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The Transannular Rearrangement of 5-Cyclodecynone

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Summary: The acid catalyzed rearrangement of 5-cyclodecynone to bicyclo[4.4.0]-1(6)-decen-2-one has been shown by carbon thirteen labeling experiments to proceed by a mechanism that does not involve an enol of 5-cyclodecynone.

It is well known [1-3] that 5-cycloalkynones undergo a facile rearrangement which requires the formation of a transannular carbon-carbon bond. Several mechanisms have been proposed for this reaction. The mechanism favored by Harding and co-workers [3,4] involves a highly strained anti-Bredt oxete **1**. An attractive alternative which avoids invoking this improbable intermediate begins with the formation of an enol **2**, which nucleophilically attacks the acetylene to form the requisite carbon-carbon bond.

As shown in Scheme I there are three possible pathways which employ the enol as a starting point. Two options feature the addition of the enol oxygen to the acetylene prior to forming the transannular carbon-carbon bond. These pathways include symmetrical anti-Bredt intermediates **3** and **4**, which should not be as strained as the oxete intermediate.

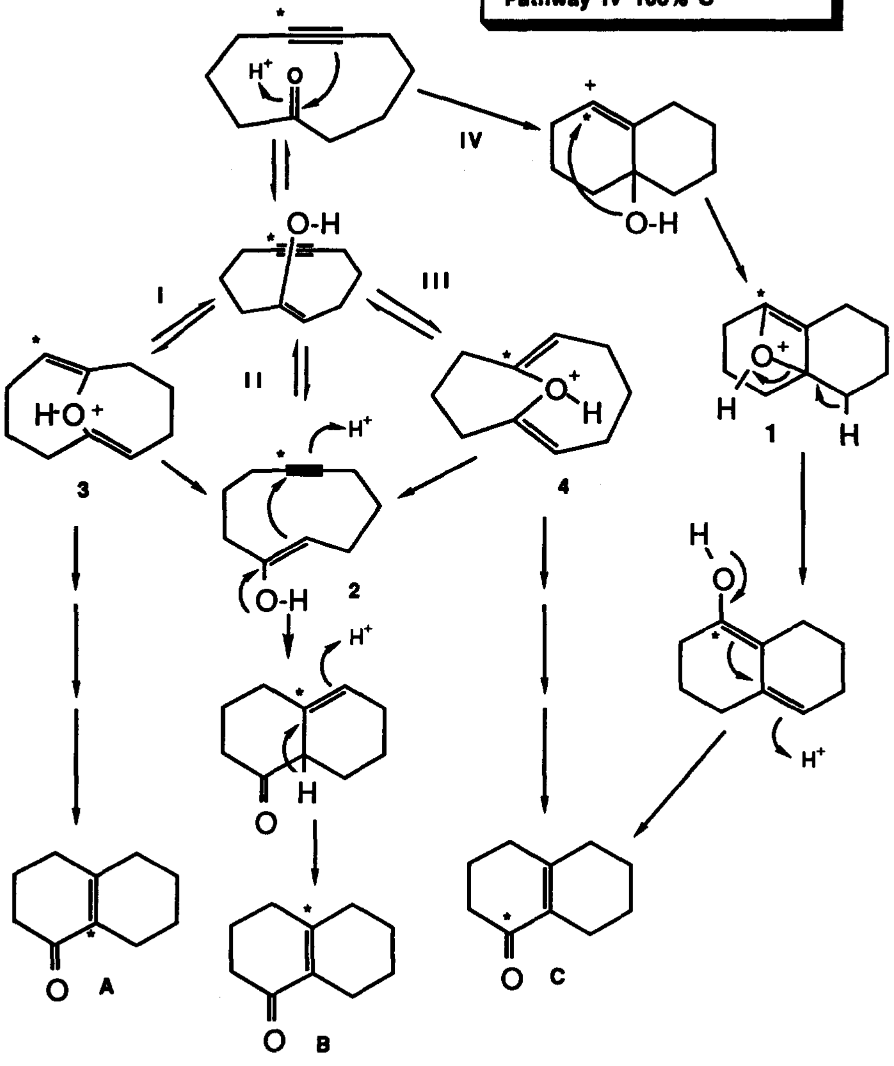
Harding[4] presented evidence in support of the oxete mechanism by showing that 6-octyn-2-one rearranged in acid to 1-acetyl-2-methyl-1-cyclopentene and 2,3-dimethylcyclohexenone. The absence of 3-ethylcyclohexenone appears to rule out the enol mechanism. Nevertheless, models of **1** demonstrate that the double bond is horribly twisted with very little overlap between the two p-orbitals.

We report here the results of a carbon thirteen labeling experiment aimed at resolving this dilemma. As shown in Scheme I a carbon thirteen placed at the number five acetylenic carbon (C-NMR 83.3 ppm) of 5-cyclodecynone will distinguish among the three enol pathways I-III and the oxete mechanism, pathway IV.

The synthesis of the required labeled 5-cyclodecynone was accomplished in nine steps (Scheme II) according to the literature procedures [3,5-7] starting from 3-bromo-1-phenylpropane and carbon thirteen labeled potassium cyanide[8] dissolved in acetonitrile with the addition of 1.0 g of 18-crown-6 ether.[9] Since

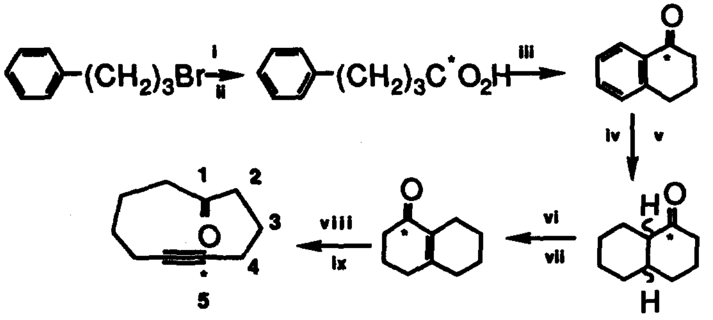
SCHEME I

Pathway I 50% A 50% B
Pathway II 100% B
Pathway III 50% B 50% C
Pathway IV 100% C



the synthesis involved so many steps we decided to use 20% enrichment of carbon thirteen. Throughout the synthesis the position of the label was determined by ^{13}C-NMR and GC-MS. Starting from 30.1 g of 3-bromo-1-phenylpropane, 1.5 g of 5-^{13}C-5-cyclodecynone were obtained. The product was >99% labeled at the number five position as judged by ^{13}C-NMR.

SCHEME II



i) KCN, CH_3CN, 18-C-6 ii) 12N HCl iii) PPA iv) H_2 Rh/Al_2O_3
v) CrO_3 vi) SO_2Cl_2 vii) LiCl, DMF viii) H_2O_2, HO^- ix) $TsNHNH_2$, CH_3CO_2H

TABLE I

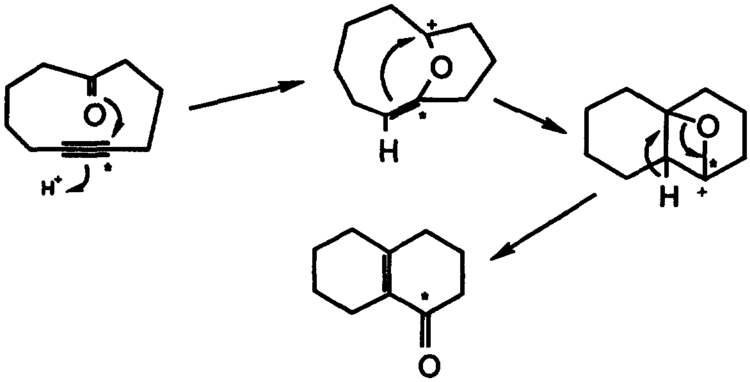
	% ^{13}C in Product		
	C1	C2	C6
CARBON NMR RESONANCE (ppm)	132	198	156
Alumina (neutral, Activity I)	0	>99	0
1.5N HCl MeOH (anhydrous)	0	>99	0
4.0N H_2SO_4 aqueous MeOH	0	>99	0

The labeled 5-^{13}C-5-cyclodecynone was subjected to three distinct reaction conditions that have been shown in the past to induce the rearrangement (Table I). One of the issues which Harding investigated was whether water was incorporated into the product. In all cases we investigated, anhydrous or aqueous, virtually all of the labeled carbon located at the number five carbon of 5-cyclodecynone was found at the carbonyl carbon of bicyclo[4.4.0]-1(6)-decen-2-one.

This result unequivocally rules out all enol pathways because these mechanisms all require at least 50% of the carbon thirteen to appear at the carbons comprising the double bond in the product (see Scheme I). This result is consistent with the Harding oxete mechanism. Harding's ^{18}O and our ^{13}C experiments clearly demonstrate that the oxygen atom in 5-cyclodecynone is the same oxygen atom in the product. At issue is the timing of the oxygen migration with intramolecular carbon-carbon bond formation. In Harding's proposal, carbon-carbon bond formation preceded oxygen migration.

Our proposal (Scheme III) begins with the formation of a bond between the carbonyl oxygen and carbon number five. According to molecular mechanics calculations the carbonyl oxygen is poised directly above the number five carbon of the acetylene in the most stable conformation of 5-cyclodecynone.

Scheme III



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