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CYCLOALKENONE FORMATION BY THE INTRAMOLECULAR ADDITION OF A α-DIAZOKETONE TO AN ACETYLENIC PI-BOND

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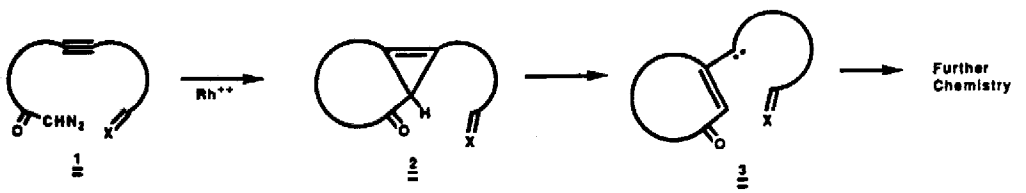
Abstract: Treatment of several ortho alkynyl substituted α-diazoacetophenone derivatives with rhodium (II) acetate results in intramolecular addition to the acetylenic pi-bond to give a transient cyclopropene which spontaneously rearranges to a vinyl carbene intermediate.

α-Diazocarbonyl compounds are valuable intermediates in organic synthesis and have been widely studied under thermal, photochemical and transition metal catalyzed conditions.[1,2] One important use of these compounds involves addition to olefinic pi-bonds.[1-6] A general review of intramolecular diazo carbonyl reactions to alkenes appeared in 1979,[2] and since then many further publications on transition metal catalyzed cycloaddition reactions have extended the scope of this methodology.[7-9] Less attention, however, has been placed upon the use of such a reaction with alkynes for the formation of substituted cyclopropenes.[10] We elected to explore the transition metal catalyzed reaction of acetylenic α-diazoketones as a method for the construction of cycloalkenones. We were particularly interested in determining whether the initially formed cyclopropene (**2**) would undergo spontaneous ring opening to give a vinyl carbene intermediate



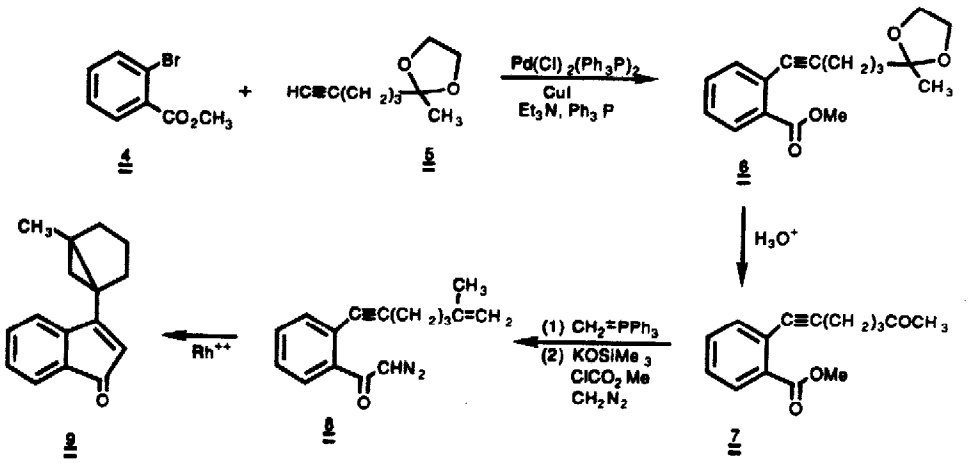
1 **2** **3**

(**3**).[11,12] The trapping of **3** with a suitably tethered pi-bond (X= CH_2 or O) would provide ready access to highly functionalized cycloalkenones. In this communication we wish to report on the successful implementation of the above strategy.[13]

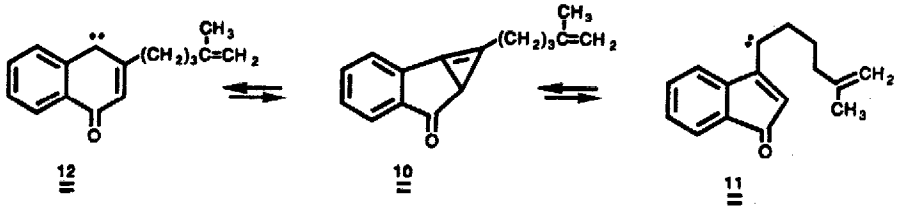
Our initial results focused on the rhodium catalyzed reaction of ortho-alkynyl substituted α-diazoacetophenone derivatives **8** and **13**. The synthesis of diazoketone **8** consisted of treating methyl o-bromophenyl benzoate **4** with acetylene **5** under typical Heck arylation conditions.[14] Hydrolysis of the ketal derived from the coupled product **6** afforded ketoester **7**. This material was readily converted to the desired diazoketone by means of a Wittig reaction followed by reacting the mixed anhydride with diazomethane (see Scheme I). Treatment of **8** with a catalytic quantity of rhodium (II) acetate at 25° C in benzene afforded indenone **9** in 60% yield. This product was identified on the basis of its characteristic 300-MHz NMR spectrum ($CDCl_3$), which showed a set of

doublets for the cyclopropyl hydrogens at δ 0.65 (J=5.0Hz) and 1.02 (J=5.0 Hz), a singlet at 1.10 (3H), multiplets centered at 1.4 (1H), 1.8 (4H) and 2.2 (1H), a singlet at 5.64 (s, 1H) and the aromatic protons at 7.0-7.4 (4H); (IR: 1710 cm^{-1}). We believe that the mechanism by which **8** is converted into **9** involves intramolecular addition of the rhodium stabilized carbenoid onto the acetylenic pi-bond to give either a vinylcarbene or possibly the highly strained cyclopropene

Scheme I

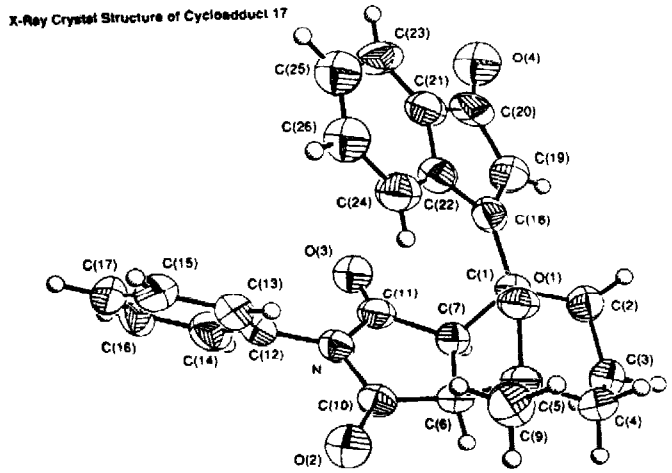


derivative **10**. It is well known that cyclopropenes ring-open to vinylcarbenes at ambient temperature,[15] and that these reactive intermediates may be trapped by alkenes both in an inter[16] and intramolecular fashion.[17] The exclusive formation of **9** suggests that this product arises by either a regiocontrolled ring opening of **10** or is the result of a reversible process which involves selective trapping of intermediate **11**.

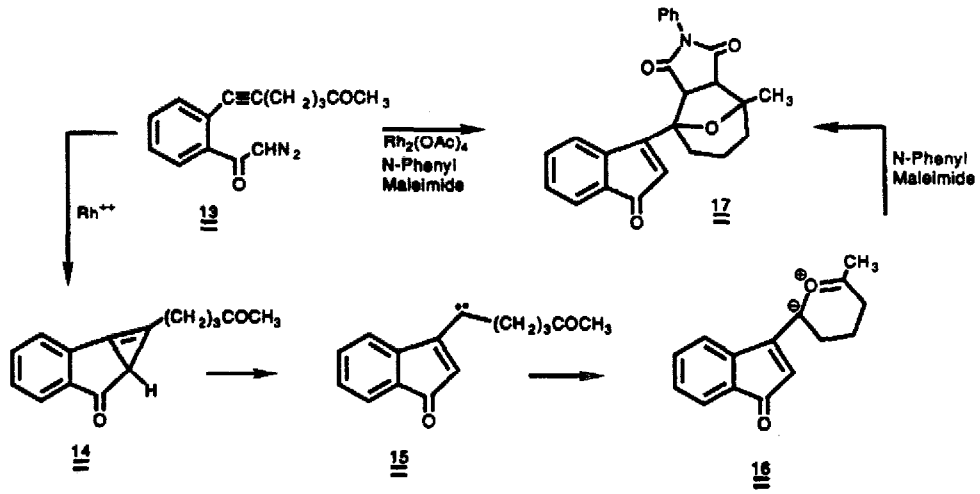


In earlier papers we have reported on the rhodium induced α-diazoketone cyclization onto a neighboring carbonyl group followed by dipolar-cycloaddition of the resulting carbonyl-ylide dipole.[18] It occurred to us that a similar cyclization-cycloaddition reaction could also occur with the vinylogous ketocarbene (i.e. **2**; X=O). In order to test this possibility, we have studied the rhodium ion catalyzed behavior of diazoketone **13**. Treatment of **13** with a catalytic amount of rhodium (II) acetate at 25° C in benzene with N-phenyl maleimide afforded cycloadduct **17**, mp 171-172° C, in good yield [NMR ($CDCl_3$, 300 MHz) δ 1.55 (s, 3H), 1.7-2.0 (m, 5H), 2.20 (m, 1H), 3.36 (d, 1H, J=7.7 Hz), 3.72 (brd, 1H, J= 7.7 Hz), 5.92 (s, 1H) and 7.1-7.5 (m, 9H)]. The structure of **17** was unequivo-

cally established by an X-ray single crystal structure analysis and the overall geometry of the molecule is shown below.



This result can nicely be accounted for in terms of the intermediacy of vinylcarbene **15** which cyclizes onto the oxygen atom of the neighboring carbonyl group to give the resonance stablized dipole **16**. Dipolar-cycloaddition of **16** across the activated pi-bond of N-phenyl maleimide affords cycloadduct **17**.



In conclusion, the facility with which the rhodium catalyzed cyclization reaction of ortho alkynyl substituted α-diazoacetophenones occurs makes this process particularly attractive for the synthesis of other cycloalkenones. We are continuing to explore the scope and mechanistic details of the rhodium catalyzed reaction of acetylenic α-diazoketones and will report additional findings at a later date.

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