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RHODIUM (II) CATALYZED CYCLIZATIONS OF α-DIAZO SUBSTITUTED ALKYNES. A NEW MODE OF REACTION

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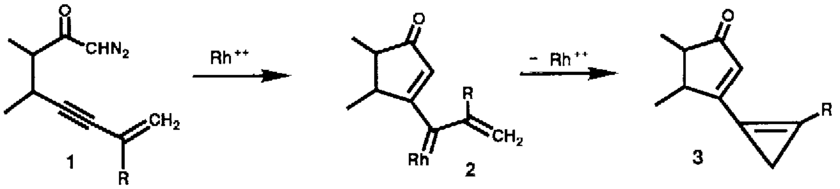
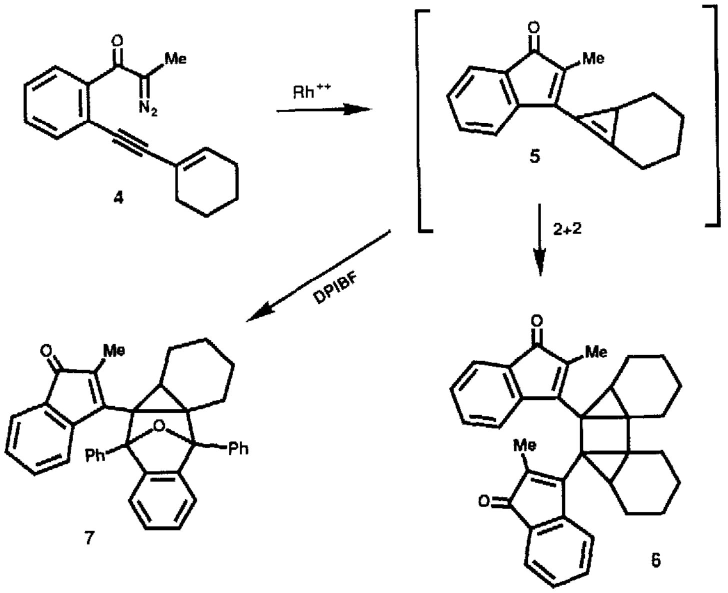
Abstract: *Treatment of several o-alkyne-enyl substituted α-diazoacetophenone derivatives with Rh_2OAc_4 results in cyclopropenyl substituted indenones which undergo a subsequent 2+2-dimerization reaction.*

Interest in the properties and reactivity of metal-carbene complexes has increased tremendously in recent years.[1] The current activity in this area stems from the role of metal carbenes in alkene metathesis[2], cyclopropanation chemistry[3] and as intermediates in an impressive array of synthetic methodology.[4] In contrast to the transition metal catalyzed intramolecular reactions of alkenyl substituted α-diazo ketones[5], which has been widely utilized in organic synthesis[6], the corresponding reaction of alkynes had until recently been far less well developed Several years ago we described a method for the formation of cycloalkenone carbenoids which involves a rhodium (II) catalyzed reaction of an α-diazo alkynyl substituted ketone [7] The process is believed to proceed by addition of a rhodium stabilized carbenoid onto the acetylenic π-bond to give the vinyl carbenoid.[7,8] The potential for many diverse chemical pathways exist through the generation and further reaction of these rhodium carbenoids. In this communication we report further on the scope of the methodology and suggest its application as a means to synthesize cyclopropenes of type 3.

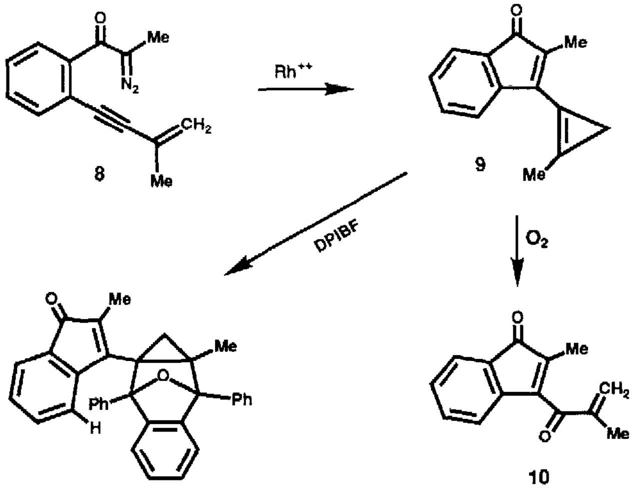


Our previous finding that o-alkynyl substituted α-diazoacetophenone derivatives produced vinyl carbenoids[7] suggested to us that these species might undergo cyclization onto an adjacent π-bond to give cyclopropenes.[9] Our initial efforts focused on the rhodium (II) acetate catalyzed reaction of α-diazo ketone 4. Treatment of 4 with a catalytic quantity of Rh_2OAc_4 in CH_2Cl_2 at 25°C afforded the 2+2-dimer 6 derived from a transient cyclopropene (5) in 73% yield The structure of dimer 6 was unequivocally established by an X-ray crystal structure analysis. That the strained cyclopropene 5 is the primary product of reaction follows from its interception by diphenylisobenzofuran (DPIBF). The *exo*-cyclopropyl adduct 7, mp 116-117°C, was obtained as the exclusive cycloadduct in 84% yield.

