically pleasing and highly symmetrical structures.

tetrahedrane

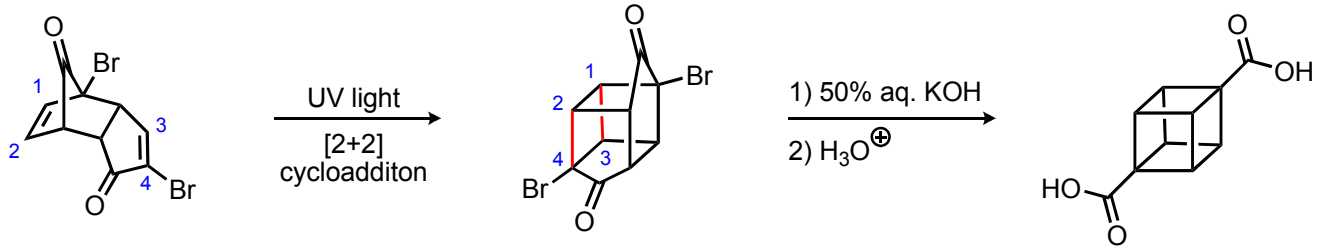
cubane



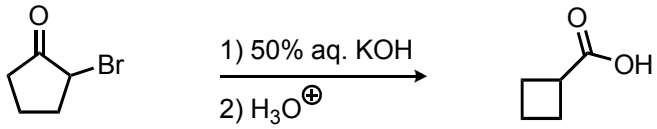
dodecahedrane

For many years, theoriticians believed that tetrahedrane and cubane would be too highly strained to exist. Indeed, unsubstituted tetrahedrane has never been prepared despite considerable synthetic effort; however, the tetra-*tert*-butyl and the tetra-trimethylsilyl derivatives of tetrahedrane have been prepared and are kinetically stable despite their extremely high energy. Cubane was first prepared in the laboratory of Philip Eaton at the Univesity of Chicago in 1964, and dodecahedrane was finally prepared in 1982 by Leo Paquette at the Ohio State University. Surprisingly, both of these compounds are perfectly stable, highly crystalline solids, and their respective syntheses are considered classics in the field of organic chemistry.

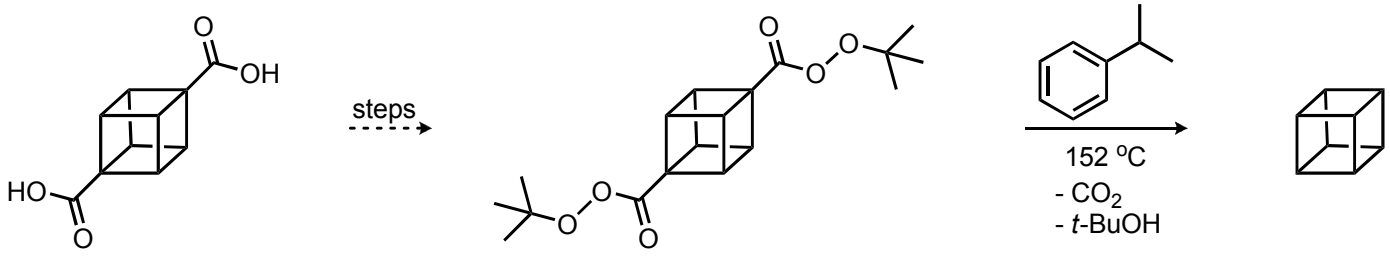
Interestingly, cubane has been produced industrially on a multi-kilogram scale, and the octanitro derivative has been investigated as a high explosive. In fact, the dimer prepared in problem 2 is a key intermediate in Eaton's 1964 synthesis of cubane. In the next step, Eaton makes use of a very powerful reaction known as a [2+2] cycloaddition in which two alkenes react upon irradiation with light to form a cyclobutane ring.



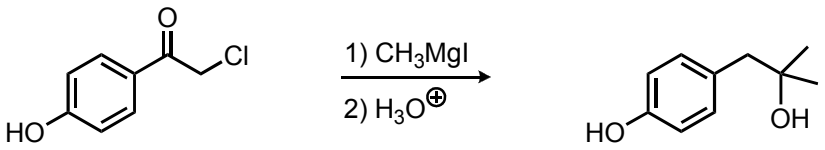
When the product of the cycloaddition was treated with concentrated aqueous potassium hydroxide at reflux, a double ring contraction occurred to give cubane 1,4-dicarboxylic acid after an acidic workup. There are two possible mechanisms for this reaction: one is known as the **Favorskii rearrangement** and involves an initial deprotonation -- the other is known as the **benzilic acid rearrangement** and involves an initial 1,2-addition. Provide a mechanism for both possible rearrangement mechanisms; to simplify the drawing, use the analogous reaction of 2-bromocyclopentanone to give cyclobutanecarboxyclic acid. Which mechanism is more likely to be operative in the cubane synthesis? How could these two possible mechanisms be distinguished using a carbon-13 labeled substrate?



4) Having prepared the 1,4-diacid derivative, we are only a double decarboxylation away from cubane. But how can we decarboxylate without an "electron sink"? It turns out that the answer is to use a radical process instead of a polar one. Propose a synthetic sequence to convert the diacid into the corresponding bis-*tert*-butyl peroxy ester. When this compound is heated in refluxing cumene (isopropylbenzene), decarboxylation occurs to give cubane. Provide a mechanism for this transformation; you may use cyclobutanecarboxylic acid to simplify your drawing (hint: the solvent also serves as a reagent in this reaction).



5) When the following α-chloroketone was treated with excess methylmagnesium iodide, an unexpected product was obtained. Provide a reasonable mechanism for this transformation.



6) The following reaction is the first step in Merck's synthesis of the selective estrogen receptor modulator drug ERa-SERM. Provide a mechanism for this transformation