Extension of the carbenoid cyclization reaction to α-diazo ketone 8 was next investigated. In this case it was possible to obtain cyclopropene 9 in 95% yield (NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 2H), 2.09 (s, 3H), 2.53 (s, 3H), 7.16-7.28 (m, 2H), 7.36 (t, 1H, J=6 5 Hz) and 7.44 (d, 1H, J=6.5 Hz)). Upon standing in the presence of oxygen, this reactive species underwent ring opening to produce indenone 10 (NMR ($CDCl_3$, 300 MHz) δ 1 74 (s,



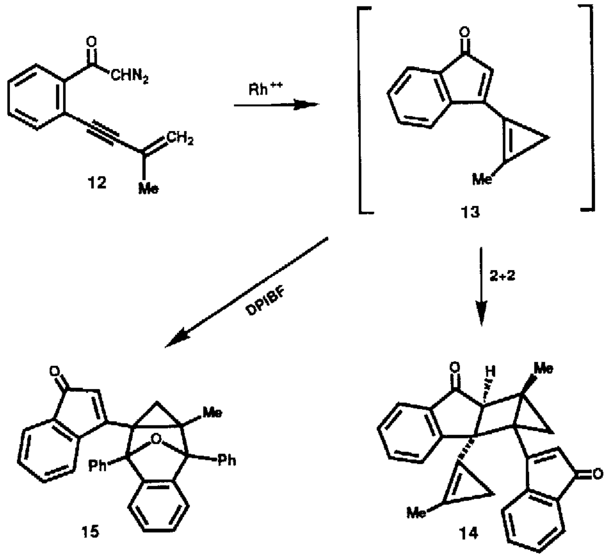
3H), 2.42 (s, 3H), 5.97 (s, 1H), 6.49 (s, 1H), 6.74 (d, 1H, J=6.0 Hz), 7.12 (t, 1H, J=7.5 Hz), 7.25 (t, 1H, J=7.25 Hz) and 7.39 (d, 1H, J=6.0 Hz)). Cyclopropene **9** was found to undergo ready Diels-Alder cycloaddition with DPIBF. The *exo*-cyclopropyl adduct **11a** is accompanied by the *endo*-isomer **11b** (85%, 2.1) and is distinguished by the shielding experienced by the *ortho*-aromatic hydrogen (4.48 ppm) because of the proximal



11a; exo
11b; endo

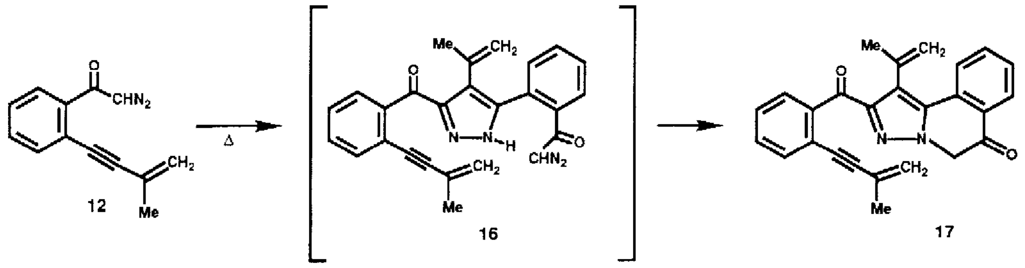
phenyl ring. The bimolecular [4+2]-reaction of substituted cyclopropenes is usually subject to strong steric preference for an *exo* transition state leading to the Diels-Alder cycloadduct.[11] The preference for *exo* approach is the result of an unfavorable steric interaction with the diene in the *endo* transition state. Only in instances in which the *endo* transition is comparable with or less sterically demanding than the *exo* transition state have products derived from *endo* approach been observed.[11] In such instances the [4+2]-cycloaddition proceeds at reduced rates and requires the use of pressure promoted Diels-Alder conditions for observable reaction [12]

An additional system which we examined involved the rhodium (II) catalyzed reaction of the closely related α-diazo ketone **12**. In this case it was not possible to isolate (nor detect) the suspected cyclopropene. Instead, this transient species (i e., **13**) readily underwent a 2+2-dimerization reaction. We initially anticipated that the dimerization of **13** would produce the tricyclo[3.1.0.$0^{2,4}$]hexane ring skeleton. This type of dimerization reaction had been studied in some detail by several groups.[13] However, we were surprised to find that the 2+2-cycloaddition of **13** takes an entirely different course to afford the novel dimer **14** in 54% yield The structure of **14** is based upon a detailed NMR analysis as well as on an X-ray crystallographic study



Bimolecular cycloaddition across the double bond in cyclopropene has been found to proceed quite readily since ring strain is reduced by 26 kcal/mol.[14] The transition state energy for the cycloaddition reaction, however, is very sensitive to both steric and electronic factors [15] FMO theory predicts that the preferred 2+2-cycloaddition path of **13** will involve reaction of the HOMO of the cyclopropene with the indenone π-bond (larger coefficients) to give the crossed dimer **14**. Introduction of a substituent group on either the indenone or cyclopropene ring generates steric interactions which retard this mode of cycloaddition. It should be noted that only the *exo*-cycloadduct **15** was isolated when the reaction of **12** was carried out in the presence of DPIBF thereby providing good support for a cyclopropene intermediate.

We have also found that the thermal reaction of **12** is significantly different from the transition metal catalyzed process. Thus, heating a methylene chloride solution of **12** in a sealed tube at 140°C in the absence of Rh_2OAc_4 afforded dimer **17** in 63% yield. Under the thermal conditions, the reaction proceeds by 1,3-dipolar cycloaddition of the diazo group of one molecule across the acetylenic π-bond of another diazo compound. The initially formed cycloadduct under-goes a proton shift to produce a transient pyrazole (i.e., **16**) which subsequently inserts into the neighboring diazo center to give **17**.



We are continuing to investigate the mechanistic details of the Rh (II) catalyzed reaction of alkynyl substituted α-diazo ketones and the use of this process for the formation of more complex ring systems. We will report our findings in due course.

